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Full Length Article

Intraocular tumours imaging with transpalpebral near-infrared LED transillumination: Pilot study

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ABSTRACT

Purpose: To determine the possible use of near-infrared(NIR) light-emitting-diode (LED) radiation for imaging intraocular tumours by transpalpebral transillumination.
Methods: This study was a pilot, open-label, prospective and non-interventional. Thirty patients (30 eyes; age 30–72 years) with uveal melanomas located in the iris, ciliary body, or choroid were under our observation. A biomicroscopy, ophthalmoscopy, transpalpebral NIR transillumination, and ultrasound examination were performed in all cases.
Results: In all cases, NIR transillumination with transpalpebral approach enables visualization of the ciliary body and accurately estimates the projection of the pars plicata and ora serrata onto the sclera. In all patients, transpalpebral NIR transillumination made it possible to image the shadow of intraocular melanoma, estimate its dimensions and location concerning the ciliary body structures.
Conclusions: We recommend the non-invasive transpalpebral NIR transillumination technique, together with traditional ultrasound imaging, to improve the accuracy of assessing the size and location of intraocular tumours.

1. Introduction

Currently, for imaging of intraocular tumours located anteriorly to the equator of the eye transillumination technique in visible light is commonly used. Application of visible light for transillumination of the globe requires the use of an invasive transcorneal or transscleral illumination pathway.[1] It is known that ocular tissues transmit the invisible near-infrared (NIR) light better than visible light. With NIR light, the eyeball can be transilluminated not only through the cornea or the sclera but also through the eyelid structures.[2,3] Transpalpebral NIR transillumination enables noninvasive ciliary body imaging and assessing the widths of ciliary body structures.[4] The technique of transpalpebral NIR transillumination makes it possible to detect shadows of the ciliary body in patients with absolute glaucoma. This allows precise positioning of the laser probe in the projection of pars plicata while performing the procedure of transscleral laser cyclophotocoagulation.[3,5] NIR transillumination in patients with penetrating eye injury allows noninvasive imaging of intraocular foreign bodies in the projection of the ciliary body and identification of their localization.[6]

2. Materials and methods

This was a pilot, open-label, prospective and non-interventional study. Thirty patients (30 eyes; age 30–72 years) with intraocular tumours (uveal melanoma) located in the iris, ciliary body, or choroid were under our observation. They underwent biomicroscopy, ophthalmoscopy, transpalpebral NIR transillumination and ultrasound examination.

The device for transpalpebral NIR transillumination consisted of a wireless near-infrared LED light source (5.0 mm infrared LED - IR333C/H0/L10 with a dominant wavelength of 940 nm; spectral bandwidth - 45 nm; beam angle - 40°; maximal radiant intensity - 45 mW/sr; Everlight Electronics Co., Ltd.), monochrome video camera (Blackfly®, Model: BFLY-PGE-13E4M-CS; FLIR Integrated Imaging Solutions Inc., with 1/1.8″, 60 FPS at 1280 × 1024 CMOS sensor e2v EV76C560) capable of recording NIR images and lens (1/3′, 3.5–8.0 MM, F1.4; Evetar M13VM358; Xiamen Leading Optics Co., Ltd.).

Examination of the patient was performed in a dark room using a wireless LED probe for ocular transpalpebral NIR transillumination. The camera was mounted opposite the test eye (Fig. 1). The distance from the

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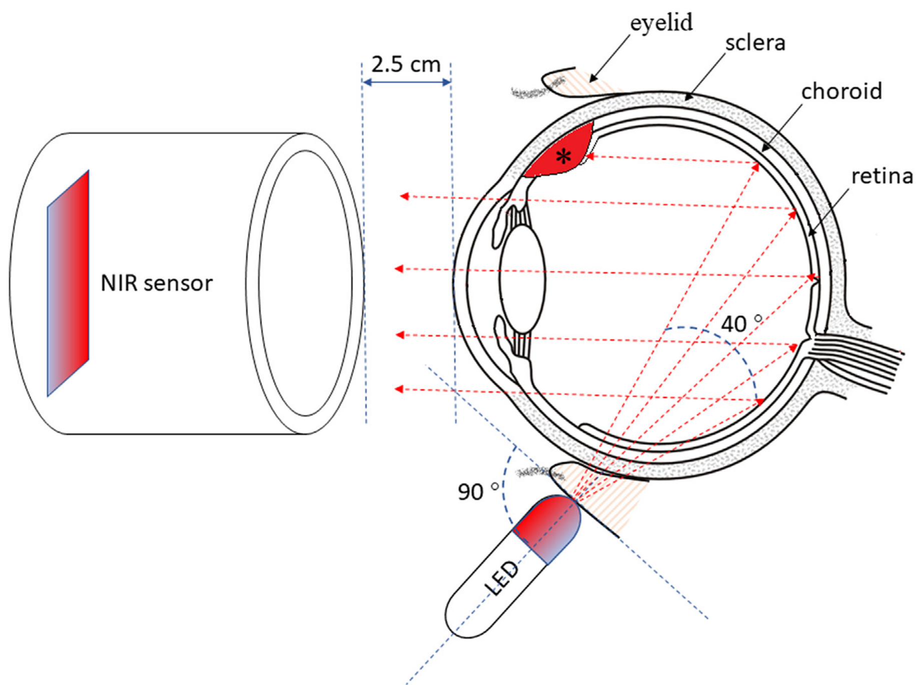

Fig. 1. Schematic representation of transpalpebral NIR transillumination of the eye. The LED contacts the skin of the eyelid without compressing the eye. A ciliary body tumour that absorbs NIR radiation is marked with a black asterisk.

lens to the surface of the eye was about 2.5 cm.

The examination was conducted without local anaesthesia. The emitting surface of the LED was in contact with the skin of the eyelid without ocular compression (Fig. 2). The eye needs to be open during the examination and to fix on the fixation mark for convenient imaging. FlyCap2 Viewer 2.13 software was used for image acquisition. Real-time images (TIF format, 1280 × 1024 pixels) or video (AVI format, 1280 × 1024 pixels, 16 bits, exposure range from 0.016 ms to 1 s) of iris and scleral shadows of the intraocular tumour, pars plicata and pars plana of ciliary body were taken and saved in the computer. The images/videos were not further processed after acquisition and were analyzed in their original format. For infrared transillumination, the characteristics of the light source and camera parameters were the same in all cases. Examination of one eye, as a rule, lasted about 30 s.

Transpalpebral NIR transillumination and ultrasound examination were used not only to visualize the intraocular tumour but also to measure its size and to estimate its location. The images were evaluated by two observers independently and in a blind fashion.

In all patients, the largest diameter of the shadow of the intraocular melanoma and the width of the shadow of pars plana and pars plicata of the ciliary body were measured by transpalpebral NIR transillumination. PhotoM 1.31 software was used for measurements of ocular structures from saved NIR images.

In all cases, the largest melanoma diameter and the tumour thickness without the sclera were measured by ultrasonography. We used the Aviso ultrasound system (Quantel Medical; Cournon d'Auvergne, France) with 10-MHz and 50-MHz linear probes for the posterior and anterior segments of the eye, respectively. The ultrasound study was performed with the patient lying on his back, and with the head of the bed raised.

The study was conducted in conformity with the principles of Good Clinical Practice, the Declaration of Helsinki, and relevant laws of Ukraine. Institutional Bioethics Committee approval was obtained before the study commencement. All participants gave written informed consent before enrolment in the study and the conduct of any study-related procedures.

The measurement results were expressed as means (M) ± standard deviations (SD). The paired Student's t-test was used to compare the size of the melanoma shadow on the NIR images with ultrasound measurements of tumour diameter. Statistical significance was set at $P < 0.05$. Statistical analysis was performed using Statistica 10.0 (StatSoft, Tulsa, OK, USA) software.

3. Results

In all cases, good quality monochrome images of the anterior segment were captured. NIR transillumination with a transpalpebral approach

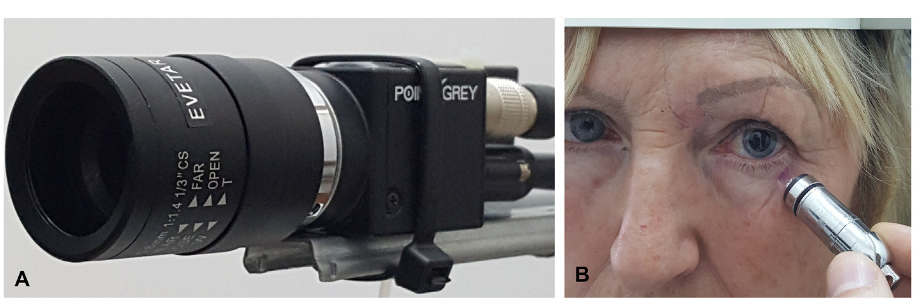

Fig. 2. A. The device for transpalpebral NIR transillumination. B. The wireless near-infrared (940 nm) LED probe position during examination with the transpalpebral approach.

made it possible to detect shadows of the ciliary body and intraocular tumour on the sclera as well as to estimate their borders.

Images of the anterior segment of the eye showed dark shadows of intraocular structures against the light background of the iris and sclera due to their NIR transmitting properties. These dark circle-shaped shadows represent the projections of intraocular structures (pupillary sphincter muscle, pars plicata of the ciliary body, ora serrata), which absorb infrared light more effectively than iris and sclera.

The shadow of pars plicata of the ciliary body was detected using the transpalpebral NIR transillumination technique in all segments of the globe in all cases. The width of the pars plicata averaged 1.7 ± 0.4 mm. The pars plana was visualized as a light wide area with radial ciliary plicae between the shadows of the pars plicata and ora serrata (Fig. 3). The width of the pars plana area averaged 4.0 ± 0.7 mm depending on the length of the eye.

In all patients, the shadow of uveal melanoma was detected and tumour location to the ciliary body structures was estimated. The ciliary body involvement was detected in all cases (Fig. 3). In some cases, the tumour shadow in relation to the scleral landmarks (conjunctival or episcleral vessels) was detected. Transpalpebral NIR transillumination allowed imaging of both pigmented and non-pigmented uveal melanomas.

In all patients, ultrasonography revealed an intraocular melanoma and made it possible to assess the location of the tumour concerning the structures of the ciliary body. The largest diameter of the shadow of the intraocular tumour averaged 7.3 ± 0.5 mm according to NIR transillumination, 6.5 ± 0.6 mm according to ultrasonography ($P = 0.02$). The melanoma thickness averaged 4.7 ± 0.5 mm according to ultrasonography examination.

4. Discussion

In 2005, Saari et al. presented a technique of digital NIR transillumination-based imaging of the iris and ciliary body. They used the incandescent lamp of the slit lamp as a source of infrared light, a filter transmitting only NIR light, optical fibre, and a retinal camera to capture the NIR images of the iris. This technique required contact of the optical fibre tip with the temporal portion of the anaesthetised sclera. Subsequently, this technique was applied in patients with iris nevus and melanoma.[7,8]

In 2013, Krohn et al. described a modified technique of NIR transillumination photography of intraocular tumours. They proposed to use a conventional digital slit lamp camera system with a replaced infrared blocking filter which transmitted the NIR light up to 1100 nm, the electronic flash unit as a source of infrared light and a flexible background illumination cable to deliver flash light to the ocular structures. A tip of the background illumination cable with a sterile transparent coating was placed directly to the anaesthetised ocular surface. This technique was used for the visualization and localization of uveal melanoma.[9]

The use of the NIR light source enables to transilluminate the eye not only through the ocular surface but even with a transpalpebral approach.[2,3,6] Our technique of transillumination photography is simple, comfortable and safe for patients. The transpalpebral approach for ocular transillumination does not require topical anaesthesia. This reduces the risk of a potential allergic reaction to the components of the eye drops. The non-contact transpalpebral transillumination excludes the risk of injury or infection to the cornea and conjunctiva. In addition, ocular transillumination with the NIR source eliminates the unwanted irritating effect of the visible bright light, which was a disadvantage of techniques mentioned above, where white light sources were used.

Using the NIR LEDs simplifies the technique of ocular transillumination and increases diagnostic safety. This diagnostic procedure does not require *optical* fibre to deliver NIR LED radiation to the eye. The LED source is a compact wireless low power device, which does not require additional infrared filters. Unlike laser sources, LEDs are not point sources of radiation and usually have widely diverging beams (in our study, the light beam angle was 40°). The absence of the blue portion of the spectrum in the NIR LED avoids photochemical injury to the retina during the examination. During NIR transillumination with a transpalpebral approach, light is transmitted through the patient's lid, sclera, and choroid. NIR images can be obtained without ocular compression by the LED probe. These factors lead to a reduction of the light intensity reaching the retina below the limits for thermal hazard.[10] To ensure better quality imaging of intraocular structures, different wavelength LEDs (810, 940 nm) can be used.

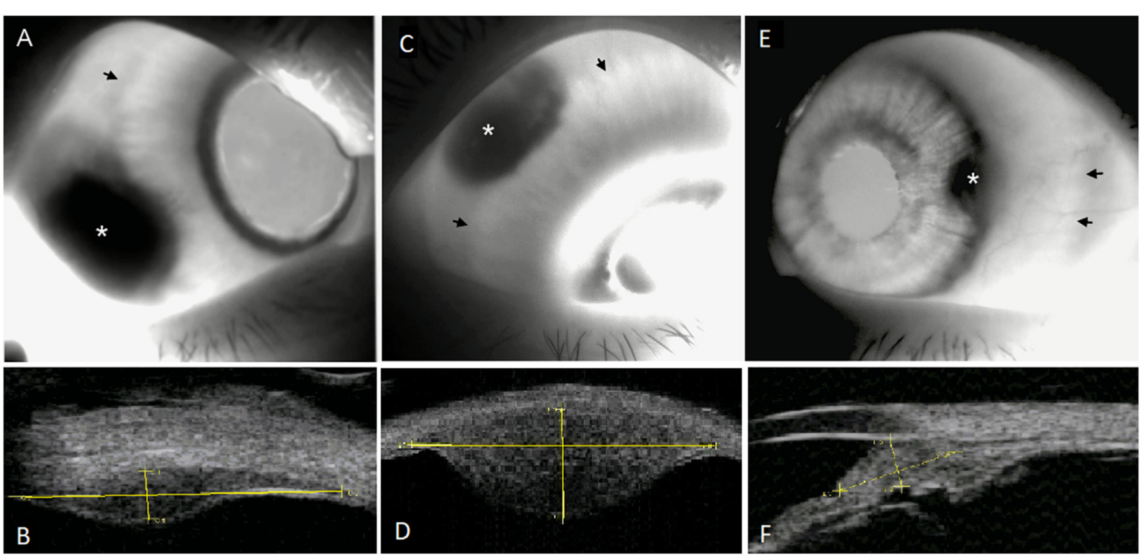

Fig. 3. A. NIR transillumination image of the uveal melanoma located in the lower temporal portion of the right eye of a 55-year-old woman. Note the irregular shadow in the projection of uveal melanoma (white asterisk) and its contact with pars plana of the ciliary body (the ora serrata is marked with a black arrow). The maximal diameter of the shadow of the tumour is 7.0 mm. B. Ultrasonographic image of the same tumour with a flat margin (the maximal diameter is 6.3 mm). C. NIR transillumination image of the uveal melanoma located in the upper temporal segment of the right eye of a 47-year-old woman. The shadow of the tumour is marked with a white asterisk and the shadow of ora serrata is marked with a black arrow. D. Ultrasonographic image of the same patient's eye. E. NIR transillumination image of the iris melanoma (with invasion to the pars plicata) located in the temporal area at the angle of the anterior chamber of the left eye of a 40-year-old woman. The shadow of the tumour is marked with a white asterisk and the shadow of ora serrata is marked with a black arrow. F. Ultrasonographic image of the same eye.

Transpalpebral NIR transillumination enables imaging of the ciliary body and accurately estimates its projection onto the sclera. In the current study, we managed to localize a melanoma shadow concerning shadows of ciliary body structures on the sclera, which allowed selecting the most appropriate treatment strategy.

In all patients, NIR transillumination, as well as ultrasound, made it possible not only to capture the image of the intraocular tumours but also to accurately estimate their dimensions. A detailed analysis in four cases (13%) revealed that the size of the melanoma shadow on NIR images exceeded the size of the tumour according to ultrasound. In these patients, ultrasonography showed an intraocular tumour of unequal thickness with a flat margin. Two of these four cases underwent enucleation followed by histopathological examination and tumour measurement. In both cases, large uveal melanoma with unequal tumour thickness and flat margins was confirmed. In these patients, the evaluation of the tumour size confirmed the higher accuracy of the measurements made by infrared transillumination. This is due to the complexity of ultrasound imaging of flat areas along the tumour margin. Thus, infrared transillumination in these patients made it possible to clarify the size of the tumour base, which is very important for the choice of treatment tactics. In the remaining 26 cases (87%), the size of the tumour according to ultrasonography (6.3 ± 0.5 mm) and infrared transillumination (6.8 ± 0.6 mm) did not differ ($P = 0.07$).

As opposed to ultrasonography, NIR transillumination enables capturing clear intraocular and scleral landmarks, which helps to perform treatment procedures precisely. For example, clear scleral landmarks made it possible to accurately position the applicator in the projection of the tumour during brachytherapy. To treat the patient with brachytherapy, we used both tumour imaging techniques.

This technique has a number of limitations in the diagnosis of non-pigmented intraocular tumours. NIR transillumination made it possible to visualize non-pigmented uveal melanomas due to the absorption of near-infrared radiation by blood components in tumour vessels.[2] In such cases, a shadow of low intensity was visualized in the projection of the tumour. However, determining the true boundaries of intraocular non-pigmented tumours seems to be a limitation of this diagnostic technique and will require further evaluation. Thus, an additional limitation of this technique is the impossibility of accurate differential diagnosis of pigmented and non-pigmented intraocular tumours.

The proposed technique of real-time transpalpebral NIR transillumination is easily repeatable and can be useful for the evaluation of dimensions and location of intraocular tumours at every follow-up visit of the patient.

5. Conclusions

We recommend the non-invasive transpalpebral NIR transillumination technique, together with traditional ultrasound imaging, to improve the accuracy of assessing the size and location of intraocular tumours.

Study Approval

The authors confirm that any aspect of the work covered in this manuscript that involved human patients or animals was conducted with the ethical approval of all relevant bodies and the study was performed in accordance with the Declaration of Helsinki , and the protocol was approved by the Ethics Committee of State Institution "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" (approval number: 6).

Author Contributions

The authors confirm contribution to the paper as follows: Conception and design of study: NP; Data collection: OZ, TK; Analysis and interpretation of results: OZ, AK; Drafting the manuscript: OZ; All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Koch FHJ, Deuchler S, Singh P, Hessling M. *Diaphanoskopie am Auge, Ophthalmologe.* 2017;114:857–864. https://doi.org/10.1007/s00347-017-0470-6.
2. Pasyechnikova N, Naumenko V, Korol A, Zadorozhnyy O. Digital imaging of the fundus with long-wave illumination. *Klin. Oczna.* 2009;111:18–20. PMID: 19517839.
3. Zadorozhnyy A, Korol A, Nevska T, Kustryn N, Pasyechnikova. Ciliary body imaging with transpalpebral near-infrared transillumination (Pilot study). *Klin. Oczna.* 2016; 118:184–186. PMID: 30088380.
4. Zadorozhnyy Y, Alibet A, Kryvoruchko G, Levytska N, Pasyechnikova. Dimensions of ciliary body structures in various axial lengths in patients with rhegmatogenous retinal detachment. *J. ophthalmol. (Ukraine)*. 2017;6:32–35. https://doi.org/10.31288/oftalmolzh201763236.
5. Zadorozhnyy O, Guzun T, Kustryn I, Nasinnyk P, Chechin A, Korol. Targeted transscleral laser photocoagulation of the ciliary body in patients with neovascular glaucoma. *J. Ophthalmol. (Ukraine)*. 2019;4:3–7. https://doi.org/10.31288/oftalmolzh2019437.
6. Kogan M, Zadorozhnyy O, Korol A, Petretskaya O, Krasnovid T, Pasyechnikova N. Visualisierung von intraokularen Fremdkörpern im Ziliarkörperbereich mittels infraroter Transillumination (Pilotstudie), Klin. Monbl. *Augenheilkd*. 2020;237: 889–893. https://doi.org/10.1055/a-1142-6502.
7. Saari JM, Nummelin K. Digital infrared transillumination imaging of iris. *J. Ophthalmic Photogr.* 2005;27:20–24.
8. Saari JM, Kivelä T, Summanen P, Nummelin K, Saari KM. Infrared transillumination imaging and fluorescein angiography of iris nevus and melanoma. *J. Ophthalmic Photogr.* 2007;29:17–20.
9. Krohn J, Ulltang E, Kjersem B. Near-infrared transillumination photography of intraocular tumours. *Br. J. Ophthalmol.* 2013;97:1244–1246. https://doi.org/10.1136/bjophthalmol-2013-303090.
10. Sieber N, Kölbl P, Lingenfelder C, Stucke-Straub K, Kupferschmid S, Hessling M. Measurement of the retinal irradiation exposure during diaphanoscopic illumination. *Curr. Dir. Biomed. Eng.* 2020;6:276–279. https://doi.org/10.1515/cdbme-2020-3070.