

## **Automated sub-retinal fluid detection comprising RPE-region using neighbouring pixel connectivity paradigm.**

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### **Abstract**

**Sub-Retinal Fluid (SRF), a categorized retinal fluid accumulation just above the Inner Hyper-Reflective Layer (HRL) of the RPE-Region has a significant correlation with visual acuity. Sub-Retinal Fluid are the indicators of Macular Hole (MH) formations. Early information regarding SRF may help in tackling the chronic cases, as surgery is the only option for treating MH. Proposed is a method to identify Retinal Pigment Epithelium (RPE) region in Optical Coherence Tomography (OCT) visualization of the retina, further based on it the retinal pathology called as Sub-Retinal Fluid is detected. This paper discusses the newly proposed method for the detection of RPE region, the non-separated region between the inner and outer Hyper-Reflective Layer (HRL). To the best of our knowledge, identification of Sub-Retinal fluid, has never been automated. The work validation is done with the ground truths (manually delineated by an expert panel). Evaluation of the system (RPE-Region detection and SRF Detection) is done independently for both the proposed methods. RPE-region detection was done on 220 images from 23 patients at different orientation styles with 90.45% correct detections whereas the sensitivity and the specificity for the SRF detection is found to be 89.74% and 89.36% respectively over 164 images from 30 patients.**

**Keywords:** Biomedical imaging, Computer aided diagnosis, Optical coherence tomography, Sub-retinal fluid, Retinal pigment epithelium.

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### **Introduction**

Retina is the light sensitive, innermost layer of the eye. The eye focuses the image of the world on the retina, starting a series of chemical and electrical events within the retina. Retina then sends the electrical signals to the brain using the nerve fibers present in it. The brain interprets these signals as visual images [1,2]. The human retina has ten distinct layers. Over the years, retinal research has greatly benefited from advances in optical imaging techniques. Fundus imaging is a 2D imaging technique. The image captured by the fundus camera, used to visualize central and peripheral retina, optic disc and macula. Retinal Optical Coherence Tomography (OCT) is a 3D imaging technique. It is a low coherence interferometry to generate cross-sectional imagery of ocular tissues.

Cross-sectional visualization obtained by retinal OCT images are very useful for identification of abnormalities in the retinal layers and in the assessment of their severity. Retinal OCT imaging comprising, Optical Coherence Tomography, images the biological structures based on the light being reflected by the tissues without disturbing their histology and spatial positions. Reflected beam of light from tissues are collected and the delay in time of flight is calculated. This delay information helps to deduce the reflection surface's

longitudinal location, the longitudinal scans known as A-scans. Number of A-scans are performed by the OCT scanner at different lateral positions to get the 2-D map of reflection, known as B-scan [3-13]. More the number of A-scans in a B-scan image, higher will be the image resolution.

### **Proposed Work**

Accurate delineation of retinal layers in the OCT scans is an important step to identify the pathologies inflicting the retina. Delineation of inner Hyper-Reflective Layer (inner HRL) from RPE is difficult because backscattering signals are high in both these layers. Inner HRL is the junction between inner and outer photoreceptor segments while outer HRL is actually the retinal pigment epithelium (RPE) (probably with choriocapillaris). The first part of the work involves accurately identifying these two layers. Under normal conditions, water flows from the vitreous cavity to the choroid. If there is a decrease in the outflow or increase in the inflow of fluid that disturbs the normal compensatory mechanism, fluid starts accumulating between the retinal pigment epithelium and the choroid, known as Sub-Retinal Fluid (SRF). SRF can lead to a sight-threatening disease known as Retinal Detachment. Early detection can save the patient from many complications. The second part of this work involves automatic detection and

delineation of SRF. The proposed work uses pixel intensity thresholding and pixel count for the same.

### RPE-region detection

**Pre-processing:** To reduce the noise, the captured scan, first smoothed with non-linear, edge-preserving bilateral filter [14,15]. The weights of the Bilateral Filter depend not only on the Euclidean distance of pixels but also on the pixel color.

$$BF[I]p = \frac{1}{W_p} \sum_{q \in S} G_{\sigma_s}(\|p - q\|) G_{\sigma_r}(\|I_p - I_q\|) I_q \rightarrow (1)$$

Where  $W_p$  is normalization factor ensuring pixel weights sum to 1.0.

$$W_p = \sum_{q \in S} G_{\sigma_s}(\|p - q\|) G_{\sigma_r}(\|I_p - I_q\|) \rightarrow (2)$$

$\sigma_s$  and  $\sigma_r$  provides filtering parameters for the image  $I$ .  $G_{\sigma_s}$  is spatial Gaussian weight controlling distant pixels,  $G_{\sigma_r}$  is Gaussian range for pixel intensity differences. The smoothed OCT scan, then converted into grey scale (say  $I_{grey}$ ). For delineating the RPE interface (RPE Layer and Choroid) in the OCT scanned B-mode images a well-established online freely available software named OCTSEG [16,17] is used. (<https://www5.cs.fau.de/our-team/mayer-markus/automated-retinal-layer-segmentation/>)

RPE Region Detection: OCTSEG delineates the RPE interface by a blue line. The blue plane of this image is subtracted from the grey scale filtered image ( $I_{grey}$ ) resulting in an image where the pixels belonging to the RPE layer have higher intensity compared to other pixels. Thresholding applied to get the RPE layer pixels. Empirically, a threshold of 35 separates the RPE layer pixels from other pixels very well. Say this image is  $I_{Thresh}$ . Applying of equation (3) results in  $I_r$ .

$$I_r(i, j) =$$

$$\begin{cases} I_{grey}(i, j) * I_{Thresh}(i, j) \quad \forall_n \text{ if } I_{Thresh}(i, j) = 0 \\ \exists_m \text{ if } I_{Thresh}(i, j) = 255 \\ I_{Thresh}(i, j) \text{ then } j = n - 1 \text{ and } i = m \end{cases} \rightarrow (3)$$

Initial values of  $i$  and  $j$  are  $m$  (number of rows) and  $n$  (number of columns) respectively, where  $m \geq i \geq 1$  and  $n \geq j \geq 1$ .

To identify the RPE region, applied thresholding to the resulting image. Empirically, a threshold of 31 segments the retinal area containing the RPE region. Connected components are then extracted from this image. For each component, it's Area, Centroid, and Perimeter is calculated. Consider the largest connected component. This removes small-scattered spots. The image so obtained ( $I_{cc}$ ) is then used as a mask to get the actual retinal tissues forming the largest connected component.  $I_{cc}$  multiplied with  $I_{grey}$ , resulting  $I_{I_{cc}}$ . To obtain the RPE region, double thresholding is used (Equation 4). This

gives most contending pixels for the RPE-Region. To extract RPE-Region completely and separate the other additional pixels, unwanted pixels removed by taking the single largest component [18-20]. Hole filling is applied to get the complete RPE region with no breakages. Consider the image as  $I_R$ .

$$I(i, j) = \begin{cases} I(i, j) = 255 & \text{if } I(i, j) > 155 \ \&\& \ I(i, j) \leq 255 \\ I(i, j) = 0 & \text{Otherwise} \end{cases} \rightarrow (4)$$

Initial values of  $i$  and  $j$  are  $m$  (number of rows) and  $n$  (number of columns) respectively, where, also it is repeated for every 'i'.

To visualize the RPE region in the original image, superimpose the extracted RPE region on the original filtered RGB image. Below shown are some example images demonstrating the performance of the system in detecting the RPE-Region.

### Sub-retinal fluid (SRF) detection

To detect the SRF region, start with the binary image  $I_{cc}$  obtained while detecting the RPE region. Then apply inverse transformation to the image. Now refer Algorithm-1.

#### Algorithm-1:

1.  $r$ =count row ( $I_{cc}$ ).
2.  $c$ =count column ( $I_{cc}$ ).
3. for  $i=1$  to  $i \leq c$
4. for  $j=1$  to  $i \leq r$
5. if  $I_{cc}(i, j) == 0$
6.  $I_{cc}(i, j) = 255$
7. break
8. else
9.  $I_{cc}(i, j) = 0$
10. end if
11. end for  $j$
12. end for  $i$
13. for  $i=1$  to  $i \leq c$
14. for  $j=r$  to  $i \geq 1$
15. if  $I_{cc}(i, j) == 0$
16.  $I_{cc}(i, j) = 255$
17. break
18. else
19.  $I_{cc}(i, j) = 0$
20. end if
21. end for  $j$
22. end for  $i$

After this further proceed as Algorithm-2.

#### Algorithm-2 (Input image I):

1.  $I_H = I_R + I_{cc}$
2. Perform hole filling operation on  $I_H$ .
3.  $I_R = I_R$ .

4. For each pixel of  $I_R$ , starting column-wise from Top Left of the image, repeat step 5.
5. If  $I_R(i,j)=255$  then, go to step 6, else move to next column
6. For  $I_H(i,j)$  to  $I_H(i-7,j)$ , if  $I_H(i,j)=255$ , then  $I_R(i,j)=255$ . Set this as  $I_T$ .
7. Now,  $I_F=I_T-I_R$ .
8.  $I_{Fi}$  =Algorithm 3 ( $I_F$ ).
9. Display connected component of  $I_H$  at location  $I_{Fi}(i,j)$ .

All the image nomenclatures in the SRF-detection Algorithm are similar to that of in the RPE-Region detection.

**Algorithm-3 (Input image I):**

Step 1 Find connected components of the image I on the basis of “8” connected neighboring pixels.

Step 2 Find the connected component having a maximum area in the image. Let this image be J.

Step 3 Return image J.

**Results**

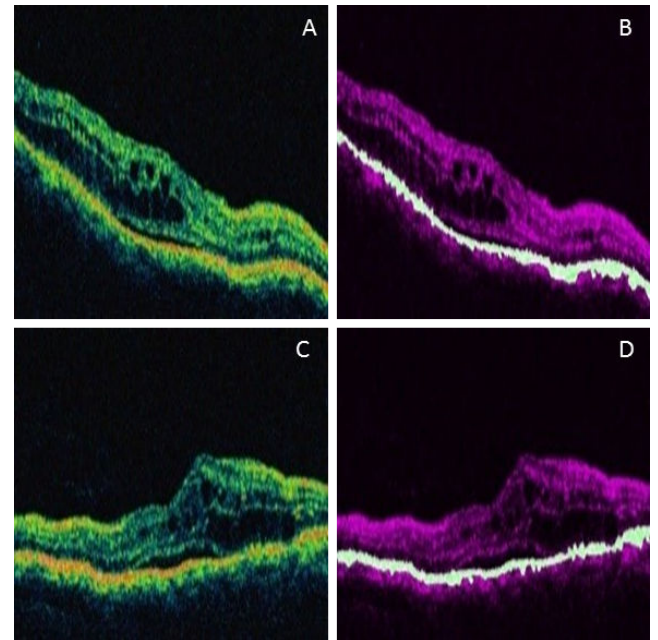
**SRF detection**

The Results are as shown in Table 1.

**Table 1.** Individual results for each patient.

Patient (P) No.	Correct Detections	Wrong Detections	Total Detections	Accuracy
01	11	Nil	11	100.00
02	4	Nil	4	100.00
03	3	Nil	3	100.00
04	8	1	9	88.89
05	2	1	3	66.67
06	4	Nil	4	100.00
07	4	Nil	4	100.00
08	8	1	9	88.89
09	1	Nil	1	100.00
10	6	Nil	6	100.00
11	9	2	11	81.82
12	3	1	4	75.00
13	3	Nil	3	100.00
14	7	Nil	7	100.00
15	3	Nil	3	100.00
16	2	1	3	66.67
17	2	1	3	66.67
18	5	2	7	100.00
19	4	1	5	71.43

20	2	Nil	2	100.00
21	9	2	11	81.82
22	9	2	11	81.82
23	24	1	25	96.00
24	1	Nil	1	100.00
25	2	Nil	2	100.00
26	1	Nil	1	100.00
27	2	Nil	2	100.00
28	2	Nil	2	100.00
29	4	Nil	4	100.00
30	2	1	2	66.67
Total	147	17	164	89.63



**Figure 1.** A&C) Bilaterally filtered images given as input to the system for RPE-region detection; B&D) RPE region detected by the system being superimposed with original bilaterally filtered RGB OCT image.

**Discussion**

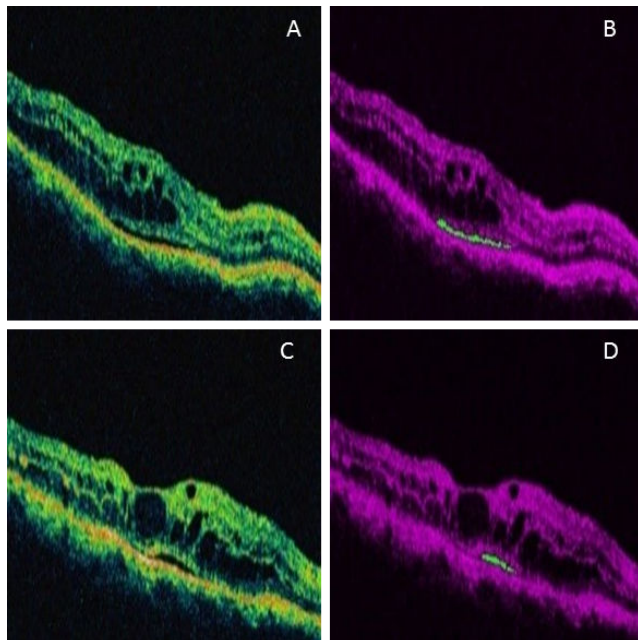
$$\begin{aligned}
 \text{Sensitivity} &= TP / (TP + FN) \\
 &= 105 / (105 + 12) \\
 &= 105 / 117 \\
 &= 89.74 \% \\
 \text{Specificity} &= TN / (TN + FP) \\
 &= 42 / (42 + 5) \\
 &= 42 / 47 \\
 &= 89.36 \%
 \end{aligned}$$

Total number of Patients=27

True Positive (TP)=105, True Negative (TN)=42

False Positive (FP)=5, False Negative (FN)=12

Figures 1 and 2 are example images demonstrating the performance of the system in detecting the RPE-Region and the SRF.



**Figure 2.** A&C) Bilaterally Filtered images given as input to the system for SRF Detection; B&D) Sub-Retinal Fluid detected by the system being superimposed with original Bilaterally Filtered RGB OCT image.

## Conclusion

As mentioned in the previous section (Results) demonstrating *via* images, the original input images to the system, ground truth images delineated manually by the expert Ophthalmologists, results from proposed method as well as the resultant images from established layer detection software (OCTSEG). In result analysis stage, software (OCTSEG), represented with its overall performance by showing the detection of all the retinal layers done by the software.

The RPE region detected by proposed method is the region in between the non-separated inner and outer HRL, which can be justified to the OCTSEG software detection such that the in-between region of the two layers i.e. the RPE (in Blue line) and the Outer Nuclear Layer (ONL). The proposed method is novel by detecting the inner HRL of RPE-region (just below the ONL of OCTSEG). It is clear from results that the proposed method is capable of detecting the RPE-region with substantially encouraging results with precise detection of non-separated inner and outer HRL.

Similarly, for the validation of results in the SRF Detection, medical panel comprising two expert Ophthalmologists, were asked to manually delineate the SRF in the images. Sensitivity

and Specificity for the SRF detection are discussed below respectively.

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