• Letter to the Editor •

Laser speckle flowgraphy findings in a patient with radiation retinopathy

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Dear Editor,

I am Satoru Kase, from Hokkaido University Hospital, Japan. Choroidal melanoma is a serious intraocular tumor, which threatens patients' vision and life. Treatments for choroidal melanoma consist of surgery and radiotherapy, the latter of which includes carbon iron beam radiation (C-iron)[1]. Recent studies have addressed that C-iron contributes to tumor suppression and elongation of metastasis-free periods and overall survival[1]. On the other hand, radiation retinopathy is one of the serious causes of vision loss following radiotherapy. The pathogenesis of radiation retinopathy is considered microangiopathy in the retina as well as choroid involved with direct irradiation. It has been reported that radiation choroidopathy happened in a patient with eyelid melanoma following extra beam radiation observed by angiography[2]. However, little is known about involvements of choroidal circulation and morphological changes after C-iron.

Ethical Approval Institutional Review Board in Hokkaido University waived approval for application of clinical researches because this is a single case report with non-invasive measurements. Written informed consent was obtained from the patient for the use of clinical images for publication in international journals. This study followed the principles outlined in the Declaration of Helsinki.

Laser speckle flowgraphy (LSFG) is a non-invasive tool, which enables ophthalmologists to evaluate intraocular blood flow. The macula is mainly perfused by choroidal vasculatures because of less distribution of retinal vessels. Therefore, macular circulation observed by LSFG is largely derived from the choroidal circulation. We have shown alteration of ocular circulation in tumor-like lesions such as sclerochoroidal calcification[3], choroidal macrovessel[4], and optic disc melanocytoma[5], using LSFG. LSFG provides high reproducibility and relative values of examined patients, referred as mean blur rate (MBR). We also demonstrated that MBR is a significant marker for longitudinal evaluation of exacerbations and treatment efficacy in retinal hemangioblastoma[6]. However, choroidal circulation observed by LSFG in radiation retinopathy has yet to be reported.

The aim of this study is to report a case with choroidal melanoma located close to the arcade, in which multimodal imaging including LSFG was employed, looking at choroidal morphology and circulation.

A 49-year-old woman complained of burry vision and metamorphopsia in her right eye. She was referred to our hospital because of an intraocular tumor in October 2018. Visual acuity was 14/20 OD and 20/20 OS. Intraocular pressure was normal OU. Fundus revealed a brownish circumscribed tumor located close to the superotemporal arcade OD (Figure 1A). Swept source optical coherence tomography (SS-OCT) revealed serous retinal detachment in the macula OD (Figure 1B). Fluorescein angiography (FA) showed heterogeneous hyperfluorescence in the tumor (Figure 1C), where indocyanine green angiography (ICGA) depicted hypofluorescence (Figure 1D).

LSFG revealed relatively warm coloration in the macula at this time, where MBR was 14.82 (Figure 2A). Magnetic resonance imaging in the tumor revealed iso-intensity and low-intensity in T1 and T2-weighted images, respectively, which was enhanced by gadolinium. 123I-IMP-SPECT demonstrated abnormal signal in the right eye. Systemic survey showed no tumor lesions elsewhere except the right eye. Based on these clinical findings, the patient was diagnosed with choroidal melanoma OD. After informed consent was obtained, she received C-iron with 60 Gy to her right eye. Her best corrected visual acuity (BCVA) was 0.9 OD 4mo after C-iron in April

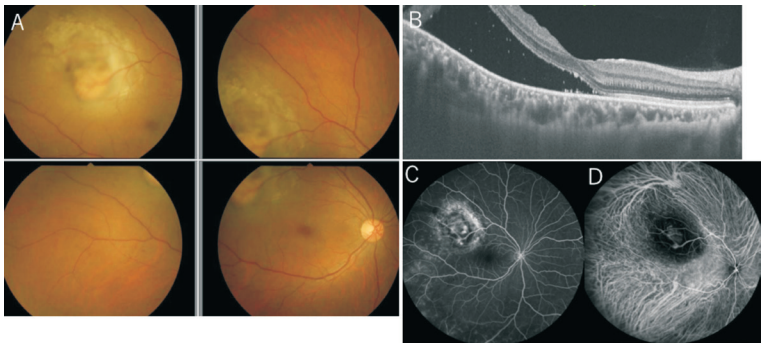

Figure 1 The patient with choroidal melanoma A: Fundus revealed a brownish circumscribed tumor located close to the superotemporal arcade OD; B: SS-OCT revealed serous retinal detachment in the macula OD; C: FA showed heterogeneous hyperfluorescence in the tumor; D: ICGA depicted hypofluorescence.

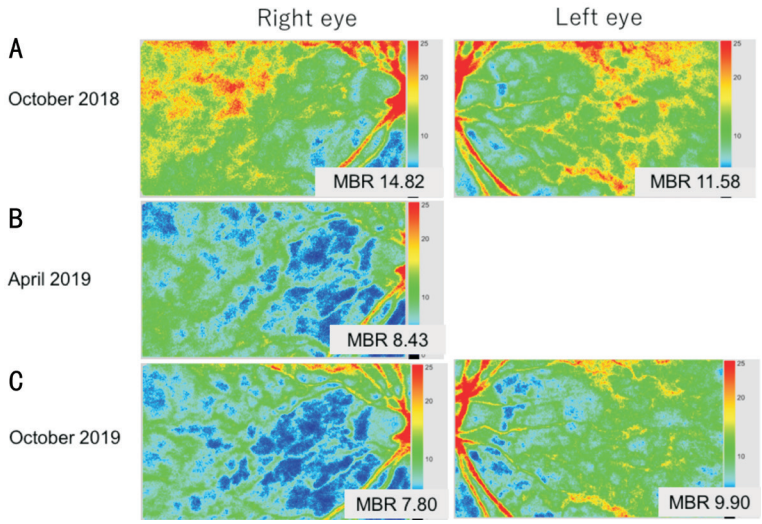

Figure 2 LSFG findings before and after the onset of radiation retinopathy A: LSFG reveals normal coloration in both eyes at an initial presentation; B: There is marked cool coloration in the right eye after heavy iron beam irradiation; C: LSFG shows cool coloration in the right eye treated with irradiation, while left reveals normal coloration.

2019. Although the choroidal tumor and the associated retinal detachment gradually regressed, MBR markedly decreased, measuring 8.43 (Figure 2B). Central choroidal thickness (CCT) and the ratio of choroidal vascular lumens in total choroidal area using a binarization method showed 20% and 2% reduction, respectively. There were no obvious findings of radiation retinopathy at this time.

In October 2019, the patient's BCVA decreased to 0.6. Fundus showed multiple cotton-wool spots in the arcade, where several retinal hemorrhages existed (Figure 3A). There was focal swelling of inner retinal layer in the vertical section of SS-OCT without retinal detachment or macular edema (Figure 3B). FA demonstrated multiple leakages from the retinal vessels as well as macular ischemia (Figure 3C). MBR in LSFG was further low OD measuring 7.80, while MBR in the left eye without treatments showed no marked changes (Figure 2C). Anti-VEGF therapy and laser photocoagulation were conducted. BCVA remained 0.3 OD in January 2021. The patient was well without systemic metastasis, and retinopathy resolved.

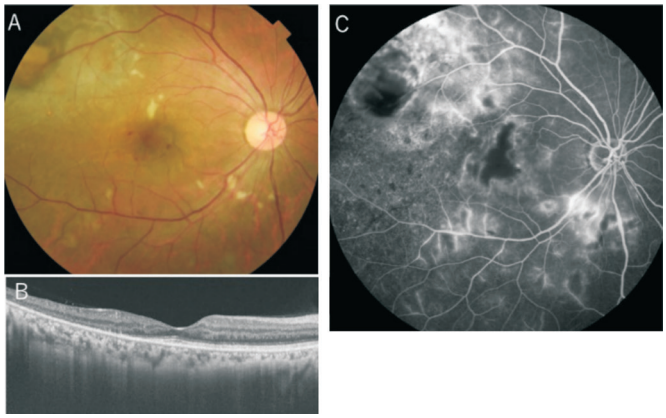

Figure 3 The onset of radiation retinopathy in a patient with choroidal melanoma treated with carbon iron beam radiation A: Fundus shows multiple cotton-wool spots in the arcade, where several retinal hemorrhages exhibit; B: There is no retinal detachment or macular edema, but is focal swelling of inner retinal layer in the horizontal section of SS-OCT; C: FA demonstrates multiple leakages from the retinal vessels as well as macular ischemia.

This study for the first time demonstrated that choroidal circulation observed by LSFG was significantly reduced C-iron posttreatment before the onset of radiation retinopathy. What's more, CCT and the ratio of choroidal vascular lumens were reduced compared to those before treatments. Next, LSFG clearly revealed markedly reduced choroidal perfusion in the macula at the onset of retinopathy. These results suggest that disruption of choroidal circulation plays a critical role in the pathogenesis of radiation retinopathy. It has been reported that macular vascular densities decreased with peripapillary capillary droplet after radiotherapy[7]. In choroidal melanoma, OCT angiography-based vessel density was negatively correlated with non-perfusion areas in the choroid following radiotherapy[8]. These studies showed that macular ischemia flowing radiotherapy could be caused by not only retinal capillary dropout but also disrupted choroidal perfusion. The current data based on LSFG and OCT suggest that radiation-induced choroidal circulation disorder was associated with reduced choroidal vascular components.

Historically, choriocapillaris perfusion was considered disrupted in the intraocular tissues apart from irradiation sites, while large choroidal vessels remained unaffected following radiation; therefore, loss of vision might not be caused by choroidal hypoperfusion[9]. Based on cellular biology, Takahashi *et al*[10] demonstrated that C-iron inhibited endothelial cell migration, adhesion and tube formation compared to conventional X-ray. This study indicates that C-iron substantially involves large choroidal vascular hypoperfusion observed by LSFG before the onset of retinopathy, because LSFG reflects relatively large choroidal vessels due to its long wavelengths emitted. The large choroidal vascular hypoperfusion simultaneously led to circulation disorders of choriocapillaris lobules, and macular ischemia with ellipsoid zone disruption. These results suggest that choroidal circulation plays a key role in the pathogenesis of radiation retinopathy and subsequent vision loss. LSFG might be a favorable tool to monitor the choroidal perfusion, which predicts macular ischemia following C-iron.

In conclusion, non-invasive LSFG clearly demonstrated a choroidal circulatory disorder before the onset of radiation retinopathy, suggesting that alteration of choroidal circulation plays a potential role in the pathogenesis of radiation retinopathy.

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REFERENCES

1 Wang Z, Nabhan M, Schild SE, Stafford SL, Petersen IA, Foote RL, Murad MH. Charged particle radiation therapy for uveal melanoma: a systematic review and meta-analysis. *Int J Radiat Oncol Biol Phys* 2013;86(1):18-26.

2 Takahashi K, Kishi S, Muraoka K, Tanaka T, Shimizu K. Radiation choroidopathy with remodeling of the choroidal venous system. *Am J Ophthalmol* 1998;125(3):367-373.

3 Mitamura M, Kase S, Ishida S. Multimodal imaging in sclerochoroidal calcification: a case report and literature review. *BMC Ophthalmol* 2020;20(1):248.

4 Kataoka K, Kase S, Noda K, Ishida S. Laser speckle flowgraphy findings in a patient with choroidal macrovessel. *Ophthalmol Retina* 2020;4(11):1123-1124.

5 Kikuchi I, Kase S, Hashimoto Y, Hirooka K, Ishida S. Involvement of circulatory disturbance in optic disk melanocytoma with visual dysfunction. *Graefes Arch Clin Exp Ophthalmol* 2019;257(4):835-841.

6 Mitamura M, Kase S, Hirooka K, Ishida S. Laser speckle flowgraphy in juxtapapillary retinal capillary hemangioblastoma: a case report on natural course and therapeutic effect. *Oncotarget* 2020;11(42):3800-3804.

7 Skalet AH, Liu L, Binder C, Miller AK, Crilly R, Hung AY, Wilson DJ, Huang D, Jia YL. Longitudinal detection of radiation-induced peripapillary and macular retinal capillary ischemia using OCT angiography. *Ophthalmol Retina* 2020;4(3):320-326.

8 Preziosa C, Corvi F, Staurenghi G, Pellegrini M. Extended field imaging optical coherence tomography angiography for the study of retinal and choroidal changes after radiation therapy for choroidal melanoma: comparison with wide-field angiography. *Retina* 2021;41(2):373-380.

9 Maguire AM, Schachat AP. Radiation retinopathy. Retina. Amsterdam: Elsevier, 2006:1483-1489.

10 Takahashi Y, Teshima T, Kawaguchi N, Hamada Y, Mori S, Madachi A, Ikeda S, Mizuno H, Ogata T, Nojima K, Furusawa Y, Matsuura N. Heavy ion irradiation inhibits *in vitro* angiogenesis even at sublethal dose. *Cancer Res* 2003;63(14):4253-4257.