SWEPT SOURCE OCT AND NEAR INFRARED REFLECTANCE PATTERNS IN CHOROIDAL NEVI.

AUTHORS:

Clara Vazquez-Alfageme¹, MD

Vasilios P Papastefanou², MD, PhD

Praveen J Patel¹, MD

Simona Degli-Esposti¹, MD

Victoria M L Cohen^{1,2}, MB BChir, FRCOphth

Mandeep S Sagoo^{1,2,3}, MB, PhD, FRCS (Ed), FRCOphth

¹ National Institute for Health and Research (NIHR) Biomedical Centre at Moorfields Eye Hospital and University College of London (UCL) Institute of Ophthalmology, London, UK.

² Ocular Oncology Service, St Bartholomew's Hospital and Moorfields Eye Hospital, London, UK.

³ University College of London (UCL) Institute of Ophthalmology, London, UK.

Corresponding author:

Clara Vazquez-Alfageme

NIHR Biomedical Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology

Moorfields Eye Hospital. 162 City Road, EC1V 2PD, London (UK)

Clara.alfageme@outlook.com

This study was conducted at Moorfields Eye Hospital, London (UK).

Financial support: The research was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Moorfields Eye Hospital NHS Foundation Trust and University College London Institute of Ophthalmology. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

No conflicting relationship exists or proprietary interest for any author for the work submitted.

The manuscript has not been submitted for publication previously. Part of this paper was presented at ARVO 2016 Annual Meeting (Seattle, WA) on the 5th May 2016 and at EVER 2016 Annual Meeting (Nice, France) on the 8th October 2016 (Awarded Best Poster – section PO).

Running head: Choroidal nevi patterns in SS-OCT and NIR.

KEY WORDS: Choroid; nevus; optical coherence tomography; near-infrared reflectance; inverse reflectance.

1 ABSTRACT:

2
3 Purpose: To describe the three distinct patterns of choroidal nevi in swept-source optical coherence
4 tomography (SS-OCT) and apply that classification to a cohort of consecutive choroidal nevi. Also, we
5 aim to describe the findings of these lesions in near-infrared reflectance (NIR) at different
6 wavelengths (820nm and 1050nm).

7 Design: Single center, retrospective, observational study.

8 Participants: 104 consecutive patients with choroidal nevi.

9 Methods: Retrospective analysis of choroidal nevi imaged with SS-OCT and NIR.

10 Main outcome measures: Lesions were classified according to OCT patterns as type A (high
11 reflectivity with optical shadowing), type B (medium reflectivity with partial visualization of the
12 scleral boundary) and type C (hyporeflective with complete visualization of the scleral boundary).

13 Results: Of 104 choroidal nevi, 97 lesions (93.3%) could be classified into one of the SS-OCT patterns.
14 49% correspond to type A, 26% type C and 18.3% type B. In NIR [820], 76% of lesions were
15 hyperreflective while at NIR [1050] most of the lesions were hyporeflective (59.6%) (inverse
16 reflectance).

17 Conclusions: Choroidal nevi present distinct patterns according to SS-OCT features. Clinical
18 implications are yet to be determined. In NIR, inverse reflectance may be a consequence of the
19 confocality of the device, rather than a property of the lesions.

20

21

22

According to a recent population-based study, 4.7% of US adults have a choroidal nevus¹. These lesions are the most frequent intraocular tumors in ophthalmic practice. Frequency aside, the importance of these lesions is twofold: the potential of malignant transformation and the occasional challenging diagnosis that they may pose. Choroidal nevi are composed of benign-appearing atypical uveal melanocytes (nevus cells). However, it is thought that most choroidal melanomas, like their cutaneous counterparts, arise from pre-existing nevi. This fact is supported by several histological studies which have found nevus cells in up to 73% of melanomas². Due to this potential of malignant transformation and the benefits of early detection of melanoma³, follow up is advised to detect possible growth, although, slow growth in benign choroidal nevus has been documented⁴. Nevus and small choroidal melanoma may exhibit overlapping clinical features such as pigmentation, lipofuscin orange pigment or subretinal fluid accumulation. Definitive diagnosis is based on histological findings in many non-ocular tumours, but biopsy of lesions in the eye is not possible nor desirable in most cases. There is an incentive therefore to develop imaging that approximates “in vivo non-invasive biopsies.”

Recent advances of ophthalmic imaging have been revolutionary. Currently, swept source laser technology for OCT (SS-OCT) allows high imaging acquisition speed (100 000 A scans/s) combined with better penetration into the choroidal and scleral tissue due its longer wavelength (1050 nm). In choroidal nevi, it has proven to be significantly better than other imaging techniques at displaying intralesional detail, as reported by Francis et al⁵. Another technique which has regained momentum is near-infrared reflectance (NIR). NIR is a variation of fundus photography using light in the near infrared spectrum (750-1400 nm) instead of visible light (400-700 nm). The longer wavelength used allows deeper penetration and better visualization of sub-retinal structures⁶. Both SS-OCT and NIR are appropriate to evaluate choroidal lesions, and with these we tried to achieve two objectives. First, we observed the features of choroidal nevi using SS-OCT. We hypothesized that nevi have

consistent, recognizable and distinct patterns on SS-OCT and classified a clinical cohort accordingly. Second, to our knowledge, a description of 1050 nm NIR in choroidal nevi has not yet been published. We aim to describe the findings with this imaging modality and compare it to the findings at 820 nm wavelength.

Methods

We retrospectively analyzed clinical data and images of consecutive patients with choroidal nevi seen in Moorfields Eye Hospital, London, UK between September 2015 and January 2016. The study fully conformed to the principles expressed in the Declaration of Helsinki, and Institutional Review Board approval was obtained (ROAD 15/021).

Data collected included patient demographics, age at presentation, sex and laterality. All patients underwent comprehensive ophthalmic assessment with slit-lamp biomicroscopy and indirect ophthalmoscopy. Diagnosis of choroidal nevus was made based on the clinical findings in funduscopy and ultrasound examination. Those lesions that exhibited predictive factors of growth into melanoma, as previously published by Shields et al.⁷ were categorized as suspicious choroidal nevi. Lesions that exhibited sufficient suspicious features for melanoma were treated as such, and therefore excluded from the cohort studied. Choroidal nevi with co-existing choroidal neovascular membranes were also excluded from the study.

Color fundus photography (TOPCON TRC-50DX Retinal Camera; Topcon Corporation, Japan), spectral domain optical coherence tomography (SD-OCT) (Heidelberg Spectralis; Heidelberg Engineering, Germany) and swept source optical coherence tomography (SS-OCT) (DRI OCT-1 Atlantis; Topcon Corporation, Japan) were performed in all subjects. Only SS-OCT images were analyzed and graded

in this study. To this end, a 5-line cross-scan with 0.25 mm spacing, centered in the lesion was obtained for every nevus. Infrared reflectance images were performed with both OCT devices, obtaining near-infrared reflectance images (NIR) at different wavelengths: 820 nm with the Spectralis OCT (NIR [820]) and 1050 nm with Atlantis DRI (NIR [1050]). It should be noted that the Spectralis OCT uses confocal scanning laser technology for imaging acquisition, capturing light only from a determined plane of interest, while DRI-OCT 1 images are non-confocal.

Based on the reflectivity pattern of the nevus displayed on SS-OCT, and the visualization of the scleral boundary, lesions were classified by a single grader into three different types: high reflectivity with optical shadowing and no visualization of the scleral boundary (type A), medium reflectivity with partial visualization of the scleral boundary (type B) and hyporeflective with complete visualization of the scleral boundary (type C), as summarized in table 1. As used by Torres et al.⁸, the RPE and vitreous served as reference to grade the strength of reflectivity of the choroidal lesion. The RPE was considered to have the highest reflectivity and the vitreous the lowest. Intermediate reflectivity between the two was graded as medium reflectivity.

NIR images of the nevi at both wavelengths were also classified as hyperreflective, isoreflective or hyporeflective according to the reflectivity patterns compared to the background reflectance. Color fundus photography was used to categorize pigmented and amelanotic (non-pigmented) nevi. No grading of pigmentation was performed in this study. Images of patients with poor quality or partial visualization of the lesion, led to the exclusion of the lesion for the analysis. Images were graded by a single observer on two separate occasions, one month apart. Repeatability was assessed using Cohen's Kappa.

Statistical analyses were performed using IBM SPSS Statistics (version 21.0, IBM Corporation, Armonk, NY, USA) and the statistical level of significance was set to $p < 0.05$. Descriptive analysis was performed on every variable of the study including mean and standard deviation (SD) for quantitative variables and, when appropriate, confidence intervals for continuous variables. Frequencies and percentages for categorical variables are provided. Qualitative variables were arranged in contingency tables and assessed with the χ^2 test or Fisher's exact test. Fisher's exact test was always performed for samples with expected values of < 5 , and Freeman-Halton extension of Fisher's was used for 2x3 and 3x3 contingency tables. Changes in quantitative variables with parametric distribution were investigated by means of Student's t-test for two groups or with ANOVA when more than 2 groups. Mann-Whitney U Test or Kruskal-Wallis were used for non-parametric data.

Results

A total of 104 choroidal nevi from 98 different patients were included in the study; 65.3% (64) patients were female and the mean age at presentation was 60.5 years. Most nevi, 93.3% (97), were pigmented and unilateral, but 6.1% of lesions were bilateral. Of 104 nevi, 8 were classified as suspicious choroidal nevi due to the presence of predictive factors of growth. The demographic data and lesion features are listed in table 2. Average nevus thickness and diameter measured by ultrasound scan were 0.8 mm (95%CI 0.71 to 0.92) and 3.9 mm diameter (95%CI 3.48 to 4.4) respectively. Ultrasound thickness distribution among groups is provided in table 3.

Classification according the pattern displayed on SS-OCT

In this cohort, 97 lesions (93.3%) could be classified into one of the three SS-OCT patterns (A, B or C). Only 7 (6.7%) did not fall into any category (table 4). The most frequent pattern was type A with 51

lesions (49%), followed by type C with 27 lesions (26%) and type B with 19 lesions (18.3%). Out of the 7 non-pigmented nevi, 3 (42.9%) did not fall under any of the categories previously mentioned. The remaining 4 were all classified as type C. Cohen's Kappa coefficient for the test-retest repeatability was 1. The presence or absence of predictive factors of growth did not significantly affect the distribution between patterns ($p=0.076$).

Classification according to the reflectivity patterns in NIR

In NIR [820], none of the lesions studied displayed hyporeflectivity. Most of them (79, 76%), were graded as hyperreflective and 25 (24%) as isoreflective (table 5). On the contrary, in NIR [1050], most of the lesions were hyporeflective (62, 59.6%), 34 (32.7%) isoreflective and only 8 (7.7%) hyperreflective. Again, the presence or absence of predictive factors of growth did not significantly affect the distribution (NIR [820] $p=0.09$, NIR [1050] $p=0.49$).

Relation between OCT patterns and NIR

We analyzed how the reflectivity in NIR [820] and NIR [1050] is distributed along the three different OCT patterns (A, B and C). In type A, 48 of 51 lesions (94.1%) exhibited hyporeflectivity in NIR [1050] and hyperreflectivity in NIR [820], with a statistically significant association between the reflectivity patterns with the different NIR wavelengths ($p<0.001$). In type B, the statistical significance was maintained ($p<0.001$). In this group, 13 of 19 lesions (68.4%) displayed hyperreflectivity in NIR [820] but hypo or isoreflectivity in NIR [1050]. In type C, there was no significant association between the two NIR wavelengths ($p=0.09$), although 11 of 27 lesions displayed isoreflectivity in both NIR and 14 of 27 exhibited hyperreflectivity in NIR [820] with iso or hyperreflectivity in NIR [1050]. Regarding the subgroup of suspicious choroidal nevi, independently of the OCT pattern, there was a significant association between reflectivity patterns and the NIR techniques ($p=0.02$).

Discussion

Choroidal nevi are the commonest fundus tumor in ophthalmic practice. Differentiating nevi from small melanomas can be challenging. As the range of fundus imaging modalities has increased, more information has become available on the characteristics of nevi and other tumors imaged with these devices. In this report, we show that most nevi can be easily classified on SS-OCT into one of the three different types, according to the reflectivity of the lesion, the presence or absence of optical shadowing and the visualization of scleral boundaries. Almost half of the lesions in this study (49%) displayed type A (hyperreflectivity with optical shadowing), followed by 26% of type C (hyporeflective lesion with complete visualization of scleral boundaries) and 18.3% of type B (medium reflectivity with partial visualization of the scleral boundary).

Several reports on the reflectivity of choroidal nevi in OCT have been published with variable results. In 2005, Shields et al.⁹ found that out of 120 nevi, 9% displayed hyperreflectivity, 29% isoreflectivity and 62% hyporeflectivity. As acknowledged by the authors, the technology used for that study (Stratus OCT 3000; Carl Zeiss Ophthalmic Systems, Dublin, CA) could only image the superficial choroid, a clear disadvantage in imaging nevi. In 2010, Torres et al.⁸ reported that 8 out of 9 pigmented choroidal nevi, assessed with enhanced depth imaging spectral domain or EDI SD-OCT (Spectralis, Heidelberg Engineering; Heidelberg, Germany), showed hyperreflectivity with optical shadowing. In contrast, 4 out of 4 amelanotic choroidal nevi displayed medium reflectivity without optical shadowing. Despite being a pilot study with a small sample, these results are closer to ours, as most of the pigmented lesions showed high reflectivity with the advantage that SS-OCT images greater depth. Finally, in 2015, using SS-OCT (DRI OCT-1 Atlantis, Topcon Medical Systems, Oakland, New

Jersey, USA) Francis et al.⁵ reported that out of a sample of 30 choroidal nevi: 53% displayed hyperreflectivity with optical shadowing and 43% had visualization of nevus/scleral interface. The current study agrees with these figures.

The reflectivity of the lesion in OCT relies on several factors. The pigment melanin is a well-known source of reflectivity in OCT, as demonstrated by Zhang et al.¹⁰. The findings of Torres et al⁸ are consistent with ours in the sense that the presence of pigmentation contributes to the reflectivity displayed in the OCT. In line with their study, all the non-pigmented choroidal nevi that we could grade (n=4) fell under type C (hyporeflective). However, in our study, the remaining 23 out of 27 nevi in type C, were pigmented and therefore we surmise that factors apart from degree of pigmentation are involved.

Cellular composition is another factor that may be involved in the reflectivity of the lesion. Nevi are composed of atypical, but benign melanocytes called nevus cells. As stated by Naumann et al.², there is an enormous cytologic variability of nevus cells, even in different portions of the same lesion. The most common cell type is the plum polyhedral nevus cell in which cytoplasm is fully loaded of melanin granules, and therefore densely pigmented. These cells tend to be in the central portion of the lesion. The second most frequent cell type is the slender spindle nevus cell, containing almost no pigment and often distributed in the outer portions of the nevus. If these cells are predominant in the lesion, nevi are only lightly pigmented. This typical distribution of nevus cell can easily explain the proposed type A, with a superficial hyperreflectivity caused by the melanin-loaded plump polyhedral cells, and the optical shadowing hiding the rest of the lesion. We hypothesize that variations in cell composition or distribution can explain the other two types: Nevi rich in slender spindle cells can constitute type C, and mixed lesions can constitute type B.

192

193 NIR fundus photography using 2 wavelengths in the near infrared spectrum (820 and 1050 nm) were
194 compared. With NIR [820], 76% of lesions were found hyperreflective and 24% isorefective. In
195 contrast, in NIR [1050], most of the lesions were hyporefective (59.6%) or isorefective (32.7%).
196 Observations of NIR [820] imaging of nevi have been made before, with a few isolated descriptions
197 supporting the hyperreflective pattern of these lesions.^{11 12}. To the best of our knowledge, no
198 descriptions of NIR [1050] have been previously published. The most striking finding is the 'inverse
199 reflectance' pattern that most of type A and type B lesions were hyperreflective on NIR [820] and
200 hyporefective on NIR [1050].

201

202 Near-infrared reflectance images are a composite of reflected and absorbed irradiation¹¹. The main
203 reflector of light in the eye is the sclera, with small contributions of the internal limiting membrane
204 (ILM), retinal nerve fiber layer (RNFL) and retinal photoreceptor layer. On the other hand, the main
205 absorbers are blood, melanin and water. The absorption spectra of the main contributors at
206 different wavelengths was reported by Elsner et al⁶. Taking this into account, the hyporefectivity of
207 the nevus displayed in NIR [1050] can be justified by the absorption of melanin which also prevents
208 light reaching the major reflector, the sclera. However, this theory does not explain the completely
209 opposite behaviour of the lesions on NIR [820]. It may be possible to attribute this phenomenon to
210 the different types of melanin present in the eye and their different optical physical properties.
211 Indeed, two different types of melanin are present in the retina-RPE-choroidal complex: eumelanin
212 (main pigment of the RPE) and pheomelanin, which constitutes with eumelanin, in different ratios,
213 the melanosomes of the uveal melanocytes¹³. However, both melanins exhibit a very similar and
214 broad linear absorption spectrum, but the main difference is the increased absorption of
215 pheomelanin at shorter wavelengths due to its reddish colour¹⁴. At longer wavelengths, the

absorption is very similar, and thus this does not constitute a feasible explanation for the ‘inverse reflectance’ phenomenon.

One possible explanation relies on the different methods of image acquisition used for the 2 wavelengths used. NIR [820] is obtained using confocal scanning laser technology, while NIR [1050] has a non-confocal capture system. With confocal image acquisition, light from a determined plane of interest is captured by the sensor, suppressing light from planes anterior or posterior to the focal plane and resulting in better contrasted images. If the plane of interest is selected above the choroidal lesion (deep retina / RPE), it is possible that information is lost from the choroid to obtain a sharper image of the retina. Moreover, the hyperreflectivity in NIR [820] may be caused, not by the choroidal lesion itself but by secondary histologic changes at the level of the RPE/choriocapilaris such as drusen formation², narrowing/obliteration of the choriocapilaris², lipofuscin accumulation¹⁵, RPE atrophy or metaplasia¹⁵. These findings suggest that NIR [1050] is a more accurate and reliable imaging technique to document choroidal nevi, as it images the lesion itself and not the secondary changes of the surrounding tissues.

Limitations of this study include the lack of histological correlation, the assessment of qualitative factors by a single grader and potential for bias caused by the excluding nevi that exceed the size of the scan parameters. Also, peripheral nevi do not often yield good quality scans, so these had to be excluded.

In summary, we have described the findings of choroidal nevi on NIR [1050] and have showed that choroidal nevi can be divided into three distinct patterns according to OCT features. It is yet to be

determined if the different patterns of choroidal nevi, as a result of a possible variation in cell composition, may have clinical implications and for this, further follow up of these lesions is needed.

References

1. Qiu M, Shields CL. Choroidal Nevus in the United States Adult Population: Racial Disparities and Associated Factors in the National Health and Nutrition Examination Survey. *Ophthalmology* 2015;122:2071–2083.
2. Naumann G, Yanoff M, Zimmerman LE. Histogenesis of malignant melanomas of the uvea: I. histopathologic characteristics of nevi of the choroid and ciliary body. *Arch Ophthalmol* 1966;76:784–796.
3. Eskelin S, Pyrhönen S, Summanen P, et al. Tumor doubling times in metastatic malignant melanoma of the uvea: tumor progression before and after treatment. *Ophthalmology* 2000;107:1443–1449.
4. Mashayekhi A, Siu S, Shields CL, Shields JA. Slow enlargement of choroidal nevi: a long-term follow-up study. *Ophthalmology* 2011;118:382–388.
5. Francis JH, Pang CE, Abramson DH, et al. Swept-source optical coherence tomography features of choroidal nevi. *Am J Ophthalmol* 2015;159:169–176.e1.
6. Elsner AE, Burns SA, Weiter JJ, Delori FC. Infrared imaging of sub-retinal structures in the human ocular fundus. *Vision Res* 1996;36:191–205.
7. Shields CL, Furuta M, Berman EL, et al. Choroidal nevus transformation into melanoma: analysis of 2514 consecutive cases. *Arch Ophthalmol Chic Ill* 1960 2009;127:981–987.

- 261 8. Torres VLL, Brugnoli N, Kaiser PK, Singh AD. Optical coherence tomography enhanced depth
262 imaging of choroidal tumors. *Am J Ophthalmol* 2011;151:586–593.e2.
- 263 9. Shields CL, Mashayekhi A, Materin MA, et al. Optical coherence tomography of choroidal nevus in
264 120 patients. *Retina Phila Pa* 2005;25:243–252.
- 265 10. Zhang Q-X, Lu R-W, Messinger JD, et al. In vivo Optical Coherence Tomography of Light-Driven
266 Melanosome Translocation in Retinal Pigment Epithelium. *Sci Rep* 2013;3.
- 267 11. Fazelat A, Desai M, Nandakumar N, et al. Enhanced, near-infrared fundus reflectance for
268 qualitative and quantitative analysis of subretinal lesions. *Exp Eye Res* 2012;96:171–177.
- 269 12. Pang CE, Freund KB. Ghost maculopathy: an artifact on near-infrared reflectance and multicolor
270 imaging masquerading as chorioretinal pathology. *Am J Ophthalmol* 2014;158:171–178.e2.
- 271 13. Hu D-N, Simon JD, Sarna T. Role of ocular melanin in ophthalmic physiology and pathology.
272 *Photochem Photobiol* 2008;84:639–644.
- 273 14. Piletic IR, Matthews TE, Warren WS. Probing Near Infrared Photo-Relaxation Pathways in
274 Eumelanins and Pheomelanins. *J Phys Chem A* 2010;114:11483–11491.
- 275 15. Shields CL, Furuta M, Mashayekhi A, et al. Clinical spectrum of choroidal nevi based on age at
276 presentation in 3422 consecutive eyes. *Ophthalmology* 2008;115:546–552.e2.

277

278

Table 1: Classification of Choroidal Nevi According to the Reflectivity of the Lesion Displayed on SS-OCT.

	Type A	Type B	Type C
Reflectivity of lesion	Highly reflective	Medium reflective	Hyporeflective
Optical shadowing *	Yes	No	No
Visualization of scleral boundary	None	Partial	Complete
Example scan			

*Optical shadowing is defined as the phenomenon caused by dense reflective material that absorbs light causing obscuration of the underlying tissues on OCT.

Table 2: Patients Demographics and Lesions Characteristics.

Characteristics		N
Patients		98
Age	Mean (years)	60.52
	Range	21-95
Sex	Male	34 (34.7%)
	Female	64 (65.3%)
Lesions		104
Laterality	Right eye	53 (51%)
	Left eye	51 (49%)
	Unilateral	92 (93.9%)
	Bilateral	6 (6.1%)
Type of lesion	Choroidal naevus	96 (92.3%)
	Suspicious choroidal naevus	8 (7.7%)
Pigmentation	Melanotic	97 (93.3%)
	Amelanotic	7 (6.7%)

Table 3: Relationship between ultrasound thickness measurements and reflectivity patterns in OCT and NIR.

		N	US (mm)	95% CI	p
Full sample		104	0.82	(0.71, 0.92)	-
OCT pattern	A	51	0.84	(0.70, 0.99)	0.001
	B	19	0.44	(0.24, 0.64)	
	C	27	1.0	(0.75, 1.25)	
NIR 830	Hyporeflective	0	-	-	0.658
	Isoreflective	25	0.84	(0.58, 1.09)	
	Hyperefective	79	0.81	(0.69, 0.93)	
NIR 1050	Hyporeflective	62	0.79	(0.65, 0.93)	0.304
	Isoreflective	34	0.8	(0.64, 0.96)	
	Hyperefective	8	1.15	(0.52, 1.78)	

Table 4: Classification according to patterns in SS-OCT.

Types		N
Full sample		104
	A	51 (49%)
	B	19 (18.3%)
	C	27 (26%)
	Others	7 (6.7%)
Choroidal nevi (absence of predictor factors of growth)		96
	A	49 (51%)
	B	18 (18.8%)
	C	22 (22.9%)
Suspicious choroidal nevi (presence of predictor factors of growth)		8
	A	2 (25%)
	B	1 (12.5%)
	C	5 (62.5%)

Table 5: Classification according to reflectivity patterns in NIR at 820nm and 1050nm.

NIR Reflectivity		N	Choroidal nevi	Suspicious choroidal nevi
NIR [820]		104	96	8
	Hyporeflective	0 (0%)	0 (0%)	0 (0%)
	Isoreflective	25 (24%)	21 (21.9%)	4 (50%)
	Hypereflective	79 (76%)	75 (78.1%)	4 (50%)
NIR [1050]		104		
	Hyporeflective	62 (59.6%)	58 (60.4%)	4 (50%)
	Isoreflective	34 (32.7%)	30 (31.3%)	4 (50%)
	Hypereflective	8 (7.7%)	8 (8.3%)	0 (0%)

300 Figure 1: Pigmented choroidal nevi in color fundus photography (A), displaying hyperreflectivity in
301 NIR [820] (B) and hyporefectivity in NIR [1050] (C) (inverse reflectance). SS-OCT (D) shows a lesion
302 with high reflectivity and optical shadowing, with no visualization of the scleral boundary (type A).

303

304

305

Figure 2: Color fundus photography (A) shows a pigmented nevus, displaying inverse reflectance in NIR [820] (B) and NIR [1050] (C). SS-OCT features (D) involve: medium reflectivity of the lesion with no optical shadowing and partial visualization of the scleral boundary (type B).

311 Figure 3: Color fundus photography (A) of a pigmented nevus, displaying hyperreflectivity in NIR
312 [820] (B) and NIR [1050] (C). SS-OCT (D) shows a lesion with low reflectivity, no optical shadowing
313 and complete visualization of the scleral boundary (type C).

314