2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Neonatal Fundus Image Registration and Mosaic Using Improved Speeded Up Robust Features Based on Shannon Entropy

Hongyang Jiang, Mengdi Gao, Kang Yang, Dongdong Zhang, He Ma and Wei Qian

***Abstract*— Fundus examination of the newborn is quite important, which needs to be done timely so as to avoid irreversible blindness. Ophthalmologists have to review at least five images of each eye during one examination, which is a time-consuming task. To improve the diagnosis efficiency, this paper proposed a stable and robust fundus image mosaic method based on improved Speeded Up Robust Features (SURF) with Shannon entropy and make real assessment when ophthalmologists used it clinically. Our method is characterized by avoiding the useless detection and extraction of the feature points in the non-overlapping region of the paired images during registration process. The experiments showed that the proposed method successfully registered 90.91% of 110 different field of view (FOV) image pairs from 22 eyes of 13 screening newborns and acquired 93.51% normalized correlation coefficient and 1.2557 normalized mutual information. Also, the total fusion success rate reached 86.36% and a subjective visual assessment approach was adopted to measure the fusion performance by three experts, which obtained 84.85% acceptance rate. The performance of our proposed method demonstrated its accuracy and effectiveness in the clinical application, which can help ophthalmologists a lot during their diagnosis.**

***Index Terms*—fundus examination, newborns, image mosaic, SURF, Shannon entropy.**

I. Introduction

According to the statistical analysis from Kunming City Maternal and Child Health Hospital that is one of the largest screening eye hospitals for neonates in China, 950 premature infants and 15,284 full-term infants were screened from March 2010 to February 2014. The abnormal ratio of term infants accounted to 20.75% and 18.63% of premature infants failed to pass the ophthalmology examination [1]. The prevalence rate was so appalling that more attention should be paid on neonatal fundus screening. More importantly, as the resource of neonatal ophthalmologists has always been scarce, improving the efficiency and accuracy of screening is much urgent. Image mosaic, as a clinical assisted diagnosis method, can not only improve the diagnostic speed and accuracy, but also reduce the visual fatigue of physicians.

Formally, physicians take at least five fundus images from one single eye in the clinic. However, the quality of neonatal fundus images is non-standard due to noncooperation of the newborn and the unstabel shooting skills of technicians. Therefore, these images are often low contrast, light imbalanced, obscure or noise-polluted. Through multiple communication with ophthalmologists, we realized that it was challenging for them to find some tiny crucial cue in the limited visual angle. Thus, the purpose of this work is to automatically and efficiently construct a fundus image with broader perspective based on a set of neonatal fundus images from different viewpoints.

Presently, there is not many studies about the neonatal fundus image mosaic available. Some researchers contribute to image mosaic of the newborns based on the retinopathy of prematurity (ROP) cases [2-4]. The retinal vessels of ROP sufferers are partly characteristics of vasculopathy manifested as vascular tortuosity or hyperplasia [5]. The whole vascular structure can be viewed more easily in the complete mosaic image. Enea Poletti et al. [3] put forward a matched and stitched method based on some frames of high quality from the ROP's video. The characteristic of sharpness and steadiness can filtrate several fundus images of high quality. Through the phased correlation and weighted fusion, the super-image mosaic of infant retinal fundus is completed. In the context of adult retinal fundus images, image registration is popular based on feature points matching, such as SURF [6-9] and scale-invariant feature transform (SIFT) [10-12] and so on. In addition, phase correlation is another commonly used registration method based on frequency-domain Fourier

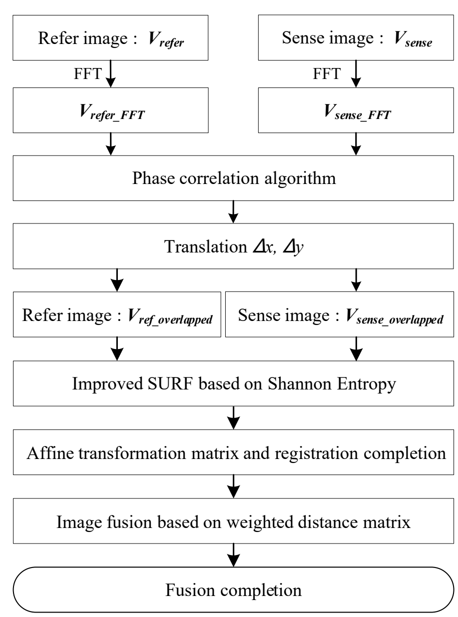

Figure. 1 An overview of proposed image registration algorithm

Hongyang Jiang, Kang Yang and Dongdong Zhang is with the Beijing Zhizhen Internet Technology Co., Ltd.

Mengdi Gao is with the Department of Biomedical Engineering, College of Engineering, Peking University, Beijing 100871, China.

He Ma is with the college of Medicine and Biological Information Engineering, Northeastern University, Shenyang 110819, China and also with the Key Laboratory of Medical Image Computing, Ministry of Education.

Wei Qian is with the College of Engineering, University of Texas at El Paso, Texas 79968, USA.

transform displacement theory [13,14]. These registration methods can be referred to in infants, but cannot be completely applicable.

In this paper, we proposed an efficient hierarchal mosaicking algorithm for neonatal fundus images with low image quality. The implementation of this method can be concluded as three steps, which can be seen in **Fig. 1**. First, we adapted the U-Net model to locate optic disc and segment retinal vessels in each image. Reference image was determined by the optic disc position. At the same time, vascular images were put forward for registration. Second, an improved SURF algorithm was applied for registration on the overlapped paired images that is located through phase correlation algorithm. Third, weighted fusion based on Euclidean distance matrix was used to complete image fusion.

II. Method

A. Preprocessing of Neonatal Fundus Images

As lack of the newborn retinal fundus images with segmentation labels, the publicly available datasets for adult were taken as the training set to train the U-Net model [15]. This study adopted DRIVE dataset [16] to develop models for optic disc and vessel segmentation. Before that, pre-treatment measures were taken for enhancing image features to perfect the segmentation performance. First, G channel of retinal fundus images was extracted and a contrast limited adaptive histogram equalization (CLAHE) method was adapted to enhance the G channel images. Second, a series of image augmentation methods were implemented to expand training set, such as rotation, crop and mirror. Patches (64 by 64) extracted from pretreated and augmented dataset were fed into the U-Net model, which further generated two segmentation maps of full vessels and optic disc simultaneously. Then, the well-trained U-Net model was migrated to segment the optic disc and retinal vessel of the newborn.

The selection of optimal reference image is an important step, which lays the foundation for image registration. According to the investigation with ophthalmologists, the image whose optic disc is closest to the center of the whole image can be taken as the optimal reference image. As the flowchart shows in **Fig. 2**, the fundus image that owns the minimum distance (***d***) as the reference image and others are sense images for registration. The effect of optic disc and vessel segmentation and the procedure of the optimal reference image selection are shown in **Fig. 3**. The top row shows five original fundus images from the same screening eye. The second line displays the segmented optic disc and vessels which is marked in red and green color respectively. For the comparatively low-quality neonatal fundus images, the deep learning-based model has stronger anti-interference ability and it is good to extract blood vessels, which contributes to optimize the performance of image registration. The third line exhibits the Euclidean distance $d_1 \sim d_5$ and d_3 is the shortest distance. Hence, the third fundus image can be considered as the optimal reference images.

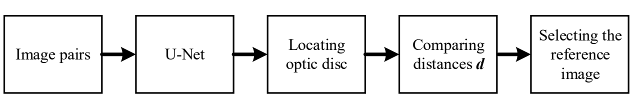

Figure. 2 A flowchart of selection of reference image.

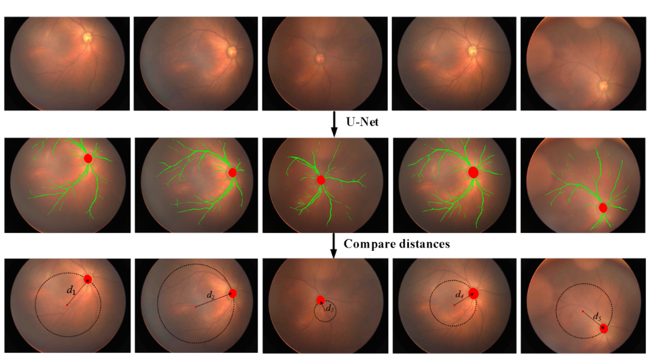

Figure. 3 The procedure of a reference image selection.

B. Pairwise Image Registration

The accurate registration was the critical factor to the image mosaic. In general, registration in newborn retinal fundus includes quite large translations and small rotations due to inevitable head tilting and ocular torsion. And scaling factor can be negligible as opposed to adult fundus acquisition [3].

Our proposed registration method can be concluded as three steps. First, the pre-processed vascular images V_{refer} and V_{sense} for the reference image I_{refer} and the sense image I_{sense} were transformed into frequency domain, V_{refer_FFT} and V_{sense_FFT}. With the phase correlation algorithm, the relative displacement Δx and Δy of I_{sense} was calculated. I_{sense} was transformed to I'_{sense} by translating $-\Delta x$ and $-\Delta y$ and the overlapped partial images between I'_{sense} and I_{refer} was obtained. Second, the fine registration with improved SURF based on Shannon Entropy was implemented on the overlapped partial images. As the feature points were searched in the local overlapped images instead of the full images, much computation time could be saved in most instances. Furthermore, two-dimensional (2D) Shannon Entropy was adopted to improve SURF, which can not only represent the aggregation characteristics but also reflect the spatial characteristics of gray distribution of an image [17]. The calculation formula is shown in equation (1), where $p_{i,j} = f(i,j)/(M * N)$. M and N represents the size of the input image, i is the gray value of the pixel and j is the mean gray value of the neighborhood. $f\ (i,\ j)$ is the frequency of the occurrence of the characteristic binary (i, j).

$$H = -\sum_i \sum_j p_{i,j} \cdot \log p_{i,j} \tag{1}$$

We calculated entropy of a square block (10 pixels width empirically) around each feature point and deleted feature points with zero entropy. It can refine the effective feature points, thus speeding up the registration time. In the end, the sense image can be transformed to a new registered image according to the affine matrix formed by the ρ, θ, $\Delta x'$ and $\Delta y'$.

C. Weighted Fusion with Distance Matrix

In this study, we introduced a weighted fusion method based on the distance matrix [3] to quickly construct a fusion image with good visual effects. The pixel (x, y) of fusion image is redefined as follows:

$$I_{merge}(x,y) = \begin{cases} I_{refer}(x,y) & \forall (x,y) \in I_{refer} \setminus I_{over} \\ I_{sense}(x,y) & \forall (x,y) \in I_{sense} \setminus I_{over} \\ f(I_{refer}, I_{sense}, x, y) & \forall (x,y) \in I_{over} = \left\{ I_{refer} \cap I_{sense} \right\} \end{cases} \tag{2}$$

where I_{merge}, I_{refer}, I_{sense}, I_{over} refers to the confusion image, reference image, sense image, overlapped region, respectively. Each pixel value in I_{over} can be determined as:

$$f(I_{refer}, I_{sense}, x, y) = \omega_{refer}(x, y) \cdot I_{refer} + \omega_{sense}(x, y) \cdot I_{sense} \quad (3)$$

where ω_{refer} and ω_{sense} are the weighted factors of reference image and sense image and sum up to const 1, which can be shown as:

$$\omega_{refer}(x, y) = \frac{d^2_{refer}(x, y)}{d^2_{refer}(x, y) + d^2_{sense}(x, y)} \quad (4)$$

$$\omega_{sense}(x, y) = \frac{d^2_{sense}(x, y)}{d^2_{refer}(x, y) + d^2_{sense}(x, y)} = 1 - \omega_{refer}(x, y) \quad (5)$$

where the distance d_{refer} and d_{sense} are the minimum Euclidean distance between the point in the overlapped region and the point in the contour of the reference and sense image.

III. EXPERIMENT AND RESULTS

A. Experiment Data

Cooperated with Kunming Maternal and Child Health Hospital, this study constructed a private experimental dataset to evaluate our proposed method. The dataset includes 20 sets of retinal fundus images from 13 screening neonates, which were taken by Retcam camera with maximum visual field 130°. Each set has at least 5 fundus images of size 1600×1200 with clear diagnosis report. The whole experimental dataset consists of a collection of 132 retinal images.

B. Performance of Pairwise Image Registration

In our experiments, the registration experimental system was configured as following: CPU Intel i7-7500U 2.7GHZ, 8G RAM, MATLAB R2017a software environment. Unlike adult retinal fundus, assessing the accuracy of the newborn retinal fundus image registration was not an easy task because of lack of ground truth. In this section, we evaluated our proposed method with both qualitative and quantitative criteria. Qualitative criterion referred to visual assessment [18, 19], which has been widely adopted to qualify the registration results. We produced chessboard images of one image pair before and after registration respectively in **Fig. 4(a)** and **4(b)**.

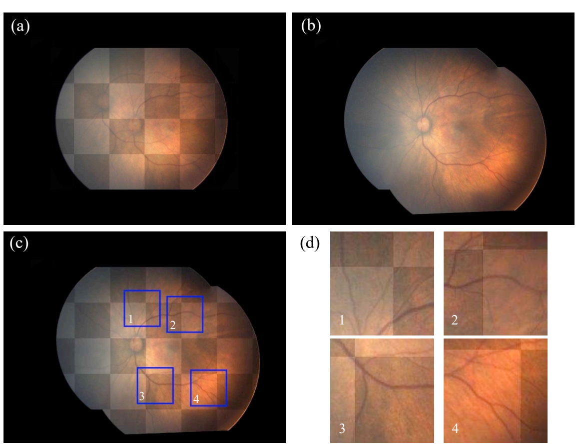

Figure 4. Average the checkerboard overlay illustration for an image pair with four zoomed areas. (a, c) The checkerboard overlay of two input images before and after registration; (b) Mosaic result; (d) zoomed-in vascular structure detail for four highlighted areas of (c).

Consequently, the blood vessel of fusion image after registration is continuous without any misplacement.

Other than direct visual assessment, quantitative criteria including normalized correlation coefficient (NCC) [20], normalized mutual information (NMI) [21], registration pairs success rate can further evaluate registration accuracy and effectiveness. NCC and NMI measured appearance difference on the overlapped partial regions between reference and registered retinal images based on intensity statistics. The success rate of registration pairs was the ratio of the number of image pairs with successful registration to the number of all image pairs [18]. Successful registration was determined with regard to the mean error value of matched points. A mean error below 5 pixels was acceptable for clinical purposes [18].

In this study, we did four groups of comparative registration experiments separately to compare performance of SURF and our proposed method, which can be illustrated in **TABLE I**. To eliminate random effects, our experiments for each group were conducted ten times, discard highest and lowest value and then found the average. The comparative results showed that the success rate of registration pairs (90.91%) based on vessel with our proposed method (Phase SURF) is optimal, especially almost twice than that based on the gray image with SURF (45.50%). The NMI and NCC of our method is 1.255 and 0.935 respectively, which are better than or just as good as others. The number of feature points pairs extracted from the vascular image is greater than that from the gray image for SURF and our method, both increasing about 4.2 times. On the other hand, the amount of feature pairs extracted from the overlapped regions are reduced 18% (registration based on gray image) and 19% (registration based on vascular image) compared with the full image. Meanwhile, the registration success rate of our method increases from 45.50% to 77.88% (registration based on gray image) and from 87.30% to 90.91% (registration based on vascular image) compared with SURF.

C. Performance of Image Fusion

To construct a well perceived wider neonatal fundus FOV, this study merged images from each eye using a novel weighted fusion method. The comparison results of neonatal fundus image mosaic can be shown in **Fig. 5**. The performance of weighted fusion based on distance matrix was apparently superior to that of weighted average fusion visually.

This study also assessed the effects of integrated neonatal fundus image mosaic method from both fusion success rate (FSR) and fusion acceptance rate (FAR). FSR refers to the ratio of the number of successful fusion eye to the number of all experimental eyes, which is largely depend on the performance of registration. FAR means the ratio of the average amount of accepted fusion eyes by three experienced

TABLE I. THE COMPARATIVE REGISTRATION RESULTS OF FOUR GROUPS. (RM=REGISTRATION MEASUREMENT GI=GRAY IMAGE, V=VESSEL, PSURF=PHASE SURF, FP=FEATURE POINTS, PSR=PAIR SUCCESS RATE)

RM	GI-SURF	GI-PSURF	V-SURF	V-PSURF
NMI	1.238±0.019	1.251±0.021	1.254±0.031	**1.255**±0.037
NCC	0.930±0.027	0.935±0.038	0.934±0.040	**0.935**±0.039
FP(pairs)	22	18	115	93
PSR	45.50%	77.88%	87.30%	**90.91%**

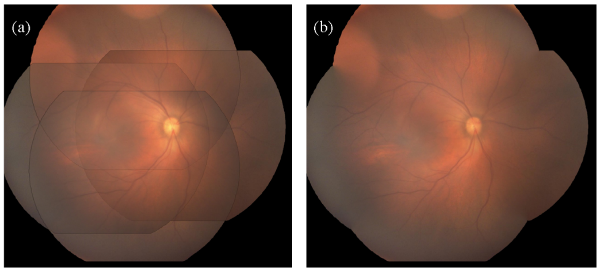

Figure 5. A mosaic image formed with 5 fundus images of the first row in Fig. 3. (a) With weighted average fusion. (b) With weighted fusion based on the distance matrix.

TABLE II. THE COMPARATIVE FUSION EXPERIMENT RESULTS OF FOUR GROUPS. (FM=FUSION MEASUREMENT, FSR=FUSION SUCCESS RATE, FAR=FUSION ACCEPTANCE RATE)

FM	GI-SURF	GI-PSURF	V-SURF	V-PSURF
FSR	0	31.82%	59.09%	**86.36%**
FAR	--	--	45.45%	**84.85%**

neonatal ophthalmologists to all the experimental eyes. The comparative fusion results of four groups are shown in **TABLE II**. Both the FSR and FAR based on vascular image with our method reached above 84%, significantly better than that of others.

Compared with adult retinal fundus images, the neonatal retinal fundus images were mostly of poor spatial resolution, low contrast and inferior quality. Hence, not too many valuable features can be extracted based on SURF, which increased the difficulties of registration. In our study, as the features of retinal vessels were obvious and stable, we utilized the famous U-Net model to segment vascular imaging for registration. Besides, the extracted feature points of the vascular imaging were merely from the overlapped region of image pairs and the feature points with zero entropy would be removed. Consequently, our method can not only decrease the number of ineffective feature points, but also improve the accuracy of matched pairs. Both FSR and FAR demonstrated the superiority of our method.

IV. CONCLUSION

In this paper, we proposed a novel and systematical method of automatically selecting the reference image, registering and fusing multiple neonatal fundus images. The comparison results of fusion acceptance rate proved the validity of our method. However, although an ultra-widefield digital pediatric retinal imaging system can acquire wider FOV of the neonatal fundus, it is rather expensive for large amounts of hospitals. Our research findings might contribute to acquire an ultra-widefield neonatal fundus image of better quality. In future, we will consider the adverse influence brought by those unqualified sense images that have serious quality problems through one kind of image screening method. Moreover, the definition of unqualified images needs to be refined with neonatal ophthalmologists in depth.

ACKNOWLEDGMENT

This study was supported by the Beijing ZhiZhen Internet Technology Co., Ltd. and it is very grateful for the Peking University to provide professional guidance on theory and experiment.

REFERENCES

[1] Li, L., Li, N., et al., "A 4-year review of neonatal ophthalmologic screening in Kunming Maternal and Child Health Hospital," *Chin Matern Child Health Care* 30(18), 2986-2990 (2015).
[2] Bontala, A., Sivaswamy, J. & Pappuru, R. R., "Image mosaicking of low quality neonatal retinal images," in *2012 9th IEEE International Symposium on Biomedical Imaging (ISBI)*, pp. 720-723, IEEE (2012).
[3] Poletti, E., Benedetti, G. & Ruggeri, A., "Super-image mosaic of infant retinal fundus: selection and registration of the best-quality frames from videos," in *2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pp. 5883-5886, IEEE (2013).
[4] Quinn G E, Vinekar A., "The role of retinal photography and telemedicine in ROP screening," *Seminars in Perinatology* WB Saunders, 43(6), 367-374 (2019).
[5] Piermarocchi S, Bini S, Martini F, et al., "Predictive algorithms for early detection of retinopathy of prematurity," *Acta ophthalmologica*; 95(2), 158-164 (2017).
[6] Bay, H., Tuytelaars, T. & Van Gool, L., "Surf: Speeded up robust features," in *European conference on computer vision*, pp. 404-417). Springer, Berlin (2006).
[7] Lukashevich, P., Zalesky, B. & Ablameyko, S., "Medical image registration based on SURF detector," *Pattern Recognition and Image Analysis* 21(3), 519 (2001).
[8] WEI L, LIN J., "Improved Fundus Image Registration Method Based on Speeded-up Robust Feature," *Computer Engineering* 12, 51 (2013).
[9] Xia H, Chen D., "Retinal Image Registration Based on Bifurcation Point and SURF," *International Conference on Service-Oriented Computing*, pp. 136-146, Springer, Cham, (2018).
[10] Guo, F., Zhao, X., Zou, B. & Liang, Y., "Automatic retinal image registration using blood vessel segmentation and SIFT feature," *International Journal of Pattern Recognition and Artificial Intelligence* 31(11), 1757006 (2017).
[11] Ghassabi, Z., Shanbehzadeh, J., Mohammadzadeh, A. & Ostadzadeh, S. S., "Colour retinal fundus image registration by selecting stable extremum points in the scale-invariant feature transform detector," *IET image processing* 9(10), 889-900 (2015).
[12] Tao Z J, Huang H., "Fundus images mosaic based on improved harris and SIFT algorithm," *Computer Engineering and Design* 33(9), 3507-3511 (2012).
[13] Foroosh, H., Zerubia, J. B. & Berthod, M., "Extension of phase correlation to subpixel registration," *IEEE transactions on image processing* 11(3), 188-200 (2002).
[14] Wang, W., Chen, H., Li, J. & Yu, J., "A registration method of fundus images based on edge detection and phase-correlation," in *First International Conference on Innovative Computing, Information and Control-Volume I (ICICIC'06)*, pp. 572-576, IEEE (2006).
[15] Ronneberger, O., Fischer, P. & Brox, T., "U-net: Convolutional networks for biomedical image segmentation," in *International Conference on Medical image computing and computer-assisted intervention*, pp. 234-241, Springer, Cham (2015).
[16] Niemeijer, M., et al., "DRIVE: digital retinal images for vessel extraction," *Methods for Evaluating Segmentation and Indexing Techniques Dedicated to Retinal Ophthalmology* (2004).
[17] Lin, J., "Divergence measures based on the Shannon entropy," *IEEE Transactions on Information theory* 37(1), 145-151 (1991).
[18] Ghassabi, Z., Shanbehzadeh, J. & Mohammadzadeh, A., "A structure-based region detector for high-resolution retinal fundus image registration," *Biomedical signal processing and control* 23, 52-61 (2016).
[19] Ritter, N., Owens, R., Cooper, J., Eikelboom, R. H. & Van Saarloos, P. P., "Registration of stereo and temporal images of the retina," *IEEE Transactions on medical imaging* 18(5), 404-418 (1999).
[20] Deng, K., et al., "Retinal fundus image registration via vascular structure graph matching," *International Journal of Biomedical Imaging* (2010).
[21] Kolar, R., Harabis, V. & Odstrcilik, J., "Hybrid retinal image registration using phase correlation," *The Imaging Science Journal* 61(4), 369-384 (2013).