Ophthalmic Plastic and Reconstructive Surgery

Characterising the occluded lacrimal punctum using anterior segment optical coherence tomography

--Manuscript Draft--

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Abstract:	Purpose: Epiphora is sometimes associated with an absent or occluded lacrimal drainage punctum (or puncta). This study uses non-invasive 'enhanced depth' anterior segment optical coherence tomography (OCT) to give improved characterisation and understanding of absent or fully-occluded puncta and the underlying canaliculus. Methods: Anterior segment spectral domain OCT images were collected prospectively from 9 lower puncta of 6 patients with epiphora and absent or fully-occluded puncta, not amenable to dilation in clinic, in order to see if a canaliculus was visible on OCT imaging below the occluded punctum. Results: An epithelial lined canalicular lumen was visible on OCT in 4 lower lid puncta from 2 patients and OCT identified 80% (4/5) of the canaliculi that were located on microscope-assisted punctal exploration. These lumen were seen within 580µm depth from the lid margin surface. A half of the eyes in which a canaliculus was identified on OCT (the 2 eyes in a single patient) had resolution of epiphora following punctoplasty, and the other patient was found to have co-existing nasolacrimal duct stenosis and required later dacryocystorhinostomy. The positive predictive value for identifying a canaliculus on lower lid punctal exploration in acquired complete punctal occlusion (excluding the congenital case) was 1, with a negative predictive value of 1. Conclusion: This study demonstrates that canaliculi can be imaged with OCT where formal access is precluded by an occluded punctum. This non-invasive investigation might help predict the likelihood of successful retrieval of a canaliculus at surgical exploration

Revision: Response to Reviewers

Reviewer Comments:

Reviewer #1: The authors present their series of obstructed puncta and OCT features of them. I congratulate them for a good work. Few minor issues that needs to be corrected include
1. The term unenterable punctum would not be completely right since it can be entered following the membrane clearance. It is best to replace this term.

This is correct as the puncta were only unenterable in the clinic, even with the use of a nettleship dilator. They were enterable once there was local anaesthetic on board and a sharp instrument. We have changed unenterable to " occluded". This has been changed on lines 1, 26, 58, 70, 91, 98, 182

2. Many of the references that the authors quoted showed membranes over the punctum clinically and the punctum being not accessible as in the current series secondary to membranes over them, hence to say that this is the first report to be describing these features would not be right. It is suggested to delete the first sentence from the discussion.

We have edited this sentence and changed 'description' to 'OCT images' in line 181.

Reviewer #3: In the space below, please enumerate specific comments and suggestions, to be shared anonymously with the authors.

this is a very interesting topic designed however; I believe that the number of studied puncta and canaliculi cannot give conclusive data as regards predictability.

We agree that the numbers are small, due to this being an uncommon situation. However, the authors felt that it was useful to discus the predictability as this is what clinicians might find useful for applying to their practice.

We have included..
"Although the number of puncta are small, the positive and negative predictive values have been calculated as an indicator for this small group of patients. Larger numbers of patients would improve the accuracy of these values." In lines 227-229 to make it clear that the numbers are small.

If the editor would prefer us to remove the positive and predictive values, we would be happy to do this under their advice.

Although it gives an idea about the patency of the vertical canaliculus, this

imaging technique cannot give an idea about the horizontal part which is very challenging and the patency of the vertical part cannot confirm the patency of the distal part. Authors already mentioned that but should elaborate it more in their conclusion

This is a very good point and we have elaborated on this in the text on lines 203-207.

“During OCT imaging, it has not been possible to visualize the horizontal canaliculus. This means that with the current OCT machines, it is not possible to assess the patency of the horizontal canaliculus. A patent vertical canaliculus does not necessarily mean that the horizontal canaliculus is patent and illustrates the limit of this mode of investigation currently.

Page 11:
Lines 152- 155 describes where the canalicular lumen was seen from the surface… could you please elaborate what does this signify.

This measurement was used to see the depth that the OCT machine could detect a lumen at rather than having a clinical implication to the outcome of the surgical exploration.

We have inserted ‘Currently, with this machine, the deepest lumen detected in this study was that starting at a depth of 301µm from the lid margin surface’ in lines 196-197.

Line 160. Do those hyper-reflective foci have any clinical significance or correlation??

We have added this to line 208-213.“Currently there is no known clinical significance of the hyper-reflective foci seen within the canaliculus. One possibility is that of make-up debris. However, they have been seen in both women and men. We presume that they represent mucous in the tears. They were noted in both the patients with a patent and non-patent nasolacrimal duct, and so do not appear to be an indicator of nasolacrimal duct patency.”

Page 13:
Line 195
You suggested that closed punctum reduces the depth of penetration while in the case with presumed congenital dysgensis, penetration was to 773 um which was higher than in cases you found the canaliculi…I'm a bit confused, could you elaborate please.

This sentence describes closed punctum (in this study) with open puncta (not see in this study, but in other studies of normal puncta).In theory, if a punctum is open (not the case in any of these patients in this publication), then the light from

the OCT machine will pass through air, whilst inside the punctum and vertical canaliculus. However, in all of the closed puncta in this study, the OCT light had to pass through semi transparent tissue at the lid surface, thus reducing the depth of penetration of the OCT light from the surface of the lid.

Where canaliculi were seen, the depth of the lumen was measured, but the presumed depth of penetration was not measured.
The presumed depth of penetration was only measured in the case where no canaliculus was seen as a guide that perhaps the canaiculus was open at a depth greater than 773µm.

To clarify this misunderstanding, we have included “within that depth” in line 172-173, and ‘as the OCT light has to pass through the semi transparent tissue of the closed punctum’ in lines 199-200.

Reviewer #4: In the space below, please enumerate specific comments and suggestions, to be shared anonymously with the authors.

Puncta and canaliculi should be labeled with arrows on Figure 3.

This submission only includes 2 figures. There is no clear definition as to where a punctum ends and a canaliculus begins, thus it would be difficult to label these two as separate anatomical areas on a punctum OCT. In these images, the surface of the punctum is closed and we have therefore used the term canaliculus for the lumen seen below this.

OCT in case 5 unhelpful regarding surgery.

We have added to lines 218-222. “Case 5 did not wish to proceed to surgical exploration. The result of surgical exploration is therefore unknown. However, she represents the clinical presentation of an occluded punctum in the presence of low tear production, and illustrates the presence of epiphora due to dry ocular surface, which was successfully treated with lubricants and not surgery.”

The authors feel this this is worthwhile keeping in for completeness for clinicians. However, we will take editorial advice and if you wish us to remove it, we will.

Why a stent in case 4?

We have added to lines 214-217 ‘In case 4, due to the extent of the occlusion and degree of incision, the intraoperative decision was made that the punctum would likely close over during the heeling process. Therefore a Mini Monoka stent was inserted to prevent re-occlusion.’

What kind of stent?

A Mini Monoka stent was inserted and explained in line 216.

Was there a papilla in case 3?

There was no papilla. “No papilla visible” has been inserted into the table on line 291, in column: patient number 3, row: clinical features of lower puncta.

Were both NLD's in case 3 stenotic?

Yes.

We have added ‘in both eyes’ in line 167 and to the table on line 291, in column: patient number 3, row: improvement in epiphora.

Reviewer Questions and Responses:
Reviewer's Responses to Questions

Title
Is the title adequately descriptive of this article?

Reviewer #1: No: The term unenterable punctum would not be completely right since it can be entered following the membrane clearance.

Reviewer #3: Yes

Reviewer #4: Yes

We have changed this to ‘occluded’

Abstract
Does the abstract adequately summarize the contents of this article? If none exists, leave blank and do not answer.

Reviewer #1: Yes

Reviewer #3: Yes

Reviewer #4: Yes

Scientific Quality
Comment on whether or not this article adds something new to the scientific literature, or offers a new interpretation or way of thinking about the problem.

Please be specific and provide details to support your conclusion

Reviewer #1: This adds more literature to the exisiting scarce literature.

Reviewer #3: This a very interesting topic where AS-OCT is used in an innovative way to address a common problem that is met in practice especially in my region. this use can be beneficial in many ways.

Reviewer #4: Too few cases to determine usefulness of this technique relating to surgical outcomes and assign predictive values.

Relevance and Interest to OPRS Readership

Reviewer #1: Moderate

Reviewer #3: High

Reviewer #4: Moderate

Originality

Reviewer #1: Good

Reviewer #3: Excellent

Reviewer #4: Good

Technical Accuracy

Reviewer #1: Good

Reviewer #3: Good

Reviewer #4: Good

Clarity of Presentation

Reviewer #1: Good

Reviewer #3: Good

Reviewer #4: Good

Use of English and Grammar

Reviewer #1: Good

Reviewer #3: Excellent

Reviewer #4: Excellent

Figures
Are all the tables/figures/illustrations essential? If none exists, leave blank and do not answer.

Reviewer #1: Yes

Reviewer #3: Yes

Reviewer #4: Yes

Tables
Are tables clearly presented?

Reviewer #1: Yes

Reviewer #3: Yes

Reviewer #4: Yes

Can any of the Tables be eliminated without loss of concept?

Reviewer #1: No

Reviewer #3: No

Reviewer #4: No

Statistics
Are statistics used appropriately and accurately?

Reviewer #1: N/A

Reviewer #3: N/A

Reviewer #4: No

References
Are references adequate and up to date? If none exists, leave blank and do not answer.

Reviewer #1: Yes

Reviewer #3: Yes

Reviewer #4: Yes

Rank this manuscript according to other manuscripts you have reviewed.

Reviewer #1: Between 90th and 99th percentile (Excellent; definitely publish)

Reviewer #3: Between 70th and 90th percentile (Good; appropriate to publish if page space allows)

Reviewer #4: Between 70th and 90th percentile (Good; appropriate to publish if page space allows)

Characterising the occluded lacrimal punctum using anterior segment optical coherence tomography

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Running Head: OCT imaging of the unenterable lacrimal punctum

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Precis: An epithelial lined canalicular lumen was visible on OCT in 4 lower lid puncta from 2 patients with occluded puncta, identifying 80% (4/5) of the canaliculi that were located on microscope-assisted surgical punctal exploration.

Word Count: 1333

Figures: 2

Tables: 1

Abbreviations:

OCT – optical coherence tomography

EDI – enhanced depth imaging

ASM – anterior segment module

IR – infrared

HEYEX – Heidelberg Eye Explorer

Keywords: Lacrimal punctum, lacrimal canaliculus, epiphora, optical coherence tomography, non-invasive.

ABSTRACT

Purpose: Epiphora is sometimes associated with an absent or occluded lacrimal drainage punctum (or puncta). This study uses non-invasive 'enhanced depth' anterior segment optical coherence tomography (OCT) to give improved characterisation and understanding of absent or fully-occluded puncta and the underlying canaliculus**.**

Methods: Anterior segment spectral domain OCT images were collected prospectively from 9 lower puncta of 6 patients with epiphora and absent or fully-occluded puncta, not amenable to dilation in clinic, in order to see if a canaliculus was visible on OCT imaging below the occluded punctum.

Results: An epithelial lined canalicular lumen was visible on OCT in 4 lower lid puncta from 2 patients and OCT identified 80% (4/5) of the canaliculi that were located on microscope-assisted punctal exploration. These lumen were seen within 580μm depth from the lid margin surface. A half of the eyes in which a canaliculus was identified on OCT (the 2 eyes in a single patient) had resolution of epiphora following punctoplasty, and the other patient was found to have co-existing nasolacrimal duct stenosis and required later dacryocystorhinostomy. The positive predictive value for identifying a canaliculus on lower lid punctal exploration in acquired complete punctal occlusion (excluding the congenital case) was 1, with a negative predictive value of 1.

Conclusion: This study demonstrates that canaliculi can be imaged with OCT where formal access is precluded by an occluded punctum. This non-invasive

investigation might help predict the likelihood of successful retrieval of a canaliculus at surgical exploration

INTRODUCTION

Epiphora is a common presenting symptom and may rarely be due to an absent or occluded lacrimal punctum (puncta) - this being either congenital absence or due to a range of acquired conditions causing complete fibrosis. In either the congenital or acquired form, there can be either isolated punctal occlusion (with a healthy underlying canaliculus), or else a concomitant canalicular stenosis or occlusion along some or all of its length[1]. Whereas a healthy canaliculus may allow normal tear drainage after punctoplasty, underlying canalicular narrowing means that punctoplasty alone is unlikely to be successful in addressing epiphora; the latter patients should be warned that canaliculo-dacryocystorhinostomy (cDCR) or insertion of a canalicular bypass tube might be required for symptomatic control.[1, 2]

Punctal occlusion may be secondary to aging, chronic inflammation (blepharitis, mucous membrane pemphigoid), infections (herpes viruses, trachoma), chronic topical therapy (glaucoma drops, mitomycin-C), systemic medications (5-flourouracil and Paclitaxel), or systemic diseases (such as cutaneous porphyria, lichen planus), local radiation, or trauma.[3] When an occluded punctum is seen in clinic, it is impossible to determine whether a healthy underlying canaliculus is present and, thereby, the prognosis for punctoplasty. In some cases of congenital punctal agenesis, the presence of a lacrimal papilla, a dimple[4] or a darker visible area behind a semi-transparent membrane may suggest a patent underlying canaliculus.

Anterior segment OCT has been used to describe healthy puncta.[5, 6, 7, 8] We report the application of spectral domain OCT with an anterior segment module, using EDI scanning protocols, for *in vivo* assessment of the occluded lacrimal punctum and associated canaliculus, together with the outcome for punctoplasty.

MATERIALS AND METHODS

Subjects and ethics.

Six patients with epiphora and one or more occluded lower lid puncta were recruited prospectively over a year. Written informed consent was obtained from all subjects and Regional Ethics Committee approval was obtained (LREC ref: 14/LO/1450; 153332 Westminster NRES Committee). Information regarding age, gender, and ethnicity, was obtained for all participants.

Image acquisition protocol.

Previously-described imaging protocols were used[5] and OCT image-sets of both lower lacrimal puncta were obtained by a single operator (H.T.), using a single Spectralis OCT device with “Anterior Segment Module” (ASM) (Heidelberg Engineering, Germany). The ASM consists of an add-on lens and dedicated software, and acquires 40,000 A-scans per second with a 7μm axial resolution in tissue, and a transverse resolution of 14μm. All images for this study were acquired using the scleral setting, a mode in which EDI-OCT can be performed. Each cross-sectional image subtended a 15º angle (eyelid length of ~8 mm), the brightness set to 25%, and single scans were acquired with the automated real

time (ART) set to between 2 and 20 frames - that is, each image comprising the average of between 2 and 20 B-scans. Images were acquired at a working distance of about 12 mm.

Each participant was firmly positioned in the OCT headrest. With both eyes open, the lower lid margin was everted (using a cotton bud, gently placed below the punctum and rolled to evert it) into a plane perpendicular to the light source. The long axis of scan acquisition was rotated to parallel the lid margin and multiple OCT and infrared (IR) images were obtained for each peripunctal area.

Qualitative and Quantitative Image Analysis

The OCT image-sets were evaluated for several morphological characteristics. Measurements were taken using Heidelberg Eye Explorer (HEYEX) software (version 1.6.8).

Positive and Negative predictive values

Positive predictive values were calculated to show the chances of locating the canaliculus during surgical exploration in those who had lumen visible on OCT. Negative predictive values were calculated to show the chances of not finding a canaliculus during exploration when no lumen was seen on OCT.

RESULTS

Using anterior segment OCT, 9 unenterable lower puncta were imaged in 6 patients (5 female; 83%) - 3 bilateral (Figure 1) and 3 unilateral (Figure 2); 4/6

patients were Caucasians and the average age was 48.5 years (range 26-66) (Table 1).

Clinical details

Epiphora had been present from between 1 and 26 years. Three patients had significant chronic blepharitis, 1 had atopic conjunctivitis, and 1 had keratitis sicca due to rheumatoid arthritis. Local conjunctival scarring, with occlusive punctal membranes, was visible in 4 lower lids of 2 patients (Figures 1C, D, K & L).

Punctal optical coherence tomography findings

A definite epithelial-lined lumen was visible beneath the occluded puncta in 4 lids from 2 patients (Patients 2 & 3; Figures 1E, F, I and J).

Patient 2's canalicula lumens were seen between the depth of 301μm and 405μm on the right and between 266μm and 580μm in the left. Patient 3's canalicula lumens were seen between the depth of 126μm and 293μm on the right and between 129μm and 302μm in the left.

The lumen sizes on OCT images were measured horizontally and vertically showing sizes of; 251μm by 43μm in patient 2's right eye, 580μm by 310μm in patient 2's left eye, 413μm by 61μm in patient 3's right eye, and 517μm by 91 μm in patient 3's left eye respectively.

Hyperreflectve foci were seen within two of the lumen seen on OCT (Figure 1F and J).

Outcomes following punctal exploration

Eight of the 9 puncta underwent punctal exploration under local anaesthesia and canaliculi were located in the 4 puncta (2 patients) where an epithelial-lined lumen was visible of OCT. Symptom resolution (bilateral) was achieved in one patient and, in the other, there was clinical evidence of nasolacrimal duct stenosis after the punctoplasty in both eyes.

Where OCT failed to detect a canalicular lumen, surgical exploration identified a lumen in only one of the four cases (Patient 4); this patient had life-long epiphora, perhaps suggesting punctal dysgenesis, rather than an acquired occlusion. In this patient the OCT scan appeared to penetrate to a depth of 773μm from the eyelid margin surface, without identifying a lumen within that depth.

Where symptoms were acquired (excluding Case 4), the positive predictive value for identifying a canaliculus on lower lid punctal exploration after OCT was 1, with a negative predictive value of 1; if the congenital case (Case 4) is included, the positive predictive value was 1 and negative predictive value was 0.75.

DISCUSSION

This appears to be the first OCT images of an epithelial-lined canalicular lumen in the presence of an occluded punctum. Although an OCT has been reported in a 14 year old with a congenital punctal membrane, imaging only demonstrated the proximal part of the vertical ampullary walls[9] and not an epithelial-lined lumen; this probably reflects the different OCT scanner used

(RTVue scanner, Optovue). The Spectralis used in this study not only had considerably greater penetration, but also had higher resolution - the latter allowing definition of a separate layer lining the lumen (presumed to be epithelium) and reinforcing canalicular identification.

In our one patient with congenital epiphora, the failure to show the canaliculus (later found at surgery) with OCT suggests that this congenital canalicular anomaly might be sited too deeply (>773μm) for the OCT penetration -- it possibly being an imperforate punctum rather than superficial membrane.[10]

More subjects are needed particularly in congenital cases to ascertain the maximum depth at which a canaliculus can be identified when scanning through a closed punctum. Currently, with this machine, the deepest lumen detected in this study was that starting at a depth of 301μm from the lid margin surface. It is highly likely that a closed punctum reduces the depth of OCT penetration when compared to an open punctum, as the OCT light has to pass through the semi transparent tissue of the closed punctum. With the emergence of intraoperative OCT, there may be scope in the future to use our proposed method to guide surgeons during initially unsuccessful punctal exploration intraoperatively.

During OCT imaging, it has not been possible to visualize the horizontal canaliculus. This means that with the current OCT machines, it is not possible to assess the patency of the horizontal canaliculus. A patent vertical canaliculus does not necessarily mean that the horizontal canaliculus is patent and illustrates the limit of this mode of investigation currently.

Currently there is no known clinical significance of the hyper-reflective foci seen within the canaliculus. One possibility is that of make-up debris. However, they have been seen in both women and men.[5] We presume that they represent mucous in the tears. They were noted in both the patients with a patent and non-patent nasolacrimal duct, and so do not appear to be an indicator of nasolacrimal duct patency.

In case 4, due to the extent of the occlusion and degree of incision, the intraoperative decision was made that the punctum would likely close over during the heeling process. Therefore, a Mini Monoka stent was inserted to prevent re-occlusion.

Case 5 did not wish to proceed to surgical exploration. The result of surgical exploration is therefore unknown. However, she represents the clinical presentation of an occluded punctum in the presence of low tear production, and illustrates the presence of epiphora due to dry ocular surface, which was successfully treated with lubricants and not surgery.

This study has shown that, in patients with occluded lower puncta, OCT can clearly identify an epithelial-lined canaliculus in 4/5 cases where a canaliculus was later identified at surgery; the one case of failed preoperative identification was probably a congenital anomaly with life-long symptoms. Although the number of puncta are small, the positive and negative predictive values have been calculated as an indicator for this small group of patients. Larger numbers of patients would improve the accuracy of these values. This study suggests that OCT might usefully predict the likely success of punctal

exploration in patients with acquired punctal occlusion, with the absence of a lumen on OCT guiding initiation of a discussion on the potential need for cDCR surgery or insertion of a canalicular bypass tube for symptomatic control.

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FIGURE LEGENDS

Figure 1: Optical coherence tomographic (OCT) and infrared (IR) images of three patients with bilaterally unenterable lower lacrimal puncta: Patient 1 (**A** Right OCT; **B** Left OCT; **C** Right IR; **D** Left IR), Patient 2 (**E** Right OCT; **F** Left OCT; **G** Right IR; **H** Left IR) and Patient 3 (**I** Right OCT; **J** Left OCT; **K** Right IR; **L** Left IR).

Figure 2: Optical coherence tomographic (OCT) and infrared (IR) images of three patients with unilateral unenterable lower lacrimal puncta: Patient 4 right eye (**A** OCT; **B** IR**)**, Patient 5 left eye (**C** OCT; **D** IR), Patient 6 left eye (**E** OCT; **F** IR).

TABLE LEGEND

Table 1: Demographics and outcomes of 6 patients with unenterable lower lacrimal puncta who underwent peripunctal OCT

TABLE 1

Characteristic	Patient number 1	2	3	4	5	6
Gender	Female	Female	Female	Female	Female	Male
Age (years)	44	40	66	26	49	66
Ethnicity	Caucasian	Indian	Asian	Caucasian	Caucasian	Caucasian
Laterality	Bilateral	Bilateral	Bilateral	Right	Left	Left
Duration of epiphora	2-3 years	3-5 years	1 year	Life-long (26 years)	3-4 years	4-5 years
Relevant ocular or medical history	Blepharitis	Hayfever Atopic conjunctivitis	Treated primary hypothyroidism	None	Blepharitis Rheumatoid arthritis; left keratitis sicca (Schirmer's 5mm left, 14mm right)	Blepharitis Rosacea
Clinical features of upper puncta	Patent to syringing	Stenotic, but patent after dilation	Patent to syringing	No visible punctum	Unrecorded	Unrecorded
Clinical features of lower puncta	Conjunctival scarring with membrane	No visible punctum; papilla present	Conjunctival scarring with membrane, no papilla visible	No visible punctum, dimple or translucent membrane	No visible punctum; papilla present	No visible punctum
Lower punctal OCT	No visible canaliculi	Epithelial-lined lumen visible bilaterally	Epithelial-lined lumen visible bilaterally	No visible canaliculus	No visible canaliculus	No visible canaliculus
Lower punctal exploration	Canaliculi not located	Canaliculi located, with punctoplasty performed	Canaliculi located, with punctoplasty performed	Upper and lower canaliculi located and stented	Not performed due to dry eye	Canaliculus not located
Improvement in epiphora	Persistent symptoms	Cured	Persistent symptoms; nasolacrimal duct stenosis demonstrated on syringing in both eyes	Cured after stent removal	Cured with long-term lubricants	Persistent symptoms

Acknowledgements

Dr Hannah Timlin had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Precis: An epithelial lined canalicular lumen was visible on OCT in 4 lower lid puncta from 2 patients with occluded puncta, identifying 80% (4/5) of the canaliculi that were located on microscope-assisted surgical punctal exploration.

Figure 1

Click here to download Figure figure 1 absent punctum OPRS.tiff

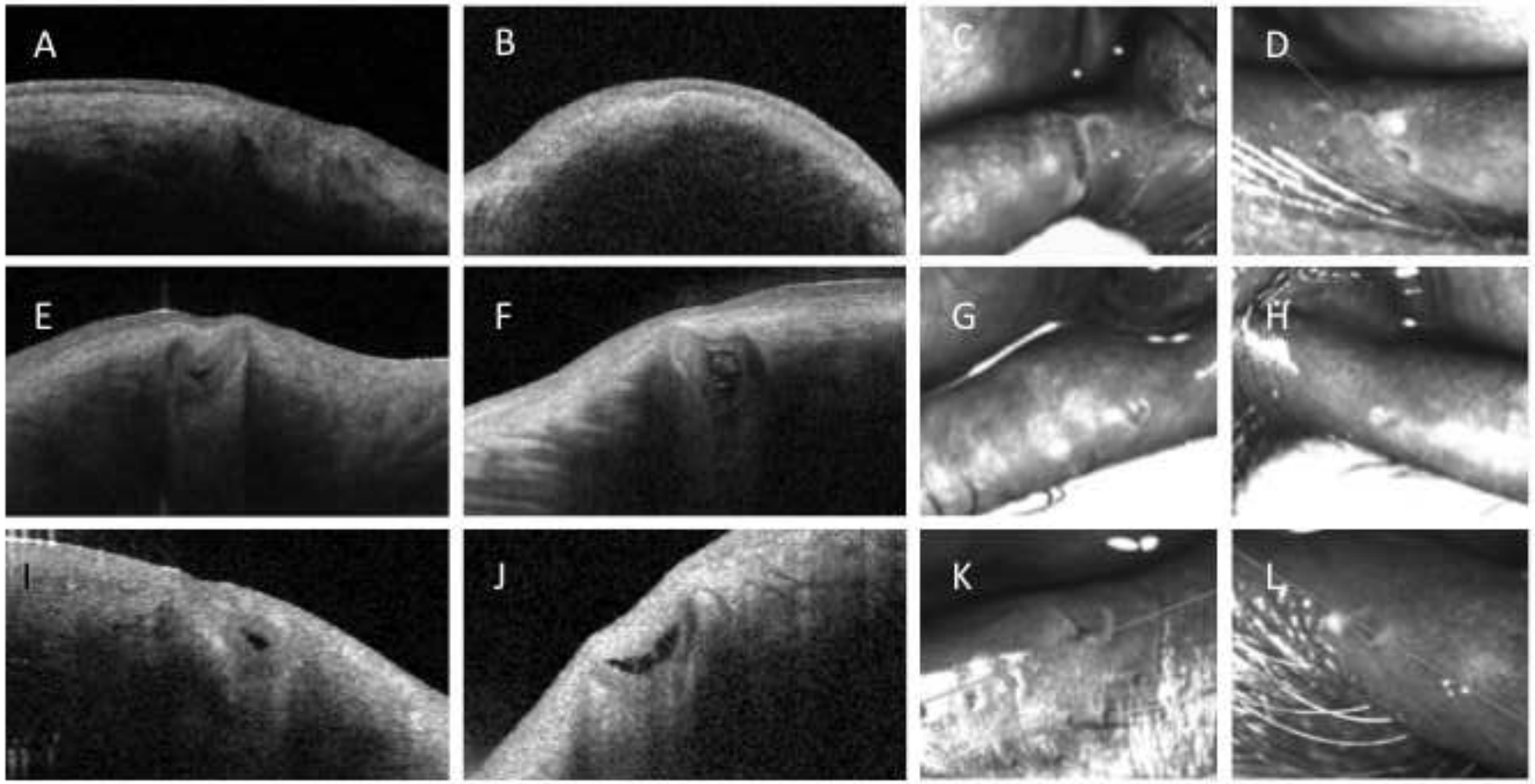
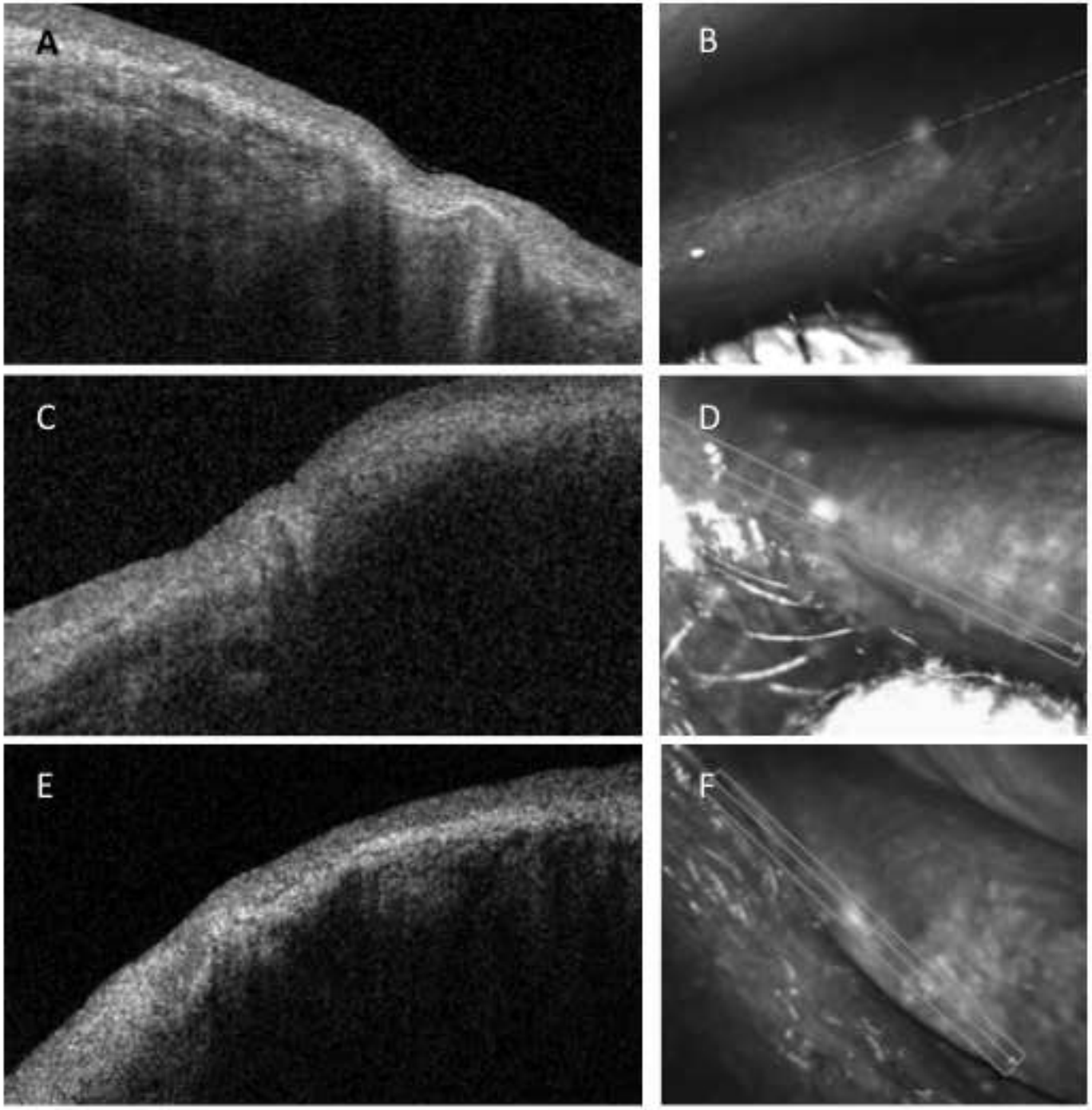


Figure 2

Click here to download Figure Figure 2 absent punctum OPRS.tiff



Table

Characteristic	Patient number					
	1	2	3	4	5	6
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Lower punctal OCT	No visible canaliculi	Epithelial-lined lumen visible bilaterally	Epithelial-lined lumen visible bilaterally	No visible canaliculus	No visible canaliculus	No visible canaliculus
Lower punctal exploration	Canaliculi not located	Canaliculi located, with punctoplasty performed	Canaliculi located, with punctoplasty performed	Upper and lower canaliculi located and stented	Not performed due to dry eye	Canaliculus not located
Improvement in epiphora	Persistent symptoms	Cured	Persistent symptoms; nasolacrimal duct stenosis demonstrated on syringing in both eyes	Cured after stent removal	Cured with long-term lubricants	Persistent symptoms