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Mapping Sentinel Vessels in Uveal Melanomas Using Laser Speckle Contrast Imaging

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Keywords
Adult ocular oncology · Anterior segment pathology · Choroidal melanoma

Abstract

Introduction: Sentinel vessels provide an important early indication of underlying ocular neoplasm. To date, there is no noninvasive technique available for imaging and mapping of their vascular supply, which remains largely unstudied. We aimed to map sentinel vessels in uveal melanomas noninvasively by laser speckle contrast imaging (LSCI). ***Case Presentations:*** This report describes a case series of 4 patients undergoing enucleation due to uveal melanoma. Perfusion was imaged using LSCI during the successive detachment of the four rectus muscles, with their ciliary arteries, and the optic nerve with its ophthalmic artery. Tumor location and possible extrascleral growth were analyzed histopathologically. Sentinel vessels in uveal melanoma could be visualized noninvasively using LSCI, appearing broader and tortuous compared to surrounding vessels. The perfusion in the sentinel vessels was 24–94% higher than in the episcleral vessels. The origin of the sentinel vessel could be determined by perfusion monitoring during the successive detachment of the rectus muscles and the optic nerve. In 3 patients, the sentinel vessel was supplied by the anterior ciliary arteries and in 1 patient by the ophthalmic artery. In one of the cases, the sentinel vessel was not visible upon visual inspection. ***Conclusion:*** This is the first study of its kind demonstrating detailed mapping of sentinel vessels in uveal melanoma using LSCI. LSCI shows potential for the detection of sentinel vessels before they are visible in slit lamp examination. Vascular changes are a hallmark of tumor growth, and noninvasive imaging with LSCI may be a useful diagnostic tool for the detection of uveal melanoma.

Introduction

Uveal melanomas are the most common primary intraocular malignant tumor in adults and represent 3–5% of all melanomas [1, 2]. A sentinel vessel, also called a feeder vessel, commonly described as a dilated episcleral blood vessel feeding the metabolically active tumor that is visible through the conjunctiva overlying it, is an early physical sign of uveal melanoma. Such findings are frequent in ciliary body melanomas, some studies suggesting them to be evident in as many as 74% of cases [3]. The episcleral arteries are branches of the anterior ciliary arteries that run along the rectus muscles and supply the conjunctiva, sclera, rectus muscles, and the ciliary body.

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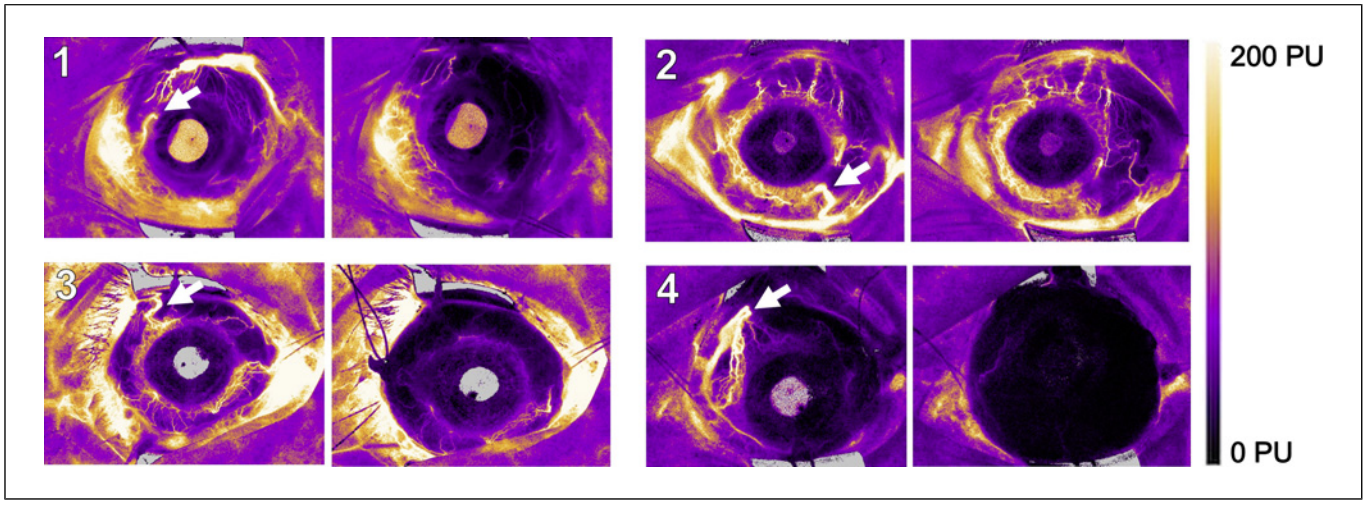

Fig. 1. Laser speckle contrast images showing the sentinel vessel (white arrows) in each of the 4 patients before (left) and after (right) their vascular supply was cut off. In patient #1, perfusion ceased after detachment of the inferior rectus muscle, and in patients #2 and #3, perfusion ceased after the detachment of the lateral rectus muscle. In patient #4, perfusion ceased after the optic nerve and its ophthalmic artery had been cut.

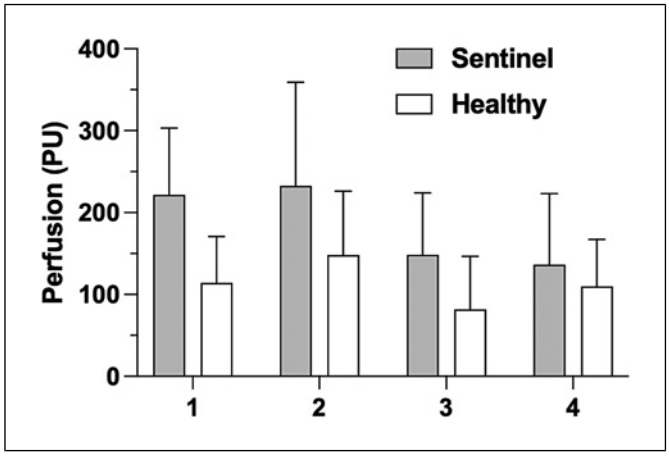

Fig. 2. Perfusion in the sentinel vessels, compared to that in healthy scleral vessels, in each of the 4 patients.

Despite the fact that they are evidently important in providing an indication of an underlying tumor, sentinel vessels have been sparsely studied. In a case report from 2016, anterior segment scleral fluorescein angiography was used to identify abnormal scleral vasculature in a patient with a ciliary body melanoma [4]. Although angiography may have the potential to identify vascular abnormalities and is generally considered safe, the method is invasive and subjects patients to the risk of allergic reactions. Today, noninvasive methods of perfusion imaging are available.

Laser speckle contrast imaging (LSCI) is a noninvasive method of measuring perfusion in real time with high spatial resolution. The technique has been used extensively in the field of ophthalmology to study retinal, choroidal, and optic nerve head circulation [5–10]. In our recent studies we have, for the first time, demonstrated that anterior segment perfusion can be mapped perioperatively with LSCI during strabismus surgery and enucleation [11–13]. However, LSCI has not yet been used to image sentinel vessels. In this study, LSCI was used during the successive detachment of the four rectus muscles, with their ciliary arteries, and the optic nerve, with its ophthalmic artery, in a case series of four eyes with uveal melanoma. The aim of the study was to evaluate the feasibility of LSCI to image and delineate the origin of sentinel vessels in uveal melanoma.

Case Report

The study was approved by the Swedish Ethical Review Authority. Four patients undergoing enucleation due to suspected uveal melanoma were recruited from the Department of Ophthalmology at Skåne University Hospital, Lund, Sweden. All patients gave their fully informed written consent. Three of the patients were male, and the median age was 63 years (range 42–77). Ultrasonography confirmed the presence of a tumor in all cases. One patient had previously undergone treatment with

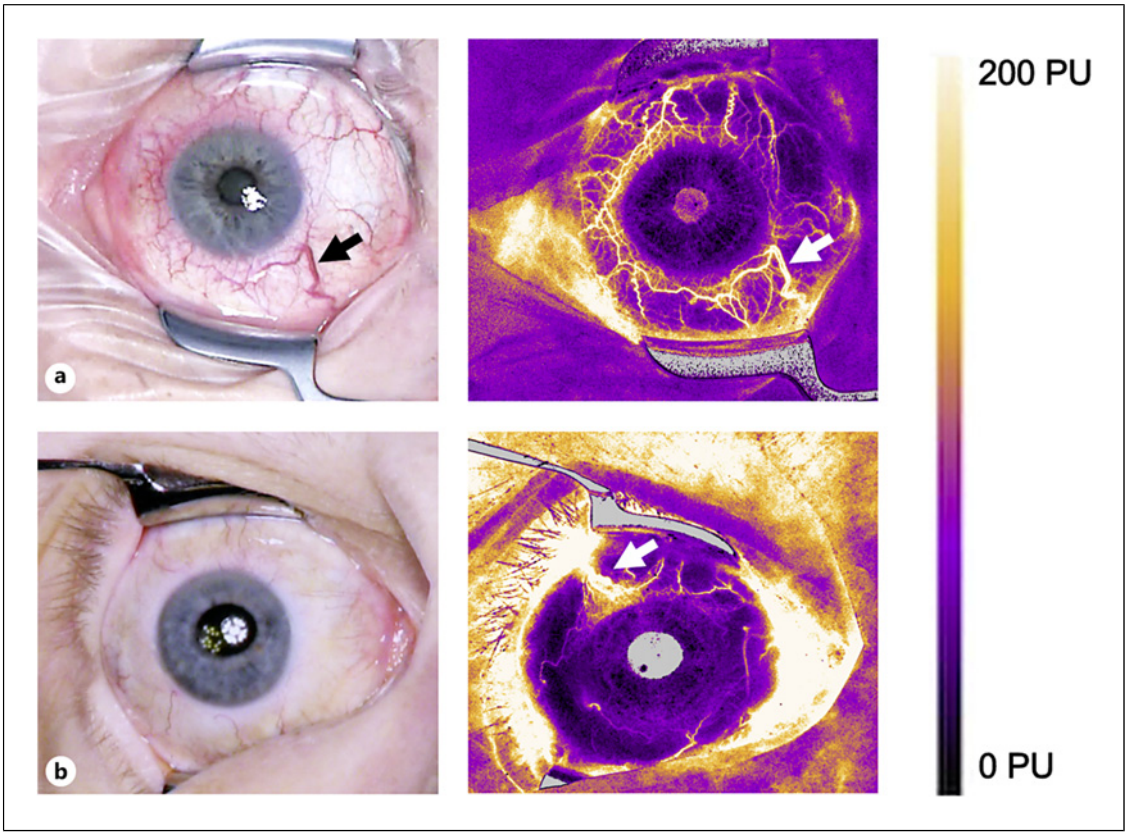

Fig. 3. Photographs (left) and laser speckle contrast images (LSCI) (right) from 2 patients where the sentinel vessel could be observed visually (**a**) and could not be observed visually (**b**), highlighting the potential of LSCI in mapping increased vascular supply to uveal melanomas.

brachytherapy. Enucleation was performed under general anesthesia according to standard procedure, and the eyes were sent for histopathological examination.

Sentinel vessels were mapped using LSCI (PeriCam PSI NR imager, Perimed AB, Järfälla, Sweden). This equipment utilizes a 780-nm laser that illuminates the surface of the eye. The light backscattered from the surface creates a dynamic speckle pattern as a result of the interference between the light backscattered from moving particles, i.e., the red blood cells in the capillaries. This creates a real-time perfusion map of the illuminated area. LSCI measurements were performed before commencing surgery, after conjunctival peritomy, and during the successive detachment of the four rectus muscles, with their ciliary arteries, and the optic nerve, with its ophthalmic artery [11–13].

Perfusion was measured in arbitrary perfusion units. Perfusion was determined in regions of interest in the image of the sentinel vessel and in a reference area of healthy scleral vasculature. The perfusion was calculated in the regions of interest as mean ± SD in each patient. The perfusion of the sentinel vessel was then expressed as a percent of that in the healthy scleral vasculature. The results from the LCSI images are shown in Figure 1, and the values of perfusion are given in Figure 2.

In patient #1, a sentinel vessel was visualized at 9 o'clock, with a perfusion that was 194% of that in healthy scleral vessels. Perfusion in the sentinel vessel ceased when the inferior rectus muscle was detached. Histopathological examination revealed a ciliary body melanoma without extrascleral growth.

In patient #2, a sentinel vessel was visualized at 5 o'clock, with a perfusion of 157% of that in healthy scleral vessels. Perfusion in the sentinel vessel ceased when the lateral rectus muscle was detached. Histopathological examination revealed a juxtapapillary choroidal melanoma at 7 o'clock by the optic nerve exit, without extrascleral growth.

In patient #3, a sentinel vessel was visualized at 11 o'clock, with a perfusion that was 181% of that in

healthy scleral vessels. Surprisingly, the abnormality of this vessel was not noticeable upon visual inspection (Fig. 3) but was evident using LSCI. Perfusion in the sentinel vessel ceased when the lateral rectus muscle was detached. Histopathological examination revealed a choroidal melanoma from 7 to 10 o' clock, without extrascleral growth.

In patient #4, a sentinel vessel was visualized at 10 o'clock, with a perfusion of 124% of that in healthy scleral vessels. Surprisingly, perfusion of the sentinel vessel only ceased after the optic nerve, with its ophthalmic artery, had been severed. Histopathological examination revealed a choroidal melanoma from 9 to 1 o'clock, without extrascleral growth.

Discussion

The present study is the first in which sentinel vessels in uveal melanomas were imaged noninvasively. There are several indications that the studied vessels are indeed sentinel vessels. The location of the sentinel vessel was correlated to the location of the intraocular tumor in all cases. The perfusion in the sentinel vessel was significantly higher than in the surrounding healthy scleral arteries in all cases. Furthermore, the appearance of the suspected sentinel vessels differed considerably from that of the surrounding vessels, primarily in terms of the width of the vessel but to some extent also in tortuosity.

The present study raises the question concerning the origin of sentinel vessels in the eye. Sentinel vessels are dilated, episcleral blood vessels, and are perceived as a valuable diagnostic clue for an underlying tumor, especially in ciliary body melanomas [14]. The episcleral arteries, in turn, are branches of the anterior ciliary arteries that run along the rectus muscles [15]. Perfusion monitoring during the successive severing of the supplying vessels, enabled determination of the origin of the sentinel vessel. In 3 of the patients, the sentinel vessel originated from the anterior ciliary arteries, as the LSCI signal ceased following detachment of a rectus muscle and its ciliary arteries. Surprisingly, in 1 patient, the perfusion in the sentinel vessel was sustained until the optic nerve and its ophthalmic artery was severed, demonstrating anatomical variation which has not been previously described.

In 1 patient, a sentinel vessel was visible with LSCI, while it was not seen on visual inspection. This suggests a clinical benefit of LSCI in diagnosing increased metabolic demand in uveal melanoma.

Conclusion

In summary, LSCI enables real-time, noninvasive imaging of sentinel vessels in uveal melanoma. The technique could possibly be used to visualize vascular anomalies undetectable upon visual inspection and slit lamp examination. LSCI may thus be a promising diagnostic tool for diseases affecting anterior segment perfusion.

Statement of Ethics

The study was approved by the Swedish Ethical Review Authority, Approval No. Dnr 2023-01067-01. Written informed consent was obtained from the participants for publication of the details of their medical case and accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Linn Engqvist: study design, data acquisition, data analysis, interpretation of data, drafted the manuscript, and modification of the manuscript with input from all authors. Ulf Dahlstrand: study design, data acquisition, interpretation of data, and revision of the manuscript. Rafi Sheikh: study design, interpretation of data, and revision of the manuscript. Malin Malmsjö: study design, interpretation of data, drafted the manuscript, revision of the manuscript, and final approval.

Data Availability Statement

The data that support the findings of this study are not publicly available as they contain information that could compromise the privacy of the research participants but are available from the corresponding author (M.M.) upon reasonable request.

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