Interretinal Symmetry in Color Fundus Photographs

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Abstract— **Symmetry can be defined as uniformity, equivalence or exact similarity of two parts divided along an axis. While our left and right eyes clearly have a high degree of external bilateral symmetry, it is less obvious to what degree they have internal bilateral symmetry. In this paper, we try to find approximate-bilateral symmetry in retina, one of the internal parts of our eye, which plays a vital role in our vision and also can be used as a powerful biometric. Contrary to previous works, we study interretinal symmetry from a biometric perspective. In other words, we study whether the left and right retinal symmetry is strong enough to reliably tell whether a pair of the left and right retinas belongs to a single person. For this, we focus on overall symmetry of the retinas rather than specific attributes such as length, area, thickness, or the number of blood vessels. We evaluate and analyse the performance of both human and neural network based bilateral retina verification on fundus photographs. By experimenting on a publicly available data set, we confirm interretinal symmetry.**

I. Introduction

Symmetry can be defined as *uniformity*, *equivalence* or *exact similarity* of two parts divided along an axis. Paired organs such as eyes, ears, hands, legs, etc., give an approximate-bilateral symmetrical look (i.e. almost identical left and right forms) to the exterior of our human body by dividing it into two parts through an imaginary left-right axis. Symmetrical left and right eyes not only give us a sense of beauty but also full field of vision and depth of perception. Even though we can easily see outward symmetry in our left and right eyes, seeing symmetry in the internal parts of our two eyes is not easy. In this paper, we try to find symmetry in retina, one of the internal parts of our eye, which plays a vital role in our vision and also can be used as a biometric.

The retina is a thin, semi-transparent, multi-layered, neural tissue that covers the two-thirds of the interior of our each eye. It is anatomically and physiologically considered as an extension of our brain. It is mainly responsible for converting incoming electromagnetic signals from the world outside of our eye into neural signals, and then handing the neural signals to the optic nerves. The neural signals, relaying through optic nerves, form images into the visual cortex of our brain, and therefore, we can have sense of vision [1], [2]. Any kind of disturbance in retina can have negative effect on our vision. Severe pathology in retina even can cause irreversible partial or complete vision loss.

In medical science, finding interretinal symmetry, i.e., symmetry between the retinas of the left and right eyes is an important topic. Because knowledge about interretinal symmetry can help the clinicians to detect development of pathology in the retinas. If any anatomic structure of retina has interretinal symmetry, then violation of that symmetry is a sign of development of pathology in retina. For example, asymmetry of the physiologic cups in the two eyes is a sign of early glaucoma [3]. When observing interretinal asymmetry clinicians can suggest patients for further thorough examination by expert ophthalmologists, and, therefore, pathology in retina can be detected faster. Investigation of interretinal symmetry also helps ophthalmologists to use one retina as a proxy of the other retina. When ophthalmologists do not have previous measurements or face difficulties to get measurements about any sick retina, they can use measurements of the opposite retina for the comparison purpose after doing any major surgery or using medicines to treat pathology in retina. For example, it is difficult to measure vascular density of retina suffering from epi-retinal membranes, retinal detachment. Measurements of interretinal symmetry of macular vascular density in normal subjects can be used as a reference value, whereas healthy retina of the patient as pre-operative retina and the retina received medical treatment as post-operative retina [4] to get an idea about the effect of the medical treatment.

In biometric, interretinal symmetry arises a possibility of developing side independent retina based person authentication system in which one side retina can be used to access a system developed for the opposite side retina. This will increase user flexibility especially when one side retina is affected by severe pathology. The study of interretinal symmetry also helps us understand how strong a biometric system would be if both side retina is used. If the left and right retina of a person were completely different then an authentication system using both side retina would be *two times stronger* than an authentication system using one side retina.

In medical science, interetinal symmetry was investigated mainly by using tomograms [5], [6], [7], [8], [4], [9][1]. Although these works revealed that interretinal symmetry indeed exists, it cannot be inferred from those studies how accurate a side independent retina based authentication system would be. Moreover, in a retina based authentication system we generally prefer to use fundus cameras rather than tomography cameras, since fundus cameras are cheaper and easier to use. In [10], [11] we reported that in color fundus photographs it is also possible to see interretinal symmetry and decide whether a pair of the left and right retinal images belongs to the same person or two different persons. We performed experiments with the help of human volunteers. We also used two similarity measurements, structural similarity and cosine similarity, to do the investigation process automatically. However, our previous works were based on the opinion of only four volunteers and on very small data sets. Moreover, simple similarity based measurements were highly prone to the orientation of optic disc and macula. Therefore, claiming anything firmly based on our findings was not possible for us.

This paper is an extension of our previous works. Here, we have reported results of 20 untrained and three trained volunteers. Untrained volunteers have been asked to find similarity between a pairs of retina without being instructed what to look or where to look. Trained volunteers have been properly instructed what to consider to find similarity. Instead of simple similarity measurement, we have trained a Y shaped neural network (YNN) to find interretinal symmetry.

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[1]Note that, in literature of medical science, *interretinal symmetry* was reported as *interocular symmetry*. Since *interocular* includes not only retina but also other parts of left and right eyes such as iris, lens, choroid, sclera, etc., therefore, we decide to use *interetinal symmetry* instead of *interocular symmetry* to be more specific.

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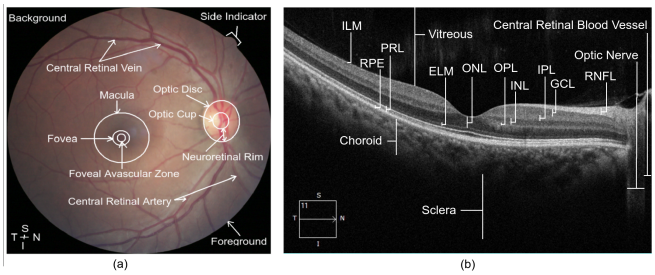

(a) (b)

Fig. 1. (a) Visibility of main anatomical structures in a color fundus photograph of a healthy right retina. Note that, the boundaries of macula, fovea, FAZ, OD, OC, NR are not accurately drawn. (b) Visibility of different layers of the retina in the left side in OCT photograph. S: Superior, I: Inferior, N: Nasal and T: Temporal.

II. Background

A. Fundus Photograph vs Tomography Photograph

As shown in Fig. 1(a), in a color fundus photograph we can see almost circular, colored foreground of a retina on dark background with its main anatomical structures such as macula, fovea, optic nerve head (ONH) or optic disc (OD), optic cup (OC), neuroretinal rim (NR), central retinal artery (CRA) and central retinal vein (CRV). CRAs and CRVs are in together known as central retinal blood vessels (CRBVs). The OD (also known as *optic nerve head* (ONH)) is the exit point of CRV and nerve fibers from the eye. The center of OD is known as OC and the area between the boundary of OD and OC is known as neuroretinal rim (NR). It is not always easy to define the boundary of OC in all fundus photographs. Macula is highly pigmented, functional center of the retina and its center is the fovea, whereas foveal avascular zone (FAZ) is the zone without CRV in the center of the fovea. Depending on the fundus camera, we may see a side indicator (i.e., triangle or oval shaped bump) always at the right side which helps us determine whether it is a left or right side retina. If OD is in the same side as the side indicator (SI) in a retinal image, then it is a right-side retinal image. If OD is in the opposite side of SI then it is a left side retinal image.

As shown in Fig. 1(b), by the optical coherence tomography (OCT), we can see that the retina is sandwiched between avascular vitreous and highly vascular choroid. Approximately 0.5 mm thick retina is composed of ten basic layers: the outer retinal pigment epithelium (RPE) layer, internal limiting membrane (INM), retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), outer limiting membrane (OLM) and photoreceptor layer (PRL). The RNFL, GCL, and IPL in together are known as ganglion cell complex (GCC) [1], [2].

B. Previous Works in Medical Science

In medical science, many studies have addressed the symmetry between the left and the right retinas (e.g., [5], [6], [7], [8], [4], [9]). Most of them consider two types of symmetry. The first is whether the right retinas from many people and left retinas from many people are *symmetric on average*, in other words, whether the left and (mirrored) right retinas follow the same probability distribution across the population. The second symmetry is the *interretinal symmetry* which means whether the right and left retinas from the same individual are correlated, i.e., whether we can expect them to be more similar than retinas from different individuals. The *average symmetry* is usually investigated by calculating the mean and standard deviation of some properties for many left and right retinas and also by checking whether the differences are statistically significant (e.g., by a *paired Student's t-test* or *Wilcoxon signed-rank test*). Interretinal symmetry has usually verified by calculating the correlation coefficient and concluding that its value is significantly larger than 0. Different kinds of tomography such as optical coherence tomography (OCT), Heidelberg retina tomography (HRT), etc., are used for different kinds of measurements. Some previous works are reported briefly in Table I where Ref: Reference, N: Number of subjects, TS: Temporal-Superior, NI: Nasal-Inferior, TI: Temporal-Inferior, ACHM: Achromatopsia, r: Pearson Correlation Coefficient and CMT: Central Macular Thickness. In all these works, no significant differences between left and right retinas were found ($p > 0.05$)[2]. And, r was significantly larger than 0 ($p < 0.001$).

TABLE I

Some previous works done by others on interretinal symmetry in medical science using tomography.

Ref. N	Parameters	Mean ± SD		p	r
		Right	Left		
[5]	Vertical OC/OD	0.31 ± 0.15	0.30 ± 0.15	0.85	-
108	Horizontal OC/OD	0.29 ± 0.14	0.29 ± 0.14	0.20	-
[6]	OD area (mm^2)	1.91 ± 0.40	1.92 ± 0.41	0.37	0.74
1276	Vertical OC/OD	0.34 ± 0.24	0.34 ± 0.24	0.39	0.66
	OC/OD	0.23 ± 0.14	0.23 ± 0.15	0.49	0.73
	NR/OD	0.77 ± 0.14	0.77 ± 0.15	0.65	0.64
	OC area (mm^2)	0.46 ± 0.33	0.47 ± 0.35	0.23	0.76
	NR area (mm^2)	1.45 ± 0.33	1.45 ± 0.33	0.92	0.64
	OC shape	-0.17 ± 0.07	-0.17 ± 0.07	0.38	0.39
[7]	RNFL thickness				
86	* TS (um)	156.6 ± 19	154.1 ± 20.5	0.13	0.71
	* NI (um)	122.9 ± 22.7	122.2 ± 23.4	0.74	0.70
	* TI (um)	160.7 ± 20.7	162.3 ± 20.7	0.28	0.82
[8]	Macual GCC				
158	thickness (um)	98.3 ± 5.5	98.1 ± 5.5	0.38	0.88
[4]	FAZ area (mm^2)	0.33 ± 0.11	0.33 ± 0.12	0.9	0.93
87	CMT (um)	241.5 ± 21.8	241.4 ± 22.0	0.68	0.93
[9]	Foveal ONL thickn.				
42	* Controls (um)	112.9 ± 15.2	112.1 ± 13.9	0.43	0.91
76	* ACHM (um)	79.7 ± 18.3	79.2 ± 18.7	0.64	0.89

III. Our Approach

None of our paired body organs have identical left and right forms. That means our human body show *approximate-bilateral* or *pseudo-bilateral* symmetry instead of *perfect-bilateral* symmetry. And this approximate-bilateral symmetry is generally less obvious inward than outward for paired organs. It is mainly true for our eyes especially when 2D fundus photographs are used for left and right retinas. The unique tree like structure of CRV spreading over the retina gives an interretinal asymmetrical look to color fundus photographs. Poor quality can increase this interetinal asymmetrical look by displaying different colors on the foreground as well as overexposing and under exposing different parts of the retina. Many factors such as experience level of the operator, operator's finger movement or shaking, different settings of fundus cameras, subject's eye movement or blinking, different amounts of light reflection by different parts of retina because of its natural curved structure, inadequate illumination, variation of pupil dilation, poor focus, and so on can result poor quality retinal images. Beside these factors, some pathology can have unilateral effect which can cause interretinal asymmetry. Therefore, in order to check interretinal symmetry using fundus photographs we do not expect to see perfect

[2]Note that, strictly speaking, this does not prove that the distribution for left and right retinas are the same.

TABLE II
DATA SETS USED IN OUR EXPERIMENTS.

Data Set	Resolution	# Pairs	Purpose
SetA	3264×4928	150	manual and automatic verification
SetB	3168×4752	7034	training volunteers and automatic verifier
SetC	3264×4928	1752	only automatic verification

mirror or reflection symmetry especially when we work on publicly available data. Instead of measuring length or area of a particular or a specific set of anatomical structures of retina as is typical in medical science we investigate if it is possible to tell whether a pair of the left and right retinas belong to a single person or to two different persons. Our assumption is that when there is substantial interretinal symmetry in such a retina pair, there is a high probability that the retinas belong to a single person. In order to support our assumption we took opinions from 23 volunteers along with one deep neural network based system.

A. Experimental Setup

We did all implementations using TensorFlow's Keras API 2.1.6-tf and Python. We used a standard PC with Intel(R) Core(TM) i9-9900K having 8 Cores and 31 GB memory, and with two NVIDIA GeForce GTX 1080 GPUs having 8 GB Memory per GPU.

We used images of Kaggle data set [12], provided by EyePACS, and publicly available via Kaggle online community of data scientists and machine learners for the competition of diabetic retinopathy detection. There are in total $42,111$ pairs of left and right retinal images (i.e., $84,222$ images). We chose 17872 images (i.e., 8936 pairs of images) with resolutions 3264×4928 and 3168×4752, because foreground of these two resolutions have complete circular shape. We prepared three sets from our chosen images for three purposes (see Table II for details).

We prepared two test sets (i.e., SetA.1 and SetA.2) using 150 pairs of SetA, and one test set using $1,752$ pairs of SetC. In SetA.1, there were only 50 positive pairs (i.e., the left and right retinal images of a pair belong to a single person) and $2,500$ negative pairs (i.e., the left and right retinal images of a pair belong to two different persons). There was no person overlap in the positive and negative pairs, as well as in the left set and right set of negative pairs. In SetA.2, there were the same positive pairs as in SetA.1 but only 50 negative pairs randomly chosen from $2,500$ negative pairs of SetA.1. Even though it was possible to make $3,067,752$ negative pairs from $1,752$ pairs of SetC, we chose $1,752$ negative pairs in order to keep a balance between the positive and negative pairs. If we used all negative pairs then we would get very low values for precision and F1 metrics.

Since background dark pixels do not provide any necessary information, therefore, at first, extra dark background was removed so that foreground could touch the boundary without loosing any important pixels of foreground. Because of different resolutions of different data sets, we re-sized all images to 256×256 by bicubic interpolation. Then we re-scaled pixel values to $[0, 1]$ for simple contrast stretching. Except that no other pre-processing was applied to any images.

B. Manual Verification

For manual verification, we considered two scenarios: (1) untrained volunteers who did not know where to look to find symmetrical properties and (2) trained volunteers who got some prior knowledge and opportunities to train themselves by seeing pairs of SetB data set. In the first case, 20 volunteers participated, whereas

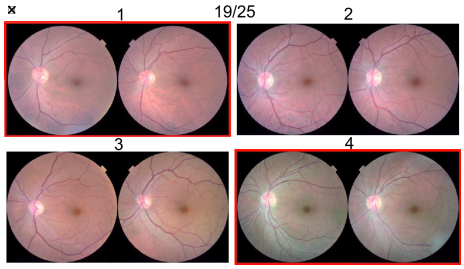

Fig. 2. An example frame for collecting volunteers' opinions. When a volunteer clicked on any pair its boundary turned into red color and it meant that the volunteer considered that pair belonging to a single person. 1, 2, 3, 4 were the pair numbers, $19/25$ was the frame number and *cross* sign was for closing the frame.

in the second case, only three volunteers. Twenty five frames were shown to each volunteer, where each frame contained four pairs of images side-by-side (as Fig. 2). Right side images were flipped to make the comparison task easier for the human volunteers. Different volunteers with ID 1-10 saw different 50 negative pairs randomly chosen from $2,500$ negative Pairs of SetA.1 so that they were not exhausted by seeing too many negative pairs.

The task of the human volunteers was to click on a pair when they thought there is high probability that pair belongs to a single person. Volunteers were allowed to select/deselect any pair as many times as they wanted and spent as much time as they wanted. But after closing any frame they were not allowed to see the previous frame any more. Twenty three volunteers participated in 23 separate sessions. None of them were aware about the true answers. All volunteers were requested not to share their assumptions with other volunteers. Trained volunteers got chance to share their assumption about any pair only when they all together tried to find similarity in a pair of retinas. As shown in Fig. 3, there were some easily recognizable positive pairs (see the 1^{st} row of Fig. 3) in SetA, which were recognized by all volunteers and some difficult pairs which made confused all most all volunteers (see the 2^{nd} and 3^{rd} row of Fig. 3).

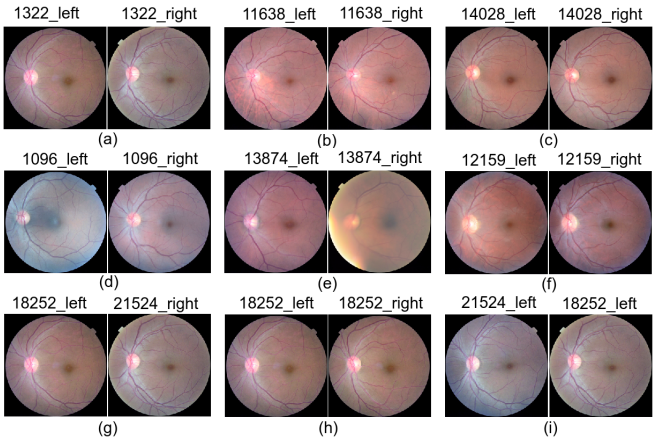

Fig. 3. 1st row: three easily recognized positive pairs [(a), (b) & (c)] recognized by all 23 volunteers. 2nd row: three difficult positive pairs. (d) a pair recognized by only 2 out of 23 volunteers, (e) a pair recognized by 3 out of 23 volunteers and (f) a pair recognized by 6 out of 23 volunteers. 3rd Row: the most difficult negative pair in SetA.2. (g) negative pair selected as positive pair by 12 out of 13 volunteers, (h) & (i) original pairs

Even though most of the untrained volunteers were not familiar with fundus photographs, they were able to see strong similarity

TABLE III

RESULTS OF MANUAL AND AUTOMATIC VERIFICATION. [AVG.: AVERAGE, TOG.: TOGETHER, U: UNTIED, T: TIED]

	SetA.1											SetA.2															SetC	
	Untrained Volunteers											Untrained Volunteers											Trained Volunteers					YNN		YNN	
Volunteer ID	1	2	3	4	5	6	7	8	9	10	Avg.	11	12	13	14	15	16	17	18	19	20	Avg.	21	22	23	Avg.	Tog.	U	T	U	T
Accuracy (%)	75	81	71	89	84	86	65	73	83	82	78.9	71	83	75	88	86	81	79	79	74	74	79.0	84	87	87	86	88	93	92	87	90
Precision (%)	72	84	96	93	85	95	61	90	100	76	85.2	84	90	74	93	91	79	91	84	80	77	84.3	87	86	89	87.3	97	88	86	80	84
Recall (%)	82	76	44	84	82	76	86	52	66	94	74.2	52	74	78	82	80	84	64	72	64	68	71.8	80	88	84	84	78	100	100	99	98
F1 Score (%)	77	80	60	88	84	84	71	66	79	84	77.3	64	81	76	87	85	82	75	77	71	72	77.0	83	87	87	85.7	87	93	93	89	91

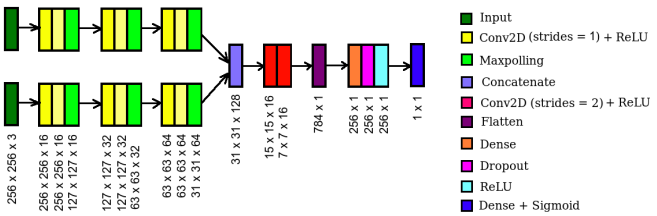

Fig. 4. Architecture of automatic verifier. Vertical text shows the output shape of the corresponding layer.

in positive pairs and strong dissimilarity in negative pairs by considering different factors some of them are color, size and shape of optic disc, how CRBVs are coming out from the optic disc, how they are spread over the retina, tortuosity of CRBVs, width of easily visible CRVs, density of CRBVs, macula, visibility of choroidal blood vessels, and so on. As shown in Table III, even the lowest performance was more than a random chance. We have noticed that the volunteers who mainly considered foreground color to find similarity had more false positives than the volunteers who mainly focused on the OD area. Foreground color of retina depends mainly on the amount of melanin in RPE layer. Different ethnic groups have different amounts of melanin, therefore, a wide color spectrum can be seen for retina. Moreover, different colored retinas for a single person is quite rare to find (actually it might happen for eyes having heterochromia iris). When retinas in a negative pair were from two different ethnic groups, volunteers were easily recognized them by color. However, negative pairs from the same ethnic was difficult to be recognized. And, confusion might occur because of different settings of cameras and image processing techniques which might make retinas from the same person having different colors.

C. Automatic Verification

We trained a deep neural network having a lying Y shaped architecture (YNN) as shown in Fig 4. During training, in each step of an epoch, one batch was prepared by taking 32 pairs from the $7,034$ positive pairs and 32 pairs from the $7,034 \times 7,033 = 49,470,122$ negative pairs. We set *mean square error* as the loss function; RMSProp with a learning rate of 0.0001 as the optimizer. For all other settings, we used the default values of TensorFlow's Keras API 2.6.1-tf. Contrary to standard verification tasks, e.g., hand written signature, face and voice, the left and right retina are, although approximately symmetric, not the same entity so it is not obvious that they should be processed in the same way. Therefore, we tried both tied and untied weights for the two legs of YNN. As shown in Table III, the tied YNN was slightly better than the untied YNN for the SetC data set.

IV. CONCLUSION

Based on our own analysis and investigation, and findings of 23 volunteers and a deep neural network, we can conclude that in good quality, high resolution color fundus photographs of left and right retina, interretinal symmetry can be seen if we focus on the color of foreground, shape and size of OD, CRBVs inside the boundary of OD and close to the OD as well as on the macula. And because of interretinal symmetry, we can say whether a pair of left and right retina belong to a single person or to two different persons. We hope, our findings would help us to develop side independent retina based biometric system in future which would give more flexibility to users specially when user's registered retina is highly affected by severe pathology.

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