Comparative study of ultrasonographic and ultrawide-field fundus for measurements of the diameter of choroidal and retinal tumors

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Research Article

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Abstract

Background

Measurement of the largest basal dimension (LBD) of intraocular tumors is important as a prognostic parameter. In order to evaluate the potential value of true color wide-field fundus photography in the measurement of tumors, we compared the measurements of the LBD of choroidal and retinal tumors by color ultra-wide-field fundus camera to clinical estimation based on indirect ophthalmoscopy and standardized ophthalmic ultrasound.

Methods

The LBD of 148 choroidal and retinal tumors of 148 patients seen at the Tongren Hospital were measured by ultra-wide-field fundus photography and compared with those measured by B-scan ultrasound and clinical estimation based on indirect ophthalmoscopy.

Results

Paired t-tests reveal that measurements from wide-field fundus photographic images are not statistically different from clinical estimation and ultrasound measurements. The results also showed that, although not statistically significant, when the tumor boundary was clear, the height 3 mm or the tumor was pigmented, the measurement value of wide-field fundus photography was greater than that measured by ultrasound. However, when the vitreous opacity, subretinal fluid or retinal detachment obscures the tumor, or the tumor is too large, or the tumor is located in the peripheral retina and close to the ciliary body, it is difficult to obtain accurate measurement by wide-field fundus photography.

Conclusions

The LBD measurement by wide-field fundus photography correlated well with ultrasonography and clinical estimation and could be used as a reliable tool for LBD measurement of choroidal and retinal tumors.

Background

The largest basal dimension (LBD) plays an important role in the staging, the proper selection of treatment, and the follow-up of intraocular tumors. Methods of clinical estimation of LBD includes indirect ophthalmoscopy, B-scan ultrasonography, and fundus photography. Ophthalmic ultrasound has been used by many ocular oncologists as the main tool for measuring the size of uveal melanoma. While
the measurement of the maximal height, especially by A-scan, is accurate, it is well known that the measurement of the basal diameter by B-scan is far less accurate.\textsuperscript{3}

Recently, a new ultra-wide-field digital fundus photography, the Clarus 500 (CLARUS 500, Carl Zeiss Meditec AG, Jena, Germany), which is a UWF retinal imaging system designed to cover up to 133° of the retina in a single image-has features of partially confocal optics and true color imaging, which is not available with the Optos.\textsuperscript{4} Clarus 500 enables true-color, high-resolution, wide-field imaging of the ocular fundus with minimal distortion\textsuperscript{4} and is especially useful in documenting intraocular tumors, especially choroidal melanoma, because in most cases the entire tumor can be photographed in one image. Special software enables the user to accurately measure the tumor diameter.

The purpose of this study was to compare the measurements of the LBD of choroidal and retinal tumors by color ultra-wide-field fundus camera to clinical estimation based on indirect ophthalmoscopy and to those obtained using conventional standardized ophthalmic ultrasound, and to explore the application value of true color wide-field fundus photography in the measurement of the LBD of tumors.

**Methods**

The participants were recruited in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Medical Ethics Committee of the Beijing Tongren Hospital and written informed consent was obtained from the patients for participation in this study and to publish study finding.

Patients with choroidal or retinal tumors who underwent indirect ophthalmoscopy, ultra-wide-field fundus imaging and ophthalmic ultrasonography at the clinic of the Beijing Tongren Hospital between 2020 and 2022 were retrospectively identified. Patients who did not have all of the specified imaging modalities on the same date or who had imaging without clear visualization of all tumor borders in all imaging modalities were excluded from the study. The age, gender, diagnosis of intraocular tumor, LBD, tumor height, tumor shape, tumor color (pigmented versus amelanotic), tumor margins (well-outlined margins versus poorly outlined margins), and presence of associated subretinal fluid were recorded. For clinical estimation, dilated fundus examination was performed by one ocular oncologist (WWB) to estimate the maximal dimensions by indirect ophthalmoscopy. For ophthalmic ultrasonography, a 18 MHz B-probe (MyLab 90, Esaote, Genova, Italy) was used. Applying the Clarus fundus camera (CLARUS 500, Carl Zeiss Meditec AG, Jena, Germany), 200 ° fields montaged images of true color, red decomposition, green decomposition and blue decomposition images were obtained, and LBD were subsequently measured using the review software.

The statistical analysis was performed using a commercially available statistical software program (SPSS for Mac, version 25.0; IBM/SPSS, Chicago, Illinois, USA). Continuous variables were presented as mean ± standard deviation. Using statistical regression and paired t-test analysis, we compare the ultrasonic measurements to wide-field camera measurements and determine whether wide-field camera
measurements provided a good correlation with clinical measurements. A p-value 0.05 was considered statistically significant.

**Results**

The study primarily included 192 individuals (89 (46.4%) men) with a mean age of 44.8 ± 15.2 years (median: 45.2 years; range: 2.4-82.3 years). Because of the following reasons, wide-field fundus true color and red photography cannot clearly or completely show the tumor and the measurement of the tumor diameter was not available in 44 patients: the tumor was too big or too close to the periphery (23 (12%) patients); retinal detachment (2 (1%) patients); severe vitreous opacity (9 (4.7%) patients) and very unclear boundary (10 (5.2%) patients). In the wide-field fundus green and blue photos, in addition to the same number of photos being excluded due to the first three reason, there were another 4 and 22 photos being excluded respectively due to unrecognizable boundary. Eventually, 148 tumors in 148 eyes were included in the present study. The demographic and clinical features are presented in Table 1. The number of photos used for measurement is 148 for true-color and red photos, 144 for green photos, and 126 for blue photos.
Table 1
Participants’ demographics and tumor features

<table>
<thead>
<tr>
<th>Gender (Female/Male)</th>
<th>81/67</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (Years)</td>
<td>44.3 ± 14.8</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>97 (65.5%)</td>
</tr>
<tr>
<td>Melanocytoma</td>
<td>7 (4.7%)</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>14 (14.8%)</td>
</tr>
<tr>
<td>Osteoma</td>
<td>6 (4.1%)</td>
</tr>
<tr>
<td>Retinal Blastoma</td>
<td>3 (2.0%)</td>
</tr>
<tr>
<td>Metastasis</td>
<td>7 (4.7%)</td>
</tr>
<tr>
<td>Nevus</td>
<td>2 (1.4%)</td>
</tr>
<tr>
<td>Other occupying lesions</td>
<td>12 (8.1%)</td>
</tr>
<tr>
<td>Tumor Shape</td>
<td></td>
</tr>
<tr>
<td>Dome</td>
<td>111 (75.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>37 (25.0%)</td>
</tr>
<tr>
<td>Tumor Height</td>
<td></td>
</tr>
<tr>
<td>3mm</td>
<td>62 (41.9%)</td>
</tr>
<tr>
<td>≥ 3mm</td>
<td>86 (58.1%)</td>
</tr>
<tr>
<td>Tumor Margins</td>
<td></td>
</tr>
<tr>
<td>Well outlined</td>
<td>92 (62.2%)</td>
</tr>
<tr>
<td>Poorly outlined</td>
<td>56 (37.8%)</td>
</tr>
<tr>
<td>Tumor Color</td>
<td></td>
</tr>
<tr>
<td>Pigmented</td>
<td>102 (68.9%)</td>
</tr>
<tr>
<td>Amelanotic</td>
<td>46 (31.1%)</td>
</tr>
<tr>
<td>Subretinal Fluid</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>51 (34.5)</td>
</tr>
<tr>
<td>Absent</td>
<td>97 (65.5%)</td>
</tr>
</tbody>
</table>
The mean of the LBD was 9.89 ± 5.58 mm (median: 8.3mm; range: 1.5 mm to 27.0mm) when clinically estimated based on indirect ophthalmoscopy, 9.51 ± 3.5mm (median: 9.76 mm; range: 2.30 mm to 17.40 mm) when measured by ultrasonography, 9.63 ± 4.57mm (median: 8.71 mm; range: 1.77 mm to 21.17 mm) when assessed by wide-field fundus true color photos, 9.51 ± 4.56 mm (median: 8.54 mm; range: 1.77 mm to 21.17 mm) for wide-field fundus red photos, 9.60 ± 4.61mm (median: 8.66 mm; range: 1.77 mm to 21.17 mm) for wide-field fundus green photos and 9.39 ± 4.56 mm (median: 8.55 mm; range: 1.77 mm to 21.08 mm) for wide-field fundus blue photos.

Paired t-tests reveal that measurements from wide-field fundus photographic images are not statistically different from clinical estimation and ultrasound measurements, except for measurements with wide-field red images (P = 0.049), green images (P = 0.035), and blue images (P = 0.015) were significantly smaller than clinical estimations. Even without statistical significance, true-color wide-field photography measurements are larger than ocular ultrasonography and are closer to clinical estimations. (Table 2)

Since the boundary of the tumor, the height of the tumor and the color of the tumor have great influence on the fundus photographic measurement, we grouped them according to whether the tumor boundary is clear, whether the tumor height is greater than 3 mm or less than 3 mm, or whether the tumor is pigmented or amelanotic, and compared the difference between the wide-field fundus photographic measurements and clinical evaluations and ultrasound measurements. The results showed that, although not statistically significant, when the tumor boundary was clear, the height 3 mm or the tumor was pigmented, the measurement value of wide-field fundus photography was greater than that measured by ultrasound (Table 3).
Discussion

The LBD of intraocular tumors is a very important parameter for evaluating prognosis and accurate measurement is even more important for practical use, such as planning the size and shape of the radioactive applicator for use in brachytherapy. Ultrasonography has been and is currently the most commonly used method for the measurement of the LBD of intraocular tumors. Although A-scan is very accurate in measuring the maximal thickness of the tumor, the accuracy of measuring the LBD is quite problematic because tumors must be greater than 0.4mm in height to be identified by ultrasound. In addition, ultrasonic measurements depend on placing the cursor on the ultrasound screen in relatively low magnifications, which could also cause some inaccuracies. Ultrasonography can be unpredictable and less accurate in the follow-up because of the difficulty in repeating the same scanning location and plan. According to the Collaborative Ocular Melanoma Study (COMS), in 644 eyes, ultrasonographic and histopathologic measurements of tumor height agreed within ± 2mm in 90% of the tumors. However, the agreement of the measured LBD between the two measurement methods was poor, with only 58% of the 664 eyes measured within ± 2mm. Peyster et al. also have suggested that the echographic measurements of the LBD are unreliable, because the exact echographic planes are difficult to reproduce. Advances in resolution and stereopsis, expanded field of view, and development of analysis tools in digital fundus photographic systems have expanded the use of the instrument into new areas of research. With montaged photos, the entire extent of a tumor can be imaged, and analytical tools can directly measure the LBD. In theory, wide-field photographic images allow for more accurate measurements of tumor size. Another benefit of fundus photogrammetry is the ability to accurately measure the distance between the tumor margin and important intraocular structures such as the optic disc and macula. This measurement can more accurately predict the likelihood of radiation maculopathy or optic neuropathy. This study suggests that tumor measurements in wide-field fundus photographic true-color images correlate significantly with both clinical assessments and ultrasound measurements. Wide-field fundus photographic true-color image tumor measurements were greater than ultrasonographic measurements when tumor boundaries were well defined, tumor height 3 mm or tumors were pigmented, although not statistically significant. This is consistent with previous research results. Kim et al. compared digital fundus photography with ultrasonography in the measurement of the basal dimension from eyes with choroidal melanoma and found that the mean basal dimension by these two methods was within 1.1 mm in 52% of eyes and 2.2mm in 95% of eyes. They found that the digital photographic analysis estimated the LBD to be greater than the ultrasonographic measurements in most of the eyes. Pe'er and colleagues also reported a larger measurements with fundus photographs than ultrasound evaluations. There may be two reasons for this. First of all, since pigmentation of the tumor is easy to recognize and since elevation in ultrasound can be recognized only above a certain size, it is assumed that measurement by a wide-field fundus camera might be more accurate for measuring the LBD of tumors well outlined. Secondly, as echographic method is less reliable in areas of the lesion 1mm in height, fundus photographs reliably capture these relatively flat portions of the tumor, resulting in a larger LBD than ultrasound.
In the present study, we found that true color and red photos show tumor boundaries better than green and blue photos. We found that tumors that did not show borders in green-light and blue-light photographs were all choroidal tumors. This may be because red light has stronger penetrating power, which can better show the details of choroidal lesions and help to show choroidal lesions. The penetrating power of green light and blue light are successively reduced, which are used to display the retina and superficial retina (such as RNFLD and macular membrane), respectively.

The measurement of wide-field fundus photography also has certain limitations. When the vitreous opacity, subretinal fluid or retinal detachment obscures the tumor, or the tumor is too large, or the tumor is located in the peripheral retina and close to the ciliary body, it is difficult to obtain accurate measurement.

In conclusion, the LBD measurement by wide-field fundus photography correlated well with ultrasonography and clinical estimation. While ultrasonography provided better measurements than fundus photography in tumors with opaque media, RD, or tumors located in the peripheral retina, wide-field could be used as a reliable tool for LBD measurement of choroidal and retinal tumors.

**Abbreviations**

LBD: largest basal dimension; COMS: Collaborative Ocular Melanoma Study; RNFLD: retinal nerve fiber layer defect; RD: retinal detachment

**Declarations**

**Ethics approval and consent to participate**

This study was conducted according to the tenets of the Declaration of Helsinki. The Medical Ethics Committee of the Beijing Tongren Hospital approved the study protocol. Written informed consent was obtained from every participant after a full explanation of the nature and possible consequences of the study.

**Consent for publication**

Not applicable.

**Availability of data and material**

The datasets obtained and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing Interests**

The authors declare no competing interests.

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Authors' contributions

Qian Wang wrote the draft of manuscript. Qiong Yang collected the clinical data. All authors reviewed the manuscript.

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Not applicable.

References


Table 3
Table 3 is available in the Supplementary Files section.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- Table3.docx