Morphology of Trabeculectomy Filtering Blebs using Anterior Segment Optical Coherence Tomography: A Comparison of Two Methods

Rita Pinto Proença[1], Joana Ferreira[1,2] and João Paulo Cunha[1,2]
[1]*Department of Ophthalmology, Central Lisbon Hospital Center, Lisbon, Portugal*
[2]*Nova Medical School, Universidade Nova de Lisboa, Lisbon, Portugal*

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Abstract: Anterior segment imaging optical coherence tomography (AS-OCT) can be a useful aid in glaucoma surgery. Recent studies have shown its importance in both the preoperative morphologic evaluation of glaucoma patients as well as postoperative evaluation of filtering bleb functionality. Our purpose is to evaluate post-trabeculectomy filtering and non-filtering bleb characteristics in both time-domain OCT (TD-OCT, Visante™, Carl Zeiss) and spectral-domain OCT (SD-OCT, Heidelberg Spectralis ® anterior segment module), assess the usefulness of AS-OCT in evaluating postoperative filtering bleb function and compare both methods results. AS-OCT as a useful exam in determining functioning and non-functioning bleb characteristics. SD-OCT with an anterior segment module had a better performance in examining fine bleb features and performed better than in previous studies in examining deeper structures.

1 INTRODUCTION

Trabeculectomy has been performed for the treatment of glaucoma since 1968. Optimal results of this surgical technique depend on the formation of a filtering bleb (Cairns JE, 1968). Bleb morphology is an indicator of shunt function and a predictor of bleb-related complications (Picht G et al., 1998; Hu C et al., 2003; DeBry PW et al., 2002; Soltau JB et al., 2000).

Color photography (Cantor LB et al., 2003; Wells AP et al., 2004), ultrasound biomicroscopy (Yamamoto T et al., 1995), confocal microscopy (Messmer et al., 2006; Labbe A et al., 2005), conventional optical coherence tomography (OCT) (Savini G et al., 2005) and time-domain anterior segment (AS) OCT (Leung CK et al., 2007; Singh M et al., 2007) have all been studied has potential exams for analysing bleb characteristics.

AS-OCT imaging has been used to correlate bleb structure and function, showing morphologic features that may help distinguish between successful and failed blebs (Singh M et al., 2007) (Meziani L et al, 2016) (Napoli PE et al., 2014). Spectral domain optical coherence tomography (SD-OCT) is an imaging modality that uses Fourier transformation of reflected light from ocular structures to determine depth data. Bleb imaging with OCT is useful as it is a non-contact imaging method, in contrast to ultrasound biomicroscopy (Drexler W et al., 1999 and 2001) (Khamar MB et al., 2014).

This study aimed to evaluate post-trabeculectomy filtering and non-filtering bleb characteristics in both time-domain OCT (TD-OCT, Visante™, Carl Zeiss) and spectral-domain OCT (SD-OCT, Heidelberg Spectralis ® anterior segment module), assess the usefulness of AS-OCT in evaluating postoperative filtering bleb function and compare both methods results.

2 MATERIALS AND METHODS

2.1 Subject Groups

Observational case series conducted at the Ophthalmology Department of the Central Lisbon Hospital Center (CHLC) between January and September of 2016.

Twenty eyes of 20 patients who had undergone limbal-based trabeculectomy with intraoperative use of mitomycin-C 0.02% and had at least 6 months of follow up were included. All patients had primary open angle glaucoma with an uncontrolled intraocular

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pressure (IOP) despite maximum medical therapy. Exclusion criteria were other types of glaucoma, previous glaucoma surgery or ocular hypotension.

Eyes were classified in 2 groups according to trabeculectomy outcome: failed blebs (FBs) and non-failed blebs (NFBs). NFBs were defined as eyes with post-operative IOP ≤ 18mmHg or a reduction of 35% in pre-operative IOP without ocular hypotensive medication. The remaining blebs were classified as FBs.

Bleb structures were assessed with both TD-OCT and SD-OCT in terms of wall thickness and reflectivity, microcysts, bleb cavity, visualization of the internal ostium, scleral flap and subflap space. IOP and slit lamp morphology were also recorded.

Patient's informed consent was obtained before participation in this study. The principles of the Declaration of Helsinki were respected and the study was approved by our institutional Ethics Committee.

2.2 Study Procedures

Patients were consecutively recruited and seen at CHLC Ophthalmology department. A complete demographic and background history was recorded. A full ophthalmological examination was performed with IOP measurement using Goldmann applanation tonometry, slit lamp examination with a particular focus in bleb pattern and fundoscopy. In the same visit patients were examined with both time-domain OCT (TD-OCT, Visante™, Carl Zeiss) and spectral-domain OCT (SD-OCT, Heidelberg Spectralis ® anterior segment module).

2.2.1 Intraocular Pressure

IOP was measured before pupillary dilation with Goldmann applanation tonometry and a mean of 3 measurements was taken.

2.2.2 Spectral Domain Optical Coherence Tomography Imaging

Blebs were examined with both time-domain OCT (TD-OCT, Visante™, Carl Zeiss) and spectral-domain OCT (SD-OCT, Heidelberg Spectralis ® anterior segment module) in the same day, by the same operator.

SD-OCT was performed using an anterior segment adaptation lens in the optical system of the scanning element to focus the OCT beam in the anterior segment.

For the imaging, the patient was seated in front of the OCT and asked to look down and fixate an external point. The lid was gently manually elevated by the observer to display the superior bulbar conjunctival bleb.

Each trabeculectomy bleb was scanned at least twice and the best image was selected. Scans were oriented radially to the corneoscleral limbus to try to include both scleral flap and maximum bleb height in the same scan.

The obtained images were analysed qualitatively. Qualitative assessment was based on visualization of bleb structures 1) wall bleb thickening relative to conjunctival-episcleral appearance, classified as thickened or not thickened 2) wall reflectivity defined as a uniform or multiform according to the presence of hyporeflective spaces in the bleb wall 3) presence of microcysts (small, round hyporeflective spaces located at the surface of the bleb) 4) bleb cavity (subepithelial hyporeflective space limited by conjunctival tissue superficial to the sclera or scleral flap 5) internal keratotrabaculectomy ostium 6) scleral flap 7) subflap space.

Bleb characteristics were analysed in FBs and NFBs in both methods.

2.2.3 Bleb Pattern

Slit lamp bleb morphology was analysed and blebs were classified as cystic, diffuse or flattened. An anterior segment photography of each bleb was recorded for documentation.

2.2.4 Statistical Analysis

Demographics and clinical characteristics of patients were described with frequencies (percentages) and with mean (SD: standard deviation).

Normality assumption of the residuals was verified using Kolmogorov–Smirnov goodness-of-fit test. Nonparametric Chi-Square test was applied to compare both methods.

A level of significance α=0.05 was considered. Data were analysed using the Statistical Package for the Social Sciences for Windows (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.)

3 RESULTS

3.1 Patient Demographics and Clinical Characteristics

A total of 20 eyes of 20 patients (13 males) were imaged. One patient was excluded due to severe hypotonia.

The FB group was comprised of 10 patients and the NFB group of 9 patients. Mean age was 67.7 ± 9.57 years in the FB group and 72.1 ± 12.01 years in the NFBs group.

Pre-operative IOP was reduced from 26.1 ± 5.97mmHg to 16.1 ± 4.1mmHg in the FB group with ocular hypotensive medication and from 27.1 ± 5.06mmHg to 13.9 ± 2.85mmHg in the NFB group.

Mean interval between trabeculectomy and study assessment was 39.33 ± 13.78 months in the FB group and 31.5 ± 20.55 months in the NFB group.

No statistically significant differences in these characteristics were found between groups.

Four patients in the FB group required additional surgery (needling). The characteristics of both groups are summarized in Table 1.

3.2 SD-OCT versus TD-OCT

Bleb characteristics were analysed in FBs and NFBs. The utility of SD-OCT versus TD-OCT imaging in showing bleb features was considered. Results are summarized in table 2. Figures 1, 2 and 3 show examples of bleb images in both methods.

In successful blebs, bleb wall thickening (88.8% vs 77.8%), multiformity (88.8% vs 77.8%), microcysts (100% vs 66.7%) and bleb cavity (88.8% vs 77.8%) were visualized in a greater proportion with SD-OCT than with TD-OCT. In spite of this trend, these values were not statistically significant.

SD-OCT showed the scleral flap, subflap space and internal ostium in a smaller proportion of blebs than TD-OCT. This difference was not statistically significant.

Table 1: Demographic and clinical characteristics of the patients by group.

	NFB (n=10)	FB (n=9)	p
Sex	2F 8M	4F 5M	-
Age (years)	67.7 ± 9.57	72.1 ± 12.01	0.54
Preoperative IOP (mmHg)	26.1 ± 5.97	27.1 ± 5.06	0.35
Postoperative IOP (mmHg)	16.1 ± 4.11	13.9 ± 2.85	0.11
Mean interval between trabeculectomy and OCT (months)	39.33 ± 13.78	31.5 ± 20.55	0.62
Additional surgery	4	0	-

Table 2: Structures visualized in FB and NFBs in both methods.

	Bleb	SD-OCT	TD-OCT	p value
Wall thickening	Total	15/19 (78.9%)	13/19 (68.4%)	0.71
	FB	8/9 (88.8%)	7/9 (77.8%)	1
	NFB	7/10 (70%)	6/10 (60%)	1
Multiform wall	Total	13/19 (68.4%)	8/19 (42.1%)	**0.19**
	FB	8/9 (88.8%)	7/9 (77.8%)	1
	NFB	5/10 (50%)	1/10 (10%)	**0.14**
Microcysts	Total	13/19 (68.4%)	10/19 (52.6%)	0.50
	FB	9/9 (100%)	6/9 (66.7%)	**0.20**
	NFB	4/10 (40%)	4/10 (40%)	1
Bleb Cavity	Total	16/19 (84.2%)	11/19 (57.9%)	**0.15**
	FB	8/9 (88.8%)	7/9 (77.8%)	1
	NFB	8/10 (80%)	4/10 (40%)	**0.17**
Scleral Flap	Total	13/19 (68.4%)	15/19 (78.9%)	0.71
	FB	6/9 (66.7%)	7/9 (77.8%)	1
	NFB	6/10 (60%)	7/10 (70%)	1
Subflap space	Total	8/19 (42.1%)	12/19 (63.1%)	0.33
	FB	5/9 (55.5%)	7/9 (77.8%)	0.65
	NFB	3/10 (30%)	5/10 (50%)	0.65
Internal ostium	Total	6/19 (31.6%)	12/19 (63.1%)	**0.10**
	FB	3/9 (33.3%)	7/9 (77.8%)	**0.15**
	NFB	3/10 (30%)	5/10 (50%)	0.65

3.3 SD-OCT in Successful versus Failed Blebs

Cystic spaces in the bleb wall were present in functioning blebs more than in non-functioning blebs in a statistically significant value ($p<0.01$).

A trend was also present for a more multiform wall in functioning blebs. Results are summarized in Table 3.

There was no other feature of failed blebs vs successful blebs statistically significant.

4 CONCLUSIONS

This is the first study to compare characteristics of functioning and non-functioning bleb in both Time-Domain OCT (TD-OCT, Visante ™, Carl Zeiss) and Spectral-Domain OCT (SD-OCT, Spectralis® Heidelberg former segment module).

Functioning blebs present thickened and multiform walls, with more microcysts, with a better visualization of the bleb cavity, greater heights of hyporeflective cavity, as well as better visualization of the scleral flap, subflap space and ostium.

Table 3: Structures visualized in FB and NFBs in SD-OCT.

	FB	NFB	p value
Wall thickening	8/9 (88.8%)	7/10 (70%)	0.58
Multiform wall	8/9 (88.8%)	5/10 (50%)	0.14
Microcysts	9/9 (100%)	4/10 (40%)	**0.01**
Bleb Cavity	8/9 (88.8%)	8/10 (80%)	1
Scleral Flap	6/9 (66.7%)	7/10 (70%)	1
Subflap space	5/9 (55.5%)	3/10 (30%)	0.37
Internal ostium	3/9 (33.3%)	3/10 (30%)	1

	FB	NFB	p value
Wall thickening	8/9 (88.8%)	7/10 (70%)	0.58
Multiform wall	8/9 (88.8%)	5/10 (50%)	0.14
Microcysts	9/9 (100%)	4/10 (40%)	**0.01**
Bleb Cavity	8/9 (88.8%)	8/10 (80%)	1
Scleral Flap	6/9 (66.7%)	7/10 (70%)	1
Subflap space	5/9 (55.5%)	3/10 (30%)	0.37
Internal ostium	3/9 (33.3%)	3/10 (30%)	1

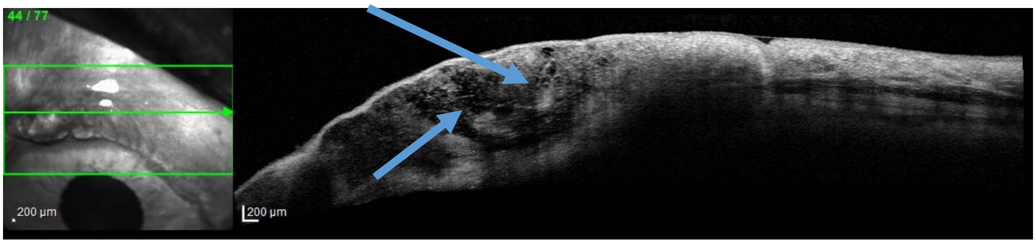

Figure 1: SD-OCT with arrows representing microcysts and bleb cavity.

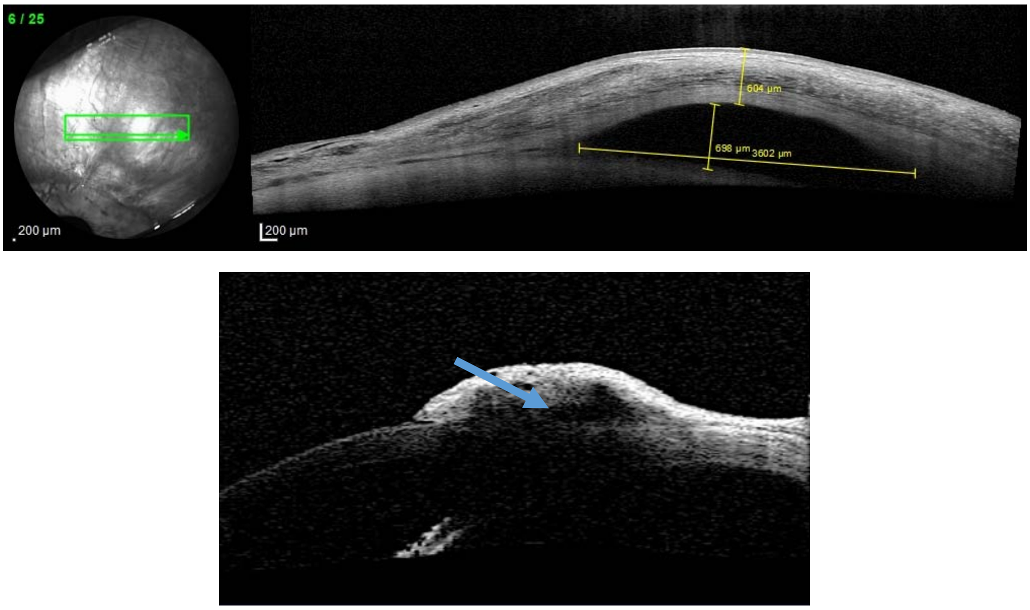

Figure 2: SD-OCT and TD-OCT of a functioning bleb.

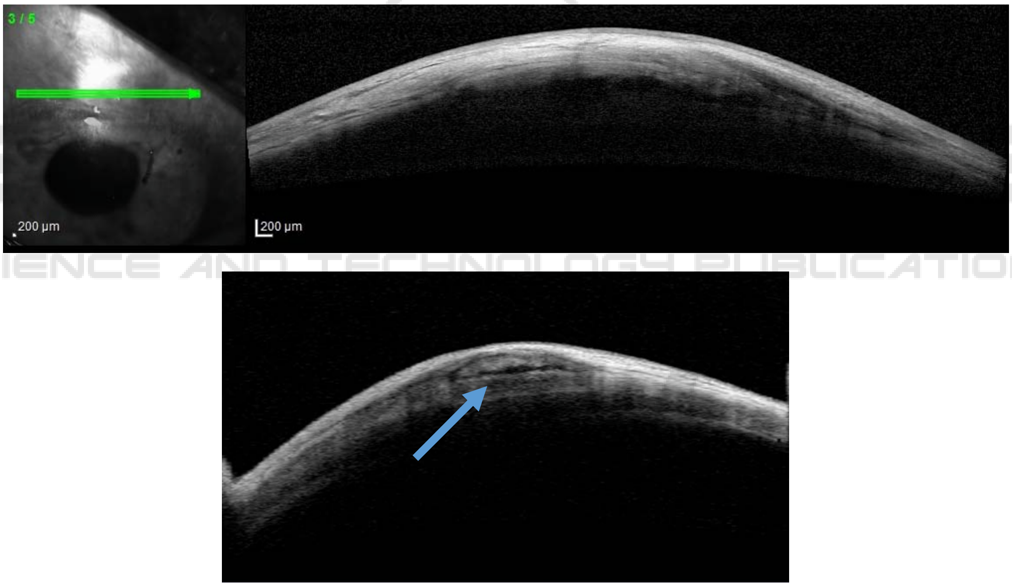

Figure 3: SD-OCT and TD-OCT of a non-functioning bleb.

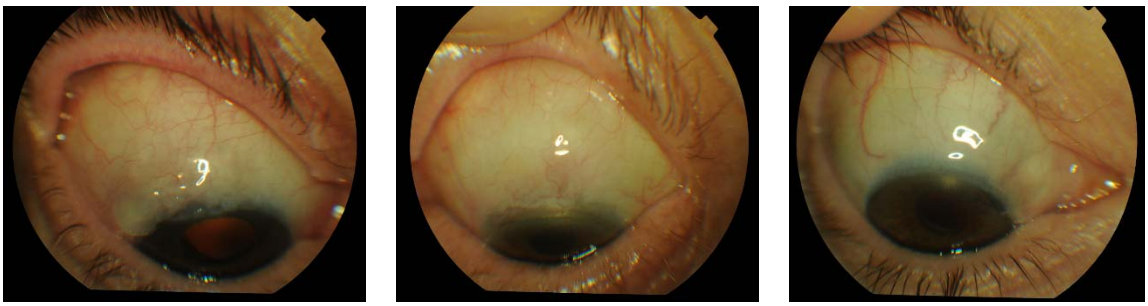

Figure 4: Anterior Segment Photography of a cystic, diffuse and flattened bleb.

Microcysts were the structure that provided a better discrimination between functioning blebs and non-functioning blebs ($p<0.01$)

SD-OCT allows better visualization of thin wall structures (multiformity, thickness and microcysts) than TD-OCT. Despite its worse performance in the observation of structures that need greater tissue penetration and its greater difficulty in obtaining wide-field images, this device has produced better results than previous studies done without an anterior segment adapter.

Some of our work limitations are the small number of patients included, different follow-up times and the higher number of anti-hypertensive medications done by patients with non-functioning blebs, which might affect conjunctival light transmission and, consequently, the exam results.

AS-OCT is a simple, non-contact, reproducible method for analysing the morphology of trabeculectomy blebs. It is a useful exam in evaluating the functionality of the bleb, aiding in the clinical characteristics observed in the slit-lamp and detecting early signs of the filtration bleb failure.

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