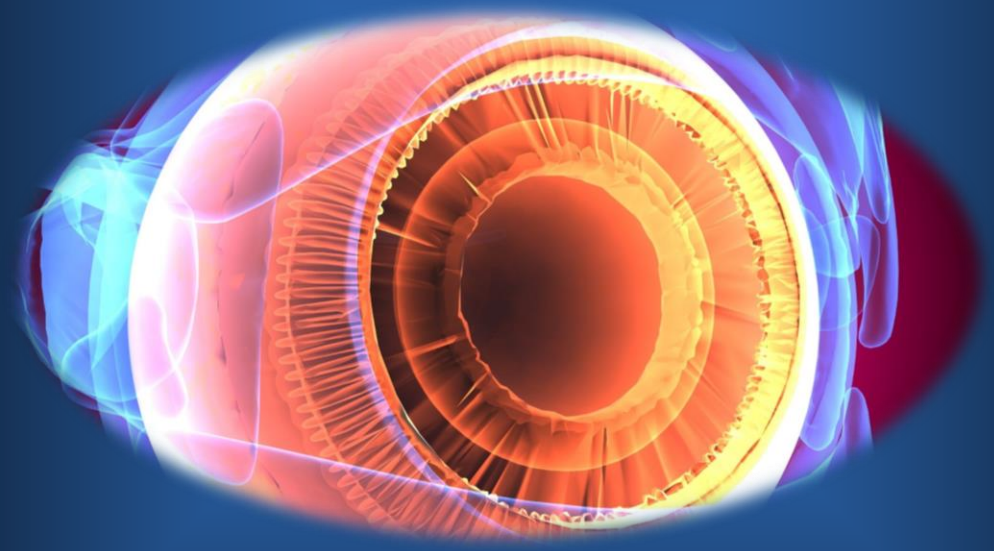
ophthal Focus

Vol 1 | Issue 9|2020



Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you 'Ophthal Focus' which contains latest and interesting news in the field of Ophthalmology.

This issue contains

- Postmortem conjunctival and nasopharyngeal swabs in SARS-CoV-2 infected and uninfected patients
- Ageing and glaucoma progression of the retinal nerve fibre layer using spectral-domain optical coherence tomography analysis
- Cilio-choroidal Melanoma: A Case Report

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in
Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

Postmortem conjunctival and nasopharyngeal swabs in SARS-CoV-2 infected and uninfected patients

COVID-19 has caused a significant health burden. Ocular manifestations, such as epiphora, conjunctival congestion or chemosis have been described to occur more frequently in patients with severe systemic manifestations. A recent meta-analysis found ocular manifestations among SARS-CoV-2 patients in 2–32%, with an overall pooled prevalence of 5.5%. The specifity of ocular tissue/fluid in detecting SARS-CoV-2 was very low in comparison with standard sample collection from nasopharyngeal swabs (NPS).

The data indicate, that neither postmortem COS nor NPS can reliably exclude donors with SARS-CoV-2, particularly, when the last positive premortem NPS was obtained 90 hr or more before death.

Corneal donation and transplantation are disrupted by concerns of SARS-CoV-2 tissue contamination and transmission. To date, no data are available on the postmortem prevalence of virus RNA in ocular and pharyngeal tissue in SARS-CoV-2 patients. In March 2020, the German Federal Institute for Vaccines and Biomedicines (PEI) recommended adjustments to donor screening due to SARS-CoV-2. Accordingly, in a prospective cohort study, potential corneal donors (uninfected with negative premortem NPS) in our institution had postmortem conjunctival (COS) and NPS taken starting March 17, 2020. In addition, Fuest et al. sampled deceased SARS-CoV-2 positive patients, with at least one positive premortem NPS (Table 1). The institutional review board of the University Hospital Aachen (EK 098/20) approved the study. All research adhered to the tenets of the

Declaration of Helsinki. Informed consent was given by next of kin. Swabs were placed immediately into a sterile transport tube containing 2–3 ml of sterile saline and analysed by reverse transcriptase–polymerase chain reaction (RT-PCR; SYNLAB, Leverkusen, Germany).

Characteristics and conjunctival (COS) as well as nasopharyngeal (NPS) swab results of the 23 SARS-CoV-2 positive deceased.

Case	Gender	Age (years)	Death to swab time NPS and COS (hr)	Result COS postmortem	Result NPS postmortem	Time Last NPS premortem (hr)	Result last NPS premortem
1	W	75	21.6	Negative	nd	42.22	Negative
2	M	83	116.32	Negative	nd	163.29	**Positive**
3	M	89	97.92	Negative	Negative	50.62	Negative
4	M	58	27.45	Negative	**Positive**	138.00	**Positive**
5	M	76	24.55	Negative	nd	71.21	**Positive**
6	M	75	10.42	Negative	nd	36.21	Negative
7	M	76	29.92	Negative	**Positive**	42.11	**Positive**
8	W	62	11.88	Negative	nd	10.36	Negative
9	W	75	14.48	Negative	nd	7.27	**Positive**
10	M	85	63.78	Negative	nd	17.55	**Positive**
11	M	71	64.92	Negative	nd	29.29	Negative
12	M	61	18.40	Negative	Negative	289.02	Negative
13	M	66	16.25	Negative	nd	80.55	Negative
14	M	61	14.35	Negative	Negative	218.98	Negative
15	M	86	8.20	Negative	**Positive**	115.13	**Positive**
16	M	75	42.17	Negative	Negative	96.40	Negative
17	W	50	70.00	Negative	Negative	378.83	**Positive**
18	M	88	10.17	Negative	**Positive**	89.18	**Positive**
19	W	64	7.58	Negative	Negative	117.58	**Positive**
20	M	66	16.97	Negative	Negative	174.10	Negative
21	M	73	68.55	Negative	Negative	55.72	Negative
22	W	68	21.25	Negative	Negative	242.02	Negative
23	W	68	16.75	Negative	Negative	168.27	**Positive**

All these SARS-CoV-2 patients were diagnosed by premortem positive NPS. The two columns to the right show the test results and the time before death of the last premortem NPS taken. nd = not done. Positive swab results are highlighted in bold.

All values are given as mean ± standard deviation (range min–max). Because of the limited number of patients and swab results, Fuest et al. decided to share our findings as a descriptive statistic for continuous variables. Categorical variables were compared using the Fisher exact test. A p-value of <0.05 was considered statistically significant (IBM SPSS Statistics for Windows, Version 25, Armonk, NY, USA: IBM Corp). Included were 70 eyes of 35 SARS-CoV-2 uninfected deceased (mean age 71 ± 10 (41–81) years, 46% females, death to swab (DTS) time 29.1 ± 16.2 (8.9–70.7) hr) and 46 eyes of 23 SARS-CoV-2 positive deceased (Table 1; mean age 72 ± 10 years, 30%

females, DTS time 34.5 ± 30.6 hr). The uninfected and infected group did not differ significantly in gender (p = 0.28), age (p = 0.7) or DTS time (p = 0.4).

SARS-CoV-2 RNA was not detected in any postmortem NPS or COS in the uninfected group. In the SARS-CoV-2 group, four out of fourteen SARS-CoV-2 postmortem NPS were positive but no virus RNA was detected in postmortem COS (Table 1). DTS time in the positive postmortem NPS cases was 18.9 ± 11.3 (8.2–29.9) hr. Table 1 also displays the latest premortem NPS of the SARS-CoV-2 positive deceased, taken at 114.5 ± 96.3 (7.3–378.8) hours before death. They were positive at 96.1 ± 41.2 (42.1–138) hr before death in all four patients, that also had a postmortem positive NPS. However, in 36% of positive premortem NPS, no postmortem NPS was acquired.

In this study, Fuest et al. observed that all postmortem COS were negative for SARS-CoV-2, even in cases, where the postmortem NPS was still positive. The absence of virus RNA in our postmortem swabs agrees with the literature on premortem samples, where only 3/315 COS = 0.95% (compared to NPS 604/849 = 71.1%) were positive even in symptomatic eyes, indicating that the human conjunctiva is not a typical site of SARS-CoV-2 replication (Lu et al. 2020; Seah et al. 2020; Ulhaq & Soraya 2020). Further studies are needed to investigate, whether other ocular structures, e.g. vitreous or iris, are more suitable to detect SARS-CoV-2 pre- and postmortem. In summary, the data indicate, that neither postmortem COS nor NPS can reliably exclude donors with SARS-CoV-2, particularly, when the last positive premortem NPS was obtained 90 hr or more before death.

Source: Fuest M et al. Acta Ophthalmol. 2020 Aug . doi: 10.1111/aos.14559. Online ahead of print.

Ageing and glaucoma progression of the retinal nerve fibre layer using spectral-domain optical coherence tomography analysis

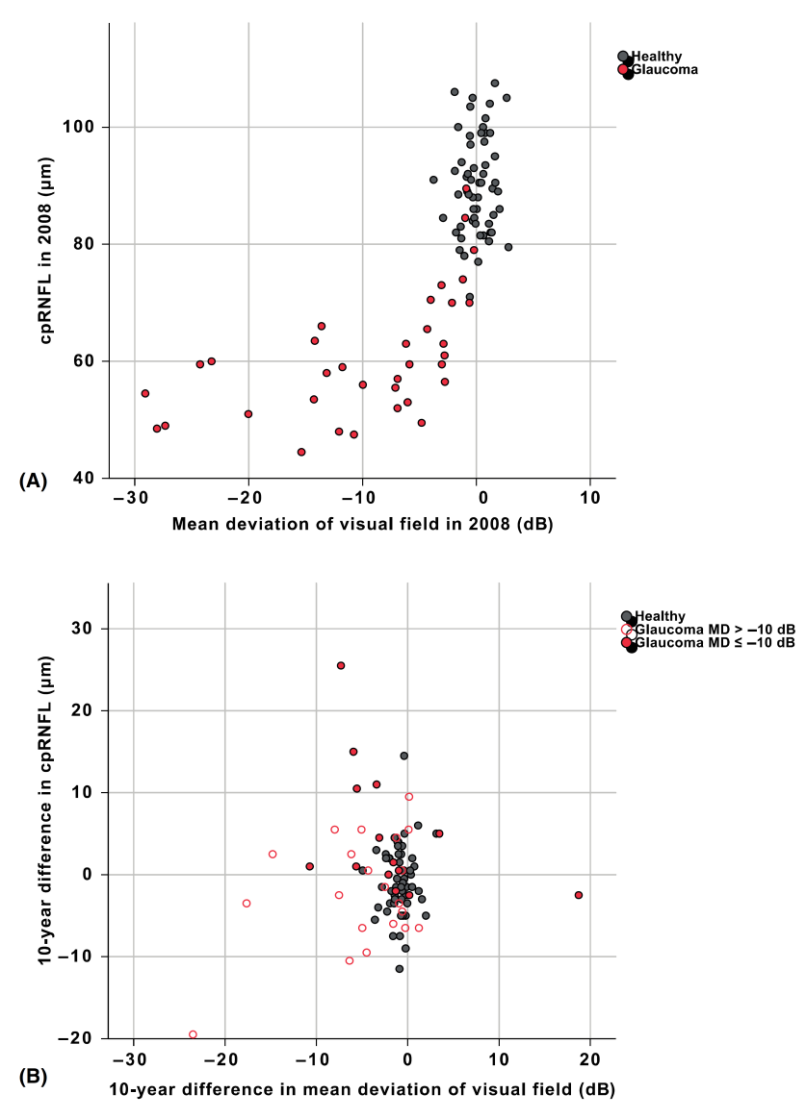
Optical coherence tomography (OCT) of the circumpapillary retinal nerve fibre layer (cpRNFL) has been shown to accurately discriminate between healthy and glaucomatous eyes. It has also been reported that OCT detected structural loss before functional changes occurred in a subset of patients. However, when monitoring glaucoma progression, the results are less conclusive. Some longitudinal studies have demonstrated that the rate of cpRNFL loss over time clearly differs between healthy and glaucomatous eyes, whereas other assessments have not shown any significant differences. The study compared the effects of ageing and glaucoma progression on the thickness of the circum papillary retinal nerve fibre layer (cpRNFL) and to evaluate the performance of a set of optical coherence tomography (OCT) progression analyses.

Considering the observations together with those made in earlier studies, it seems that using OCT for glaucoma followup may not be straightforward.

The cpRNFL was measured twice by OCT at each of two visits made 10 years apart in 69 healthy individuals and 49 glaucoma patients. Both visits also included Humphrey 24-2 SITA standard testing. The change in cpRNFL thickness was analysed by linear regression, and a sub-analysis was performed on glaucoma patients with a perimetric mean deviation better than −10 dB at the first visit. The proportion of individuals whose OCT progression analyses indicated progression was also evaluated for the same groups.

The average cpRNFL thickness deteriorated by a mean of −0.16 µm/year in the healthy cohort, increased by 0.03 µm/year in the glaucoma cohort, and

deteriorated by −0.24 µm/year in eyes with less severe glaucoma; there were no statistically significant differences between the groups. For 17 (30%) of 56 healthy individuals, at least one of the three different OCT progression analyses incorrectly indicated progression.



(A) Despite the large range in measurements of the thickness of the circumpapillary retinalvnerve fibre layer (cpRNFL) for healthy individuals, there was very limited overlap with values noted for glaucoma patients. (B) There was a lack of correlation between the difference in mean deviation values and cpRNFL measurements, and a large proportion of the visual fields in glaucoma eyes deteriorated over time

Rate of change in visual fields by difference in mean deviation and VFI, and rate of change in average circumpapillary retinal nerve fibre layer thickness.

Rate of change	Healthy individuals (n = 58)	All glaucoma patients (n = 35)	Glaucoma with MD ≥10 dB (n = 21)
Mean MD difference from 2008 to 2018, dB (95% CI)	−0.84 (−1.20 to −0.48)	−3.84 (−6.14 to −1.54)	−5.20 (−8.11 to −2.30)
Median VFI rate of change, %/year (min, max)	0.00 (−0.51, 0.40)	−1.18 (9.07, 5.16)	−1.60 (9.07, −0.08)
Mean cpRNFL difference from 2008 to 2018, µm* (95% CI)	−0.84 (−1.95 to 0.26)	0.70 (−2.04 to 3.44)	−2.10 (−5.18 to 0.99)
Mean cpRNFL rate of change, µm/year (95% CI)	−0.10 (−0.21 to 0.02)	0.07 (−0.21 to 0.35)	−0.21 (−0.54 to 0.12)
Signal strength adjusted mean cpRNFL rate of change, µm/year (95% CI)	−0.16 (−0.25 to 0.06)	0.03 (−0.24 to 0.31)	−0.24 (−0.53 to 0.05)

cpRNFL = circumpapillary retinal nerve fibre layer, MD = mean deviation, n = number of individuals, VFI = visual field index.
* Median interval between visits was 9.7 years, ranging from 9.3 to 10.0 years.

The results show a small effect of age on the cpRNFL, and they reveal a higher rate of thinning in glaucoma patients with mild to moderate disease defined by their visual fields, but still limited and statistically nonsignificant. Our findings also suggest a thickening of the cpRNFL in eyes with severe glaucoma. The OCT progression analyses generated a substantial number of false positives. Considering the observations together with those made in earlier studies, it seems that using OCT for glaucoma followup may not be straightforward.

Source: Ohnell HM et al. Acta Ophthalmol. 2020 Aug. doi: doi.org/10.1111/aos.14553

Cilio-choroidal Melanoma: A Case Report

A 74-year-old woman presented with gradual diminution of vision and pain in the left eye (OS) for the past 6 months. She was diagnosed to have complicated cataract in the left eye and was advised cataract surgery elsewhere. Her best corrected visual acuity in the right eye was 20/60, while it was just perception of light in the left. Anterior segment evaluation of OS

showed total cataract with multiple posterior synechiae and irregular nonreactive pupil [Figure 1]a. Multiple pigmented lesions were noted at 11 and 2:30'O clock position which was considered to be primary acquired melanosis (PAM). View of the fundus was completely obscured because of complicated total cataract. Right eye was otherwise normal.

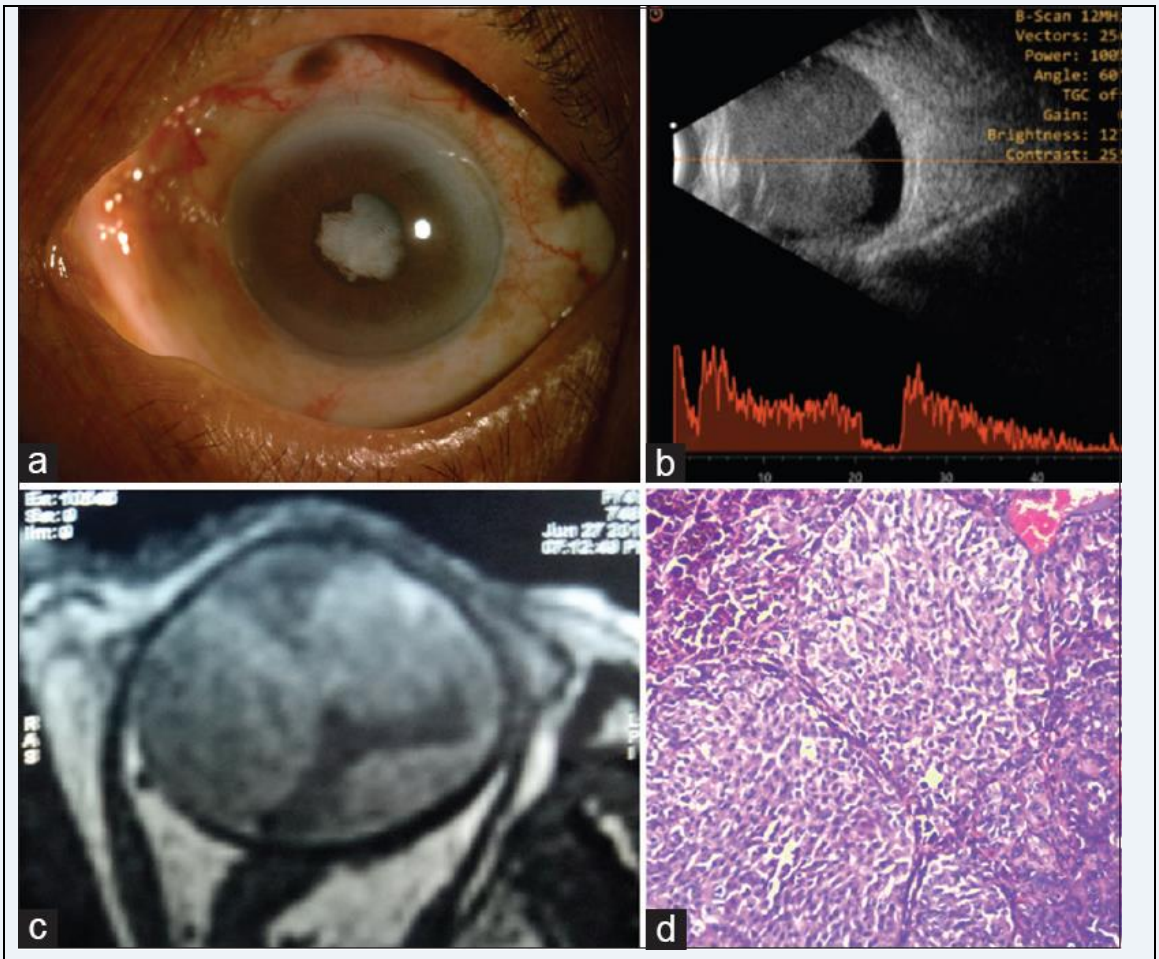


Figure 1: (a) Diffuse slit lamp photograph showing total cataract, posterior synichiae with irregular pupil. (b) Ultrasound B scan showing large intraocular mass with high surface reflectively and diffuse internal low reflective echoes, suggestive of ciliochoroidal melanoma. (c) MRI axial cut showing a large intra ocular mass displaying T1 hyperintensity. (d) Microphotograph (Hematoxylin and Eosin 20X) showing a tumor arising from ciliary body and choroid. The tumor cells exhibit nuclear atypia and anaplasia, and are predominantly of epitheloid variety. Findings are suggestive of ciliochoroidal melanoma

Ultrasound B-scan of OS revealed a large homogenous retino-choroidal mass filling the entire vitreous cavity associated with retinal detachment [Figure 1]b. Magnetic resonance imaging (MRI) of the orbit showed a large dome shaped cilio-choroidal lesion in the nasal and superior quadrant of OS, displaying hyperintense signal on T1 weighted images, suggestive of ciliochoroidal melanoma [Figure 1]c. The pigmented lesions over the sclera were now suspected to be extrascleral extension. The patient underwent enucleation with ball implant of OS under general anesthesia. The conjunctiva around the suspected pigmented lesions was left intact and peritomy was carried out with 5 mm clear margin. Histopathology showed a pigmented tumor arising from the ciliary body and choroid and extending over the optic nerve; however there was no invasion of the optic nerve. The tumor cells were predominantly composed of epitheloid cells with high nucleo-cytoplasmic ratio and prominent nucleoli [Figure 1]d. Extrascleral extension was noted however the overlying conjunctiva in these areas was spared. The findings were suggestive of cilio-choroidal melanoma. Metastatic workup in the form of chest X-ray, ultrasound abdomen and pelvis and liver function test was negative. The case was diagnosed to be of Cilio-choroidal Melanoma (OS).

Choroidal melanoma is the most common primary intraocular malignancy in adults. Usually melanoma can present with various manifestations and can mimic other lesions leading to a diagnostic ambiguity. Hence, a strong clinical suspicion with appropriate imaging is warranted. Cases of uveal melanoma mimicking panophthalmitis and bleeding anterior staphyloma have been described earlier in literature. Studies have reported a case of uveal melanoma presenting as staphyloma and complicated cataract in a 45-year-old female, in similarity with the present case. Our case highlights the necessity of meticulous examination and importance of ultrasound in all cases presenting as dense cataract which preclude fundus examination. The

possibility of harbouring an intraocular mass in all such cases cannot be totally ruled out and they should not be planned for cataract surgery unless an ultrasound screening has been done. With high mortality and a poorer prognosis, choroidal melanoma is indeed a tumor which needs early recognition with prompt treatment.

Source: Alam MS et al. Indian J Ophthalmol 2020;68:1519