



UNIL | Université de Lausanne

Unicentre

CH-1015 Lausanne

<http://serval.unil.ch>

Year : 2019

Evolution and patterns of choroidal thickness changes in rhegmatogenous retinal detachment

Giacuzzo Clarice

Giacuzzo Clarice, 2019, Evolution and patterns of choroidal thickness changes in rhegmatogenous retinal detachment

Originally published at : Thesis, University of Lausanne

Posted at the University of Lausanne Open Archive <http://serval.unil.ch>

Document URN : urn:nbn:ch:serval-BIB_5E0A75C25D2A9

Droits d'auteur

L'Université de Lausanne attire expressément l'attention des utilisateurs sur le fait que tous les documents publiés dans l'Archive SERVAL sont protégés par le droit d'auteur, conformément à la loi fédérale sur le droit d'auteur et les droits voisins (LDA). A ce titre, il est indispensable d'obtenir le consentement préalable de l'auteur et/ou de l'éditeur avant toute utilisation d'une oeuvre ou d'une partie d'une oeuvre ne relevant pas d'une utilisation à des fins personnelles au sens de la LDA (art. 19, al. 1 lettre a). A défaut, tout contrevenant s'expose aux sanctions prévues par cette loi. Nous déclinons toute responsabilité en la matière.

Copyright

The University of Lausanne expressly draws the attention of users to the fact that all documents published in the SERVAL Archive are protected by copyright in accordance with federal law on copyright and similar rights (LDA). Accordingly it is indispensable to obtain prior consent from the author and/or publisher before any use of a work or part of a work for purposes other than personal use within the meaning of LDA (art. 19, para. 1 letter a). Failure to do so will expose offenders to the sanctions laid down by this law. We accept no liability in this respect.



UNIL | Université de Lausanne

Ecole doctorale

UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Hôpital Jules-Gonin, Fondation Asiles des aveugles

Service d'ophtalmologie - Rétine chirurgicale

**Evolution and patterns of choroidal thickness changes in
rhegmatogenous retinal detachment**

THESE

Préparée sous la direction du Professeur Thomas J. Wolfensberger

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Clarice Giacuzzo

Médecin diplômée d'Italie
Originnaire d'Italie

Lausanne
2019

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse *Monsieur le Professeur Wolfensberger*
Co-Directeur de thèse
Expert *Monsieur le Professeur Francois-Xavier Borruat*
Vice-Directeur de l'Ecole doctorale *Monsieur le Professeur John Prior*

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

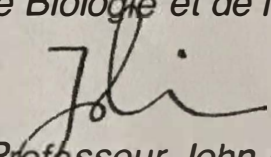
Madame Clarice GIACUZZO

intitulée

***Evolution and patterns of choroidal thickness changes in
rhegmatogenous retinal detachment***

Lausanne, le 23 mai 2019

*pour Le Doyen
de la Faculté de Biologie et de Médecine*



*Monsieur le Professeur John Prior
Vice-Directeur de l'Ecole doctorale*

EVOLUTION AND PATTERNS OF CHOROIDAL THICKNESS CHANGES IN RHEGMATOGENOUS RETINAL DETACHMENT

CLARICE GIACUZZO, MD,* CIARA BERGIN, PhD,* JELENA POTIC, MD,*† EDWIGE FORESTIER,* ALEJANDRA DARUICH, MD,* JEAN-ANTOINE POURNARAS, MD,* LAZAROS KONSTANTINIDIS, MD,* THOMAS J. WOLFENSBERGER, MD*

Purpose: To evaluate the changes in choroidal thickness (CT) before and after a successful pars plana vitrectomy for rhegmatogenous retinal detachment (RD), and to compare the evolution of CT with respect to the extent of RD.

Methods: Fifty-four patients were divided into three groups: peripheral macula-on RD (>3 mm from the fovea; 14 eyes); paracentral macula-on RD (fovea-sparing; ≤3 mm from the fovea; 14 eyes); and macula-off RD (involving the fovea; 26 eyes). Choroidal thickness was measured at 1 month (M1) and 3 months (M3) postoperatively, preoperatively in macula-on RDs, with enhanced depth imaging optical coherence tomography, from the nasal side (+2.5 mm) to the temporal side (−2.5 mm) of the fovea.

Results: In peripheral macula-on RD, the intereye difference in CTs showed thickening throughout follow-up (subfoveally: preoperatively = 19.6% ± 43.9%, M1 = 22.9% ± 27.5%, M3 = 18.2% ± 35.6%). In paracentral macula-on RD, the intereye difference in CTs showed a thinning throughout follow-up (subfoveally: preoperatively = −7.8% ± 21.9%, M1 = −5.5% ± 26.1%, M3 = −9.3% ± 19.4%), as well as in the macula-off RD (subfoveally: M1 = −14.1% ± 18.7%, M3 = −9.9% ± 15%).

Conclusion: The extent of RD was related to the evolution of the CT before and after surgery. Further studies are necessary to clarify the relationship between the changes in CT and the effects of circulatory alterations, vitrectomy, and RD.

RETINA 00:1–9, 2018

By delivering nutrients and removing waste products, the choroid circulatory system plays an essential role in the pathogenesis of multiple diseases of the posterior segment of the eye.¹ Enhanced depth imaging in optical coherence tomography (OCT) provides cross-sectional images of the retina, which extend to the posterior border of the choroid. From these images, the choroidal thickness (CT) can be measured reliably.² The CT has been correlated with the axial length (AL) of the eye and patient age.^{3,4} Moreover, based on OCT images, associations have been established between the CT and chorioretinal diseases, such as central serous retinopathy and age-related maculopathy.^{5,6} During retinal detachment (RD), many metabolic processes are disrupted, which may affect choroid circulation. Modifications in choroidal circulation have been shown to modify the CT in the fovea.⁷ Preoperative observations in patients with RD have

shown modifications in the CT.^{8,9} Postoperatively, after both pars plana vitrectomy (PPV) and scleral buckling treatments, changes in the subfoveal CT have been observed, which have been attributed to surgical inflammation and/or RD.^{10,11}

Previous studies have indicated that disruptions in retinal metabolism, due to RD and/or subsequent surgical interventions, could induce transient choroidal thickening. However, this process has not been well characterized. This study aimed to investigate morphologic changes in CT by measuring the thickness preoperatively and postoperatively over a much more extended area (51 loci across the central 5 mm of the retina) than previously studied. In addition, this report was the first to compare the effect of RD on CT between three disease groups; eyes with peripheral macula-on RD; eyes with paracentral macula-on RD; and eyes with macula-off RD.

Methods

This prospective, observational, monocentric study was conducted at the Jules-Gonin Eye Hospital, University of Lausanne, at the Department for Vitreoretinal Surgery. The study period was from March 2015 to March 2017. The study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Canton Vaud, Switzerland (protocol no 483/14). Written informed consent was obtained from participants after we explained the nature and possible consequences of the study. We recruited patients who had undergone surgery for rhegmatogenous RD. We excluded patients older than 99 years or younger than 18 years; those with preexisting ocular disease or macular disorders (epiretinal membrane, macular edema, and macular holes); those with previous ocular surgery, other than cataract surgery in either eye; those with proliferative vitreoretinopathy, Stage C; those with posttraumatic RD; and those with RD that had lasted longer than 30 days. We also excluded patients when the OCT images were low quality or blurred, and the choriocleral interface could not be traced. We excluded patients with a spherical equivalent higher than -12 diopters and patients without a complete set of images. A total of 54 eyes of 54 patients were included in analysis. The patients were divided into three groups, according to the extent of RD, as follows: peripheral RD with macula-on (>3 mm from the fovea, $n = 14$); paracentral RD with macula-on (fovea-sparing, ≤ 3 mm from the fovea, $n = 14$); and macula-off RD (central RD, involving the fovea, $n = 26$).

Patient Follow-up

All patients underwent ophthalmic examinations before, and 1 and 3 months after the surgery. The examinations included measurements of the best-corrected visual acuity (BCVA), intraocular pressure

From the *Jules-Gonin Eye Hospital, Vitreoretinal Surgery Unit, Fondation Asile des Aveugles, University of Lausanne, Lausanne, Switzerland; and †Clinic for Eye Diseases, Clinical Center of Serbia, Department of Ophthalmology, School of Medicine, University of Belgrade, Serbia.

Presented at 17th Euretina Congress in Barcelona, Spain, September 7–10, 2017.

None of the authors has any financial/conflicting interests to disclose.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Reprint requests: Thomas J. Wolfensberger, MD, Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Fondation Asile des Aveugles, Avenue de France 15, 1000 Lausanne 7, Vaud, Switzerland; e-mail: thomas.wolfensberger@fa2.ch

(with Goldmann applanation tonometry), anterior segment and fundus examinations (with slit-lamp biomicroscopy), and an AL measurement (with the IOL Master 500; Carl Zeiss Meditec, Dublin, CA).

Images

Optical coherence tomography images were taken preoperatively in both macula-on groups, and at 1 and 3 months postoperatively in all eyes. A single horizontal enhanced depth imaging in OCT scan through the fovea was obtained for each eye. Contralateral eyes served as control eyes. The extent of RD was measured manually with an OCT map scan (Spectralis HRA + OCT; Heidelberg, 30° ART, 5.9×5.9 mm). The CT was measured with proprietary software, using the horizontal line scan in the area between 2.5-mm nasal and 2.5-mm temporal from the fovea. Briefly, we aligned the external limiting membrane segmentation to the posterior choroidal boundary and assessed the “outer retinal layer” to extract the CT systematically (the distance between Bruch membrane and the outer border of the choroidal stroma).

The repeatability of CT measurements was assessed by two coauthors (C.G. and E.F.) who measured CTs on the same images, manually, from 10 patients who represented the range of RD types at all 51 loci. No significant differences were found between observers ($P > 0.05$). Henceforth, all CT measures were performed by a single observer (multivariate analysis of variance).

Choroidal thickness measurements were compared between those taken at baseline and those taken at each postoperative visit. We also compared measurements between treated and contralateral eyes. Choroidal thickness was measured at 51 points that spanned the central 5 mm, from -2.5 mm to $+2.5$ mm, with a horizontal separation of 0.1 mm. We defined three regions: the nasal macular region, which comprised 11 points, starting at 1 mm and ending at 2 mm from the fovea, respectively, on the nasal side; the temporal macular region, which comprised 11 points, starting at 1 mm and ending at 2 mm from the fovea, on the temporal side (-2 mm to -1 mm); and the subfoveal region, which comprised 5 points along the 0.4-mm diameter of the fovea (-0.2 mm to 0.2 mm).

Surgical Procedure

Surgeries were performed by four vitreoretinal surgeons in our hospital. Patients received local anesthesia. All patients underwent a 3-port, 23-gauge PPV, and retinal breaks were treated with cryotherapy or argon laser photocoagulation during surgery. More

Table 1. Baseline Characteristics of the Patient Cohort in Relation to Retinal Detachment Extension

	Peripheral (Mac-On)		Paracentral (Mac-On)		Macula-Off	
Age, mean Y ± SD	63.4 ± 8.5		55.1 ± 6		60.5 ± 9.6	
Male, %	74.1		63		67.4	
Duration of symptoms (days)	9.4 (range 0–23)		8.7 (range 0–26)		6.4 (range 1–21)	
Patients with >6 clock hours detachment % (N)	14% (2/14)		21% (3/14)		50% (13/26)	
Phakic, %	71		85		61.5	
	TE	FE	TE	FE	TE	FE
SE, mean D ± SD	-1.6 ± 2.8	-1.7 ± 3	-2.8 ± 2.1	-1.9 ± 1.8	2.51 ± 4	1.60 ± 3.9
AL, mean mm ± SD	25.6 ± 1.9	25.1 ± 1.7	25.5 ± 1.2	25.4 ± 1.1	24 ± 5.2	23.8 ± 5.6
IOP, mean mmHg ± SD	14.7 ± 3	15.6 ± 4.8	16.3 ± 3.2	16.3 ± 1.8	13.9 ± 4.3	15.6 ± 4.8

D, diopters; FE, fellow eye; IOP, intraocular pressure; Mac-on, macula-on; SE, spherical equivalent; TE, treated eye; Y, years.

precisely, retinal tears were treated with cryotherapy in 37 patients, with both argon laser photocoagulation and cryotherapy in 16 patients, and with only argon laser photocoagulation in one patient. All patients received fluid–gas exchange and either a sulfur hexafluoride or perfluoropropane internal gas tamponade. All patients received local treatment with antibiotics and corticosteroids for 1 month after surgery.

Anatomical success was defined as the total reattachment of the retina, observed with binocular

indirect ophthalmoscopy. The final anatomical success rate was 100% at the end of the follow-up period.

Statistical Analyses

Statistical analyses were performed to assess data on sex, age, lens status, symptom duration, extent of RD, macular condition, changes in the logarithm of the minimum angle of resolution of the BCVA, refractive errors, AL, intraocular pressure, retinal thickness, and CT measured preoperatively, at 1 month, and at 3 months after surgery. The multiple measures in each

Table 2. Mean CT values and Percentage of Change in CT Over Fellow Eyes (FEs) in Peripheral, Paracentral, and Macula-Off RD

		Peripheral (macula-on)			Paracentral (macula-on)			Macula-off		
		Macula region			Macula region			Macula region		
		Temporal	Sub-foveal	Nasal	Temporal	Sub-foveal	Nasal	Temporal	Sub-foveal	Nasal
Mean CT values (µm)	FE	188.5 ±41.8	172.7 ±42.2	148.1 ±47.0	236.5 ±74.3	230.6 ±81.0	181.6 ±70.4	234.6 ±57.9	235.2 ±70.3	198.3 ±71.6
	Preop	200.3 ± 66.0	202.0 ± 75.5	160.9 ±59.6	225.5 ±86.1	220.9 ±74.5	181.8 ±78.1			
	TE	210.1 ± 71.4	208.4 ± 57.8	158.3 ±68.8	220.9 ±80.3	204.8 ±68.7	170.7 ±65.4	198.6 ±60.4	201.3 ±70.9	171.6 ±72.7
	M1 TE	205.5 ± 78.1	200.2 ± 61.4	161.2 ±59.7	226.4 ±81.4	206.0 ±72.7	170.2 ±61.6	207.7 ±58.8	210.3 ±67.1	178.6 ±73.5
		Peripheral (macula-on)			Paracentral (macula-on)			Macula-off		
		Macula region			Macula region			Macula region		
		Temporal	Sub-foveal	Nasal	Temporal	Sub-foveal	Nasal	Temporal	Sub-foveal	Nasal
Percentage change in CT over FE	Pre-op	7.5 ± 22.2	19.6 ± 43.9	14.2 ± 36.3	-7.7 ± 24.9	-7.8 ± 21.9	-3.2 ± 14.3			
	M1	11.8 ± 26.8	22.9 ± 27.5	9.2 ± 22.2	-5.4 ± 22.4	- 5.5 ± 26.1	1.1 ± 33.6	-15.7 ± 15.0	- 14.1 ± 18.7	-11.8 ± 22.8
	M3	9.4 ± 33.4	18.2 ± 35.6	9.5 ± 21.4	-1.8 ± 25.7	- 9.3 ± 19.4	-2.1 ± 28.5	-11.2 ± 17.0	- 9.9 ± 15.0	-7.5 ± 27.0

The lightly shaded areas denote a general thinning of the choroid, whereas a darker shade denotes thickening of the choroid (in blue peripheral RD, in green paracentral RD, and in red macula-off RD).

FE, fellow eye; M1, month 1; M3, month 3; Preop, preoperative; TE, treated eye.

region for each patient were evaluated with the analysis of variance for repeated measures. We considered *P* values below 0.05 as statistically significant. The statistical analysis was performed in R version 2.15.120.

Results

Baseline Characteristics

The demographic and clinical characteristics of patients are shown in Table 1. In the peripheral RD group, the mean age at the onset of RD was 63.4 ± 8.5 years. The median BCVA was 0.0 (interquartile range [IQR]: 0–0.1) (20/20), both before and after surgery (*P* = 0.37). In the paracentral RD group, the mean age was 55.1 ± 6.0 years, and the median preoperative

BCVA was 0.08 (IQR: 0–0.2) (20/25), which improved to a postoperative BCVA of 0 (IQR: 0–0.1; *P* = 0.08) (20/20). In the macula-off RD group, the mean age at the onset of RD was 60.5 ± 9.6 years, and the BCVA improved significantly from 2 (IQR: 1.3–2.3) (20/2000) preoperatively to 0.2 (IQR: 0.1–0.3) (20/32) postoperatively (*P* < 0.001). The BCVA in contralateral eyes remained stable at 0.0 (IQR: 0.0–0.1) (20/20) throughout the follow-up.

Mean Submacular Choroidal Thickness Throughout Follow-up in Groups with Different Extents of Retinal Detachment at Baseline

The preoperative mean CT at the subfoveal location in the peripheral RD group was 202 ± 75.5 μm, and the postoperative mean subfoveal CTs at Months 1 and 3 were 208.4 ± 57.8 μm and 200.2 ± 61.4 μm,

Submacular choroidal thickness and extent of retinal detachment

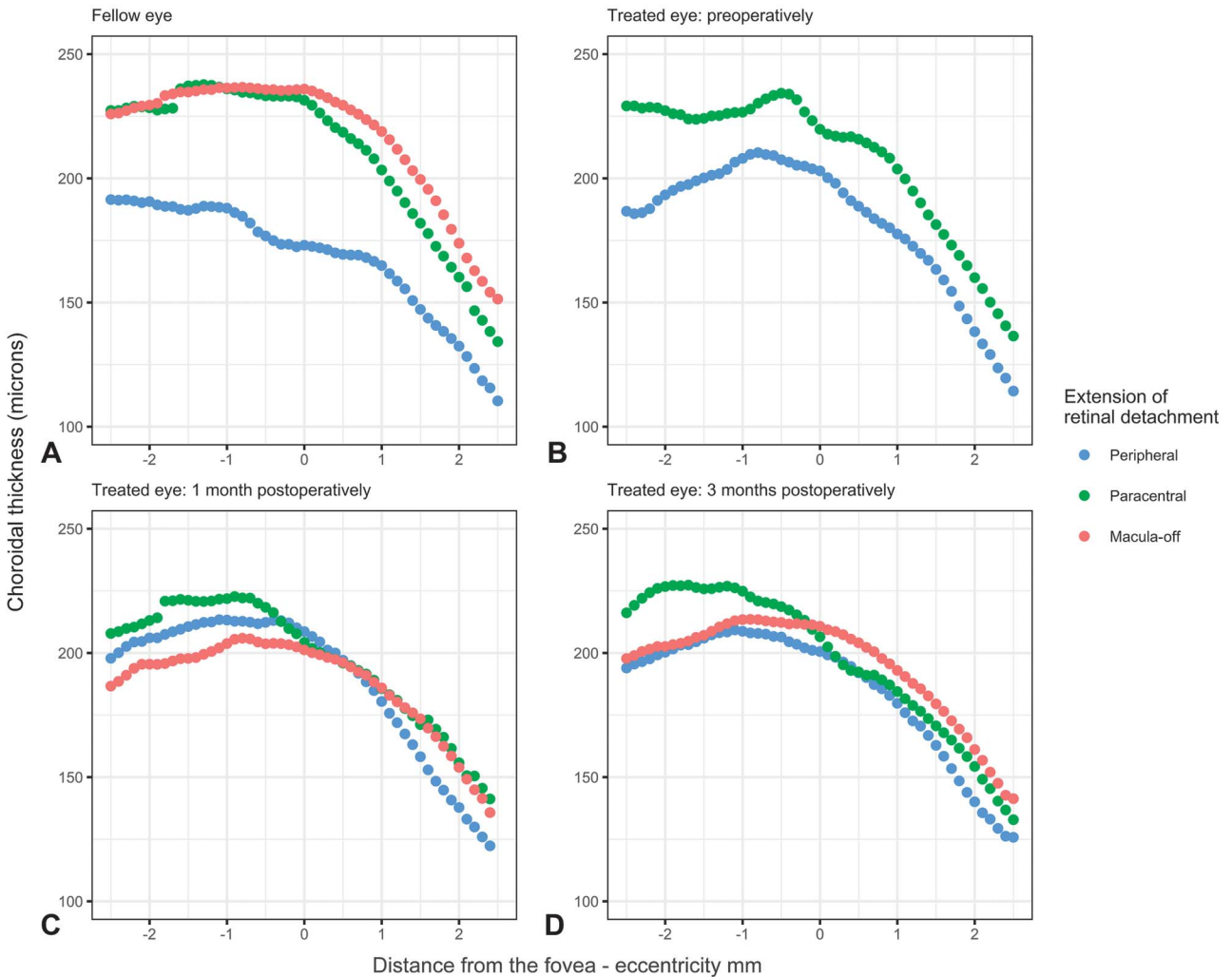


Fig. 1. Choroidal thickness (CT) in peripheral, paracentral, and macula-off RD. **A.** Fellow eye. **B.** Treated eye preoperatively. **C.** Treated eye 1 month postoperatively. **D.** Treated eye 3 months postoperatively.

Submacular choroidal thickness and extent of retinal detachment

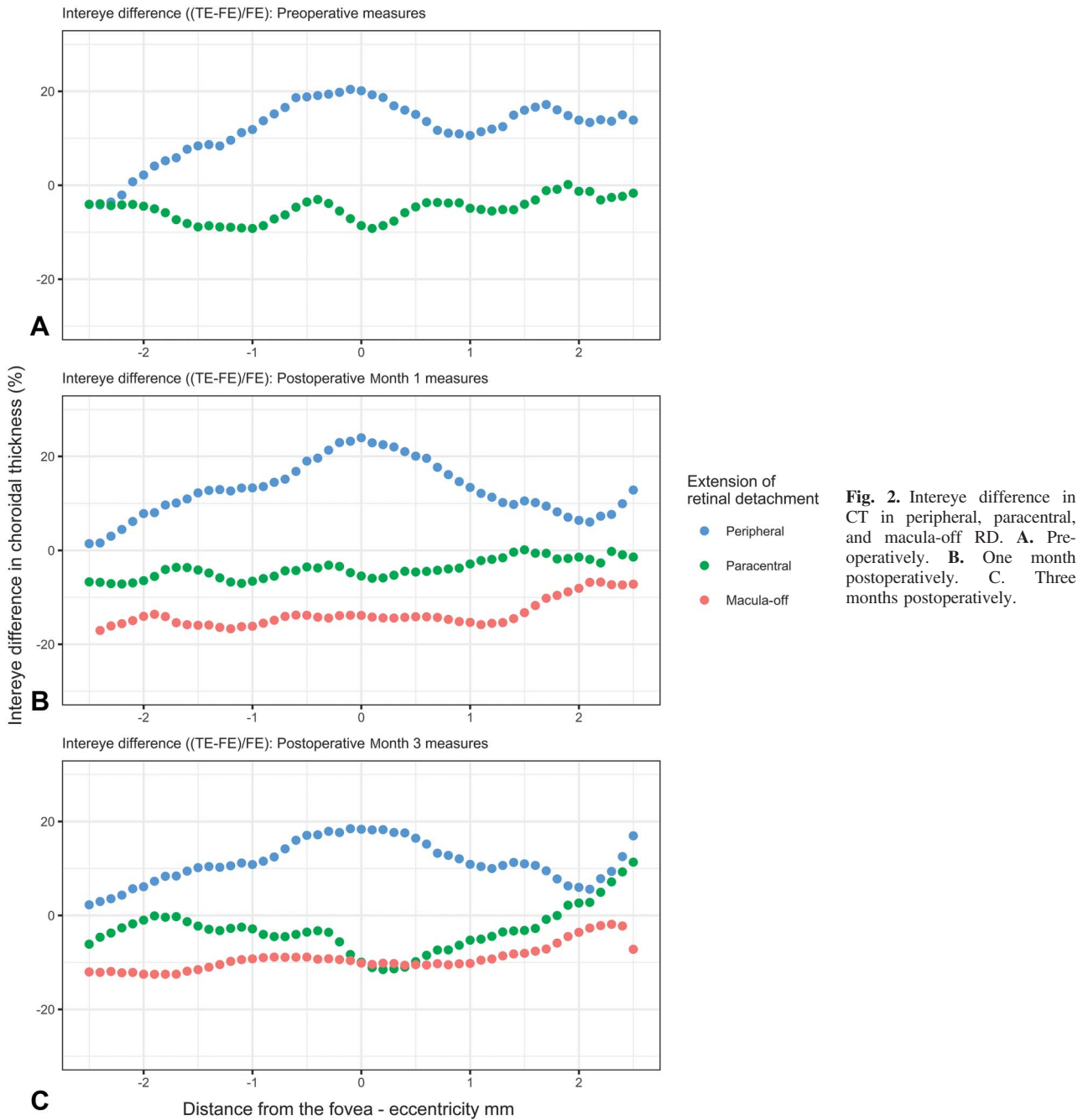


Fig. 2. Intereye difference in CT in peripheral, paracentral, and macula-off RD. **A.** Preoperatively. **B.** One month postoperatively. **C.** Three months postoperatively.

respectively. In the paracentral RD group, the mean CT was thicker at the subfoveal location preoperatively ($220.9 \pm 74.5 \mu\text{m}$) than in the peripheral RD group, but similar to that of the peripheral RD group at 1 and 3 months postoperatively ($204.8 \pm 68.7 \mu\text{m}$ and $206 \pm 72.7 \mu\text{m}$, respectively). The mean subfoveal CTs in the macula-off RD group at 1 and 3 months were also similar to those of the peripheral RD group postoperatively ($201.3 \pm 70.9 \mu\text{m}$ and 210.3 ± 67.1

μm , respectively). In the contralateral eyes, the mean subfoveal CT was thinner in the peripheral RD group ($172.7 \pm 42.2 \mu\text{m}$) than in the paracentral or macula-off RD groups ($230.6 \pm 81.0 \mu\text{m}$ and 235.2 ± 70.3 , respectively; $P < 0.01$ and $P < 0.01$, respectively; Table 2). In the contralateral eyes, no significant differences were found in the preoperative, 1-month, and 3-month examinations. The mean CTs at the foveal, nasal, and temporal locations in the three different

Table 3. Summary Statistics for Mean CT Between Fellow Eye (FE) and Treated Eye (TE), and of the Percentage of Change in CT Over FE in Peripheral, Paracentral, and Macula-Off RD

	Peripheral (Macula-On)			Paracentral (Macula-On)			Macula-Off		
	Macula Region			Macula Region			Macula Region		
	Temporal	Subfoveal	Nasal	Temporal	Subfoveal	Nasal	Temporal	Subfoveal	Nasal
Mean CT values (μm) FE versus TE at M1	0.001	0.000	0.16	0.10	0.04	0.27	0.000	0.000	0.000
Percentage change in CT over FE	Peripheral vs. Paracentral			Paracentral vs. Macula-Off			Macula-Off vs. Peripheral		
	Macula Region			Macula Region			Macula Region		
	Temporal	Subfoveal	Nasal	Temporal	Subfoveal	Nasal	Temporal	Subfoveal	Nasal
Preop	0.000	0.000	0.000	0.000	0.002	0.75	0.000	0.000	0.62
M1	0.000	0.000	0.23	0.000	0.10	0.82	0.09	0.000	0.06
M3	0.000	0.000	0.02	0.004	0.10	0.82	0.09	0.000	0.06

FE, fellow eye; M1, month 1; M3, month 3; TE, treated eye.

groups at the three different preoperative and postoperative time points are summarized in Table 2 and Figure 1.

Intereye Difference in Mean Choroidal Thickness Nasally, Centrally, and Temporally Throughout Follow-up

In the peripheral RD group, the intereye difference in CTs at the subfoveal location showed a thickening throughout follow-up (preoperative = $19.6\% \pm 43.9\%$, 1 month = $22.9\% \pm 27.5\%$, and 3 months = $18.2\% \pm 35.6\%$). In the paracentral RD group, the intereye difference in subfoveal CTs showed a thinning throughout follow-up (preoperative = $-7.8\% \pm 21.9\%$, 1 month = $-5.5\% \pm 26.1\%$, and 3 months = $-9.3\% \pm 19.4\%$). In the macula-off RD group, the intereye difference in subfoveal CTs showed a more pronounced thinning at 1 month ($-14.1\% \pm 18.7\%$) and 3 months ($-9.9\% \pm 15\%$). The intereye differ-

ences in mean CTs at the subfoveal, nasal, and temporal locations and in the three different groups at different preoperative and postoperative time points are summarized in Table 2 and Figure 2.

At 1 month postoperatively, the peripheral RD group showed a significant thickening in the subfoveal CT ($P < 0.01$) compared with contralateral eyes. Conversely, the paracentral and macula-off RD groups showed significant thinning in the subfoveal CTs ($P = 0.04$, $P < 0.01$, Tables 2 and 3 and Figure 3).

The summary statistics show the significance of the observed differences in the mean CT values between the treated eyes and the contralateral eyes and the significance of the percentage of change in CTs in the peripheral, paracentral, and macula-off RD groups compared with the corresponding contralateral eyes (Table 3).

Using univariate analysis, we observed that preoperative subfoveal CT in the fellow eyes was significantly associated with AL ($P = 0.02$), extension

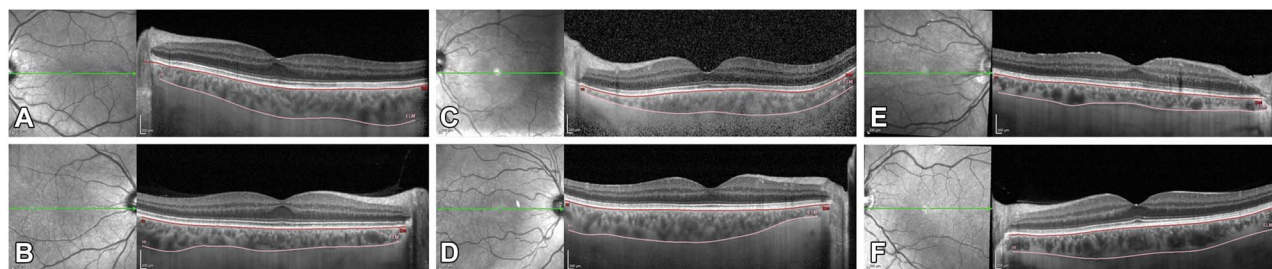


Fig. 3. Enhanced depth imaging spectral domain OCT images demonstrated CT in patients with peripheral, paracentral, and macula-off RD 1 month after surgery. **A.** Choroidal thickness in the treated eye (TE) of peripheral RD. **B.** Choroidal thickness in the fellow eye (FE) of peripheral RD. Choroidal thickness showed a thickening in the TE over the FE. **C.** Choroidal thickness in the TE of paracentral RD. **D.** Choroidal thickness in the FE of paracentral RD. A thinning of CT in the TE over the FE is observed. **E.** Choroidal thickness in the TE of macula-off RD. **F.** Choroidal thickness in the FE of macula-off RD. A marked thinning of CT in the TE over the FE is observed.

of RD ($P = 0.01$), and borderline significantly associated with age ($P = 0.056$). There was no association observed with sex and subfoveal CT ($P = 0.28$). On multivariate analysis, age ($P = 0.03$), AL, (0.001) and extent of RD (0.03) were independent predictive factors of subfoveal CT in fellow eyes; however, inversely, only subfoveal CT of the fellow eye was a predictive factor for the extent of RD ($P = 0.01$).

Discussion

In this study, we characterized the correlation between the extent of RD and the CT by measuring 51 loci across the macula, preoperatively and postoperatively, with a horizontal separation of 0.1 mm. In previous studies, CT was measured only at the subfoveal area, not across the macula. Our method allows us to examine also the paramacular CT because CT is known to vary topographically with respect to the distance from the macula and optic nerve head.¹² Also, as this included 51 measures from the same patient, we could improve the reliability of our measures by using analysis of variance. Moreover, we separated the study eyes into three groups according to the extension of RD (verified using OCT): peripheral RD (>3 mm from the macula), paracentral RD (<3 mm with the fovea fully attached), and macula detachment (macula-off). Choroidal thickness is more affected by systemic factors; therefore, the possibility of systemic factors driving RD motivated our choice, and this grouping had not been described previously in the literature.

It has been reported that in healthy eyes, there is no significant interocular difference in CT.¹² Because the second eye is considered healthy in patients with RD, we examined the relative changes of CT with respect to RD by comparing operated with the healthy fellow eye. Given the large intrasubject variation in CT, we considered that this approach would give a much better estimation of change due to CT. We observed that, when RD extended toward the macula (paracentral RD), the CT was thinner than that in contralateral eyes; moreover, when RD caused the macula-off condition, the CT was even thinner (relative to fellow eye). Conversely, in peripheral RD, we observed that the CT was thicker than in contralateral eyes. Surprisingly, in the contralateral eyes of patients with peripheral RD, the CT was markedly thinner than that in the contralateral eyes of patients with either paracentral or macula-off RD. This large difference in CT of fellow eyes of patients with RD between groups was not expected. Thus, patients with

peripheral RD may be at lower risk of developing macula-off RD, because of the thinner baseline CT.

The architecture of the choroidal vasculature might partly explain the recovery trajectories observed. Previously, Nickla and Wallman⁷ demonstrated that modulations in ion and fluid flow across the retina and retinal pigment epithelium into the choroid modulated the CT. Similarly, RD was shown to disrupt retinal metabolism and ionic transfer into the choroid, resulting in CT modifications, which resolved once the retina was reattached. Several studies have shown that the CT increased immediately after surgery, and that resolution was achieved within 3 months of surgery.^{9–11} Those findings were consistent with our hypothesis that, after retinal reattachment, the CT will return to the measurements observed in the contralateral eye. Akkoyun and Yilmaz¹¹ studied patients who underwent different types of surgical interventions for RD. They showed that a transient increase in subfoveal CT occurred 1 week postoperatively, after both PPV and scleral buckling. The authors suggested that this transient increase in CT may have been induced by scleral and choroidal inflammation after laser photocoagulation in the PPV group, and with scleral compression reducing blood flow and increasing hemostasis in the choroidal circulation in the scleral buckling group.¹¹

Somewhat surprisingly, we observed that CT changes were very different in eyes with peripheral RD than in those with paracentral or macula-off RD. In particular, the CT in contralateral eyes was significantly thinner in the peripheral RD group than in the paracentral and macula-off RD groups (Table 2). This finding suggested that either systemic factors influenced the extent of RD or that eyes with peripheral RD were at lower risk of extensive RD, because of the thinner baseline CT. After PPV with a silicone oil tamponade for treating RD, the subfoveal CT decreased after surgery.⁸ This thinning might have been related to increased uveoscleral outflow and intraocular inflammation caused by the RD. However, that study was based on an analysis of a group of patients with either macula-on or macula-off RD (63% vs. 37%). Our results indicate that there would be patients with significant increases (peripheral RD) and decreases in CT (macula-off RD), as such changes in CT would be masked in this mixed cohort.

Another study suggested that the width and size of the buckling material could affect changes in the choroidal circulation, which could result in long-term increases in the subfoveal CT in patients with macula-off RD.¹³ Finally, a randomized clinical trial of cryotherapy versus laser photocoagulation in scleral buckle surgery showed that the postoperative aqueous flare was higher after cryotherapy than after laser

photocoagulation.¹⁴ All our patients were treated with cryotherapy, except one who was treated only with laser photocoagulation in the paracentral RD group. Therefore, the different patterns in CT evolution that we observed among the three different RD groups were not related to the laser treatment used.

The CT has been reported to be thickest under the fovea in a healthy population.³ That finding was correlated with the vascular architecture, which is shaped to sustain the high metabolic demand of the macula. The outer retina in the nasal macula is relatively thin, due to increases in the overlying layers of nerve fibers in this region; consequently, a significant component of the nasal macula is sustained by the retinal vasculature. Accordingly, the nasal macula places lower metabolic demand on the choroidal vasculature; indeed, it has been shown that this area had a thinner CT than other areas of the macula.³ In our study, the healthy contralateral eyes in the peripheral macula-on RD group showed a submacular CT that was thinner than the average measurements found in the literature. This unexpected finding could not be explained by the mean age, AL, or spherical equivalent.

Similar to other groups, we observed a high inter-observer correlation, high repeatability, and high intervisit reproducibility in the CT measurements.^{15–18} The mean intereye CT difference in the peripheral RD group was elevated across the central 0.4 mm, and that elevation began to resolve at 3 months after surgery. In the paracentral RD group, at 1 month after vitrectomy, the CT was thinner than that of the contralateral eye, mainly in the foveal region. At 3 months, the intereye CT difference continued to resolve temporally and nasally, but not centrally. In the macula-off RD group, at 1 month postoperatively, the mean intereye CT difference showed significant thinning compared with contralateral eye at all locations, particularly the subfoveal and temporal locations. This thinning also started to resolve at 3 months postoperatively.

Although the results of this study are notable, there are several limitations that should be highlighted. First, we analyzed a small number of patients. Future studies with larger sample sizes are needed to confirm the different patterns of CT evolution that we observed before and after RD treatment. Furthermore, several studies have reported that the CT undergoes diurnal fluctuations of 8.5% to 13.9%.^{19–21} All our patients were imaged shortly after presentation, with no systematic selection bias for the RD type or imaging time. Therefore, although diurnal fluctuation might be a likely source of noise, it was not likely to mask the observed CT changes associated with RD type. However, ideally, all imaging should be performed at approximately the same time of day. Furthermore,

there is currently no automated software that can segment and automatically extract CT measurements. We used a manual technique to measure the outer border of the choroidal stroma. To delineate the profile of the CT, we aligned the external limiting membrane boundary to the posterior choroidal boundary and used the measures calculated by the device to estimate the thickness of the modified “outer retinal layer.” In this way, we were able to extract the CT systematically. In many eyes, the chorioscleral interface is blurred on OCT images, which makes measuring the CT more challenging. However, this obstacle may be removed in the future with the recent advances in imaging technology, particularly the use of longer wavelength light sources, which allow for deeper penetration. Finally, because the fovea relies exclusively on the choroidal vascular system, greater changes in the choroid may represent larger impacts on retinal health, with negative consequences on visual acuity, in patients with RD.¹

In conclusion, this study was the first to report CT changes associated with RDs in the subfoveal and submacular choroid. We found that the CT varied significantly, depending on the extent of RD, both before and after successful surgical treatment. The origin and clinical implications of these different recovery pathways remain unknown, but influencing factors might include effects from circulatory alterations, treatment choice, and the extent of RD.

Key words: retinal detachment, choroidal thickness, intereye difference, optical coherence tomography, enhanced depth imaging (EDI), vitrectomy.

References

1. Kur J, Newman EA, Chan-Ling T. Cellular and physiological mechanisms underlying blood flow regulation in the retina and choroid in health and disease. *Prog Retin Eye Res* 2012;31:377–406.
2. Mrejen S, Spaide RF. Optical coherence tomography: imaging of the choroid and beyond. *Surv Ophthalmol* 2013;58:387–429.
3. Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. *Am J Ophthalmol* 2009;147:811–815.
4. Ruiz-Medrano J, Flores-Moreno I, Pena-Garcia P, et al. Macular choroidal thickness profile in a healthy population measured by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci* 2014;55:3532–3542.
5. Imamura Y, Fujiwara T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. *Retina* 2009;29:1469–1473.
6. Koizumi H, Yamagishi T, Yamazaki T, et al. Subfoveal choroidal thickness in typical age-related macular degeneration and polypoidal choroidal vasculopathy. *Graefes Arch Clin Exp Ophthalmol* 2011;249:1123–1128.

7. Nickla DL, Wallman J. The multifunctional choroid. *Prog Retin Eye Res* 2010;29:144–168.
8. Sayman Muslubas I, Karacorlu M, Hocaoglu M, et al. Subfoveal choroidal thickness change after pars plana vitrectomy in recent onset rhegmatogenous retinal detachment. *Retina* 2016;36:2371–2376.
9. Kimura M, Nishimura A, Yokogawa H, et al. Subfoveal choroidal thickness change following segmental scleral buckling for rhegmatogenous retinal detachment. *Am J Ophthalmol* 2012;154:893–900.
10. Miura M, Arimoto G, Tsukahara R, et al. Choroidal thickness after scleral buckling. *Ophthalmology* 2012;119:1497–1498.
11. Akkoyun I, Yilmaz G. Choroidal thickness after scleral buckling surgery versus pars plana vitrectomy in macula-off rhegmatogenous retinal detachment. *Klin Monbl Augenheilkd* 2014;231:1029–1033.
12. Chen FK, Yeoh J, Rahman W, et al. Topographic variation and interocular symmetry of macular choroidal thickness using enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci* 2012;53:975–985.
13. Odrobina D, Laudanska-Olszewska I, Gozdek I, et al. Influence of scleral buckling surgery with encircling band on subfoveal choroidal thickness in long-term observations. *Biomed Res Int* 2013;2013:586894.
14. Veckeneer M, Van Overdam K, Bouwens D, et al. Randomized clinical trial of cryotherapy versus laser photocoagulation for retinopexy in conventional retinal detachment surgery. *Am J Ophthalmol* 2001;132:343–347.
15. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 2008;146:496–500.
16. Ikuno Y, Maruko I, Yasuno Y, et al. Reproducibility of retinal and choroidal thickness measurements in enhanced depth imaging and high-penetration optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52:5536–5540.
17. Rahman W, Chen FK, Yeoh J, et al. Repeatability of manual subfoveal choroidal thickness measurements in healthy subjects using the technique of enhanced depth imaging optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52:2267–2271.
18. Vuong VS, Moisseiev E, Cunefare D, et al. Repeatability of choroidal thickness measurements on enhanced depth imaging optical coherence tomography using different posterior boundaries. *Am J Ophthalmol* 2016;169:104–112.
19. Brown JS, Flitcroft DI, Ying GS, et al. In vivo human choroidal thickness measurements: evidence for diurnal fluctuations. *Invest Ophthalmol Vis Sci* 2009;50:5–12.
20. Chakraborty R, Read SA, Collins MJ. Diurnal variations in axial length, choroidal thickness, intraocular pressure, and ocular biometrics. *Invest Ophthalmol Vis Sci* 2011;52:5121–5129.
21. Tan CS, Ouyang Y, Ruiz H, Sadda SR. Diurnal variation of choroidal thickness in normal, healthy subjects measured by spectral domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2012;53:261–266.