EARMARKING RETINAL CHANGES IN A SEQUENCE OF DIGITAL COLOR FUNDUS PHOTOGRAPHS

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Abstract: This paper presents a novel approach for earmarking retinal changes in a sequence of digital color fundus photographs, using Principal Component Analysis (PCA) and a temporal color-coded scheme so as to improve the representation of the global effect of these changes — its aim is to assist graders in detecting alterations on digital color photographic follow-up time-sequences of the human retina. The color-coded scheme was developed so that: the earliest earmarking color of areas which have been detected in multiple instances in the follow-up timeline is kept; areas which have suffered changes but have returned to their original appearance are earmarked with a specific color-code. The composite image formed by the projection of the color-code image onto the baseline image used as reference then guides the grader's attention to changes detected on the fundus photographs.

Introduction

The evaluation of sequential temporal series of retinal images of the same eye is a widely used diagnostic tool for the study of signs of visible retinal changes. In fact, retinal lesions, such as haemorrhages, exudates and others, and their progression through time are important indicators of serious systemic diseases, such as diabetes or hypertension/sclerosis [1].

The aim of the present work is to assist graders engaged in the evaluation of these temporal series in detecting changes on digital color photographic follow-up time-sequences. A novel approach for automatically earmarking retinal changes in a sequence of digital color fundus photographs has been developed using Principal Component Analysis (PCA) and a temporal color-coded scheme so as to improve the representation of the global effect of these changes.

Materials and Methods

Sequences of $N = 5$ digital color fundus photographs taken every six months during a two-year follow-up period were collected using a Zeiss FF450 fundus camera, equipped with a 3CCD detector to produce 50^{o} field-of-view, 768×576 pixels RGB color images centered on the macula. All images were preprocessed so as to correct for poor illumination conditions (figure 1) in the following manner:

(1) a PCA of the original image was carried out using the method described in [2], which considers each RGB component as an independent variable, and its first principal component scaled and transformed so as to reduce the image-space data to a gray-scale image;
(2) this gray-scale image was processed using the method proposed by Foracchia *et al.* in [1], thus improving contrast and brightness conditions;
(3) the Value component of the Hue-Saturation-Value (HSV) representation of the original image was replaced by the result of the previous step;
(4) the HSV output resulting from the previous step was transformed back into RGB space, resulting in an enhanced retinal image.

Each of the enhanced retinal images obtained by this procedure were subsequently processed even further so as to obtain the following data (besides their RGB representations):

- an intensity image taken from the Value component of the HSV representation space of the enhanced image (corresponding in practice to the result of step 2 on the procedure described earlier on), which is used for difference-image computations;
- a gray-scale image resulting from a reduction of the enhanced image's RGB space using the PCA method presented in [2] as described above, which is used for feature detection purposes (e.g., vessel segmentation, optic disc and fovea detection, etc.).

To simplify the following description, these data and the original RGB representations will be referred to indiscriminately as "the image"; each one can be differentiated from all others easily by context.

Following the preprocessing stages, the retinal vascular tree was segmented by means of differential geometry [3]. Vessel bifurcations, intersections and cross-overs

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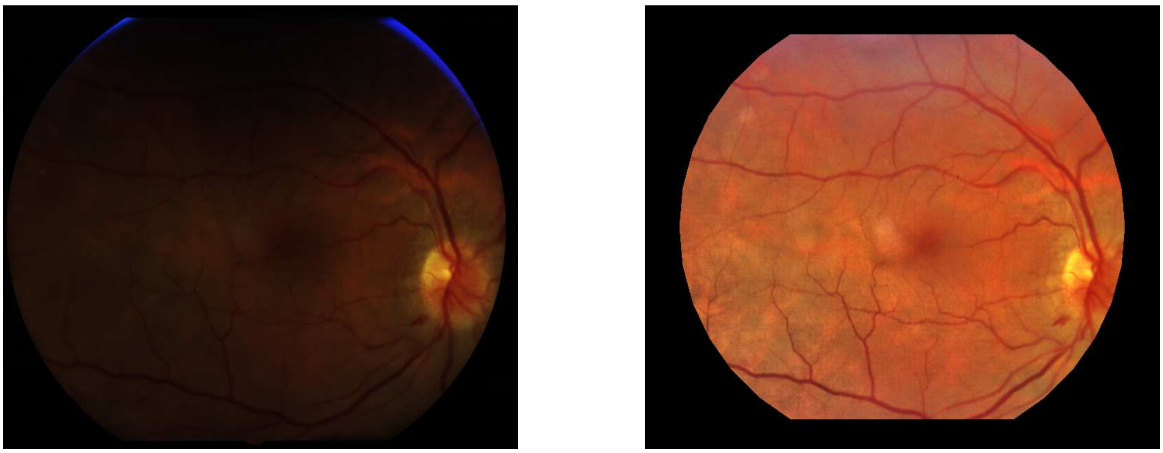

Figure 1: Example of results of the enhancement of an image suffering from extremely poor illumination conditions — a small portion of the retinal margin is cropped to avoid borderline effects. On the left: original image; on the right: after enhancement.

were then used as landmarks for a two-step image registration process consisting of a rough first approximation using a rigid transformation followed by a refinement using a perspective transformation. A summarized description of this process is given in the following lines; for more details on the subject, please refer to [4].

Rigid registration is accomplished by first estimating translation, followed by rotation. More specifically, while the translational part of the rigid registration is given by the position displacement of the fovea between both images, the rotation is determined by computing the translation on the polar representation of the vascular tree, using a robust phase-correlation approach [5].

As a prelude to the final registration step, the results of rigid registration can be used by a modified version of the procedure established in [6] to obtain initial pairings of landmarks and to remove vessel bifurcation and intersection segmentation outliers by eliminating hypothetic locations from one image without counterparts on the other. After this is done, the Moore-Penrose pseudo-inverse matrix is used to compute the perspective transformation given by

$$\mathbf{P} = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & 1 \end{bmatrix} \quad (1)$$

After all images were registered using the baseline image (1st image) as reference, a tunable blurring low-pass filter was used to avoid the effects of focusing and registration errors (typically of pixel accuracy), and the differences between each of the former and the latter were computed inside their overlapping region, thus providing a means of detecting changes for a particular instant in time during the follow-up (figure 2). These were thresholded so that only significant alterations were taken into account, and are referred to as *difference-images*. The threshold value is also user-tunable. Finally, each of the $N-1$ difference-images ($I^i_{difflinear}$) were non-linearly scaled through $I^i_{diff} = \log(I^i_{difflinear})$ so as to amplify the effect of smaller retinal changes.

To achieve a better representation of the global effect of changes in the retina, it is possible to consider each difference-image (I^i_{diff}) as a band of a hyperspectral image. Thus, extending the PCA method described before to encompass $N-1$ dimensions, the most significant principal components were then combined, scaled and transformed into gray-scale images for each instant in time (after the 2nd visit), which were in turn processed so that the contribution of each spectral component (i.e. each difference-image) was assigned a specific coloration, as shown in the example presented on figure 3. The region of interest (ROI) used for processing was the intersection of all overlapping regions used for difference computations, as described above — as a result of the cumulative area intersections, throughout the follow-up the ROI will never expand over time, only maintain or shrink. Each of these images can be effectively considered as a representation of the evolution history of retinal changes depicted by the corresponding set of difference-images. For this reason, each of them is usually referred to as *difference evolution images* and the whole set of images for a particular follow-up is called *difference evolution sequence*.

Finally, the resulting image was projected onto the baseline image (although projection on any image from the follow-up would be possible), with the purpose of eventually guiding the grader's attention to changes detected on the fundus photographs.

Results

On figures 4 and 5, results are presented for two follow-up cases which had previously been chosen to be representative of a healthy subject and a subject presenting a clinically significant macular oedema resulting from diabetic retinopathy, respectively. More specifically, their

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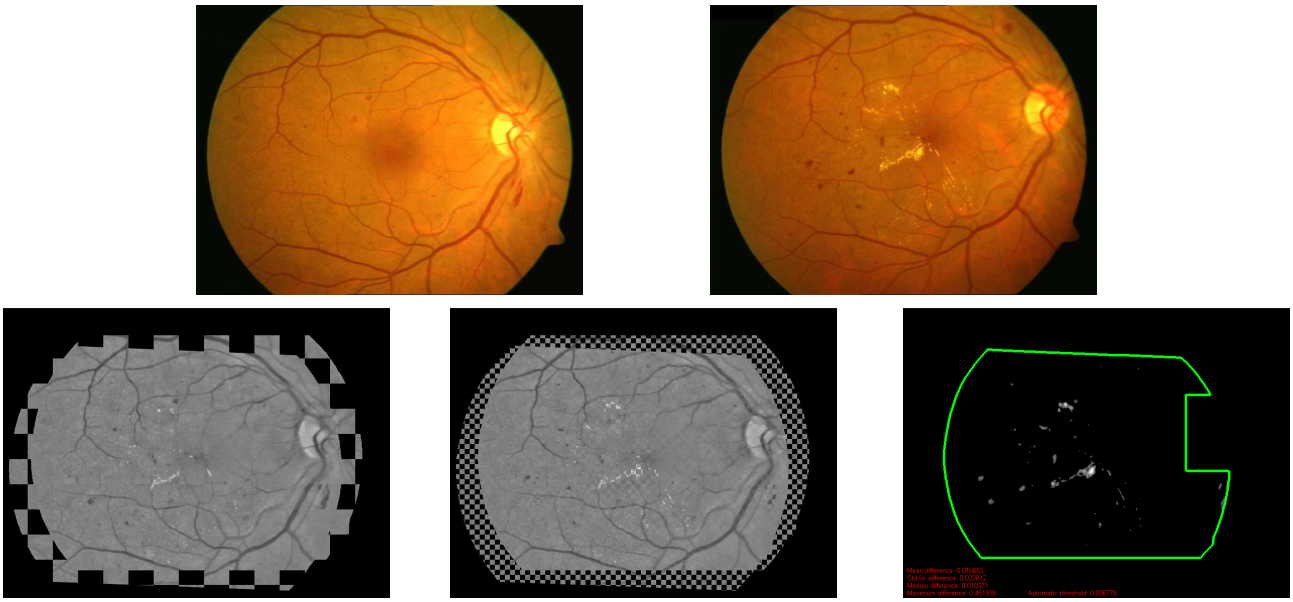

Figure 2: Alignment assessment (two images on bottom left) of the result of registration between a particular image (top right) and the baseline image (top left), and respective difference-image (bottom right).

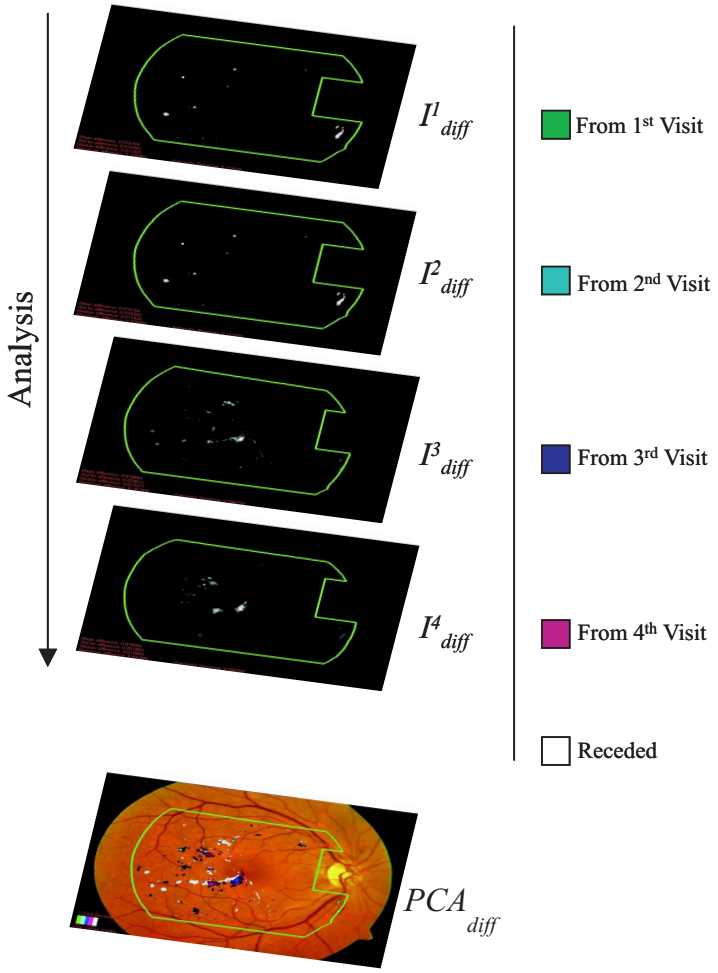

Figure 3: Principal Component Analysis for difference evolution study. As shown on the diagram, each difference-image is considered as a band of a hyperspectral image and the 1st principal component is taken, and this is in turn used for earmarking the baseline image, as shown. The color-scheme code used for earmarking is also presented, relating each color with its corresponding difference-image.

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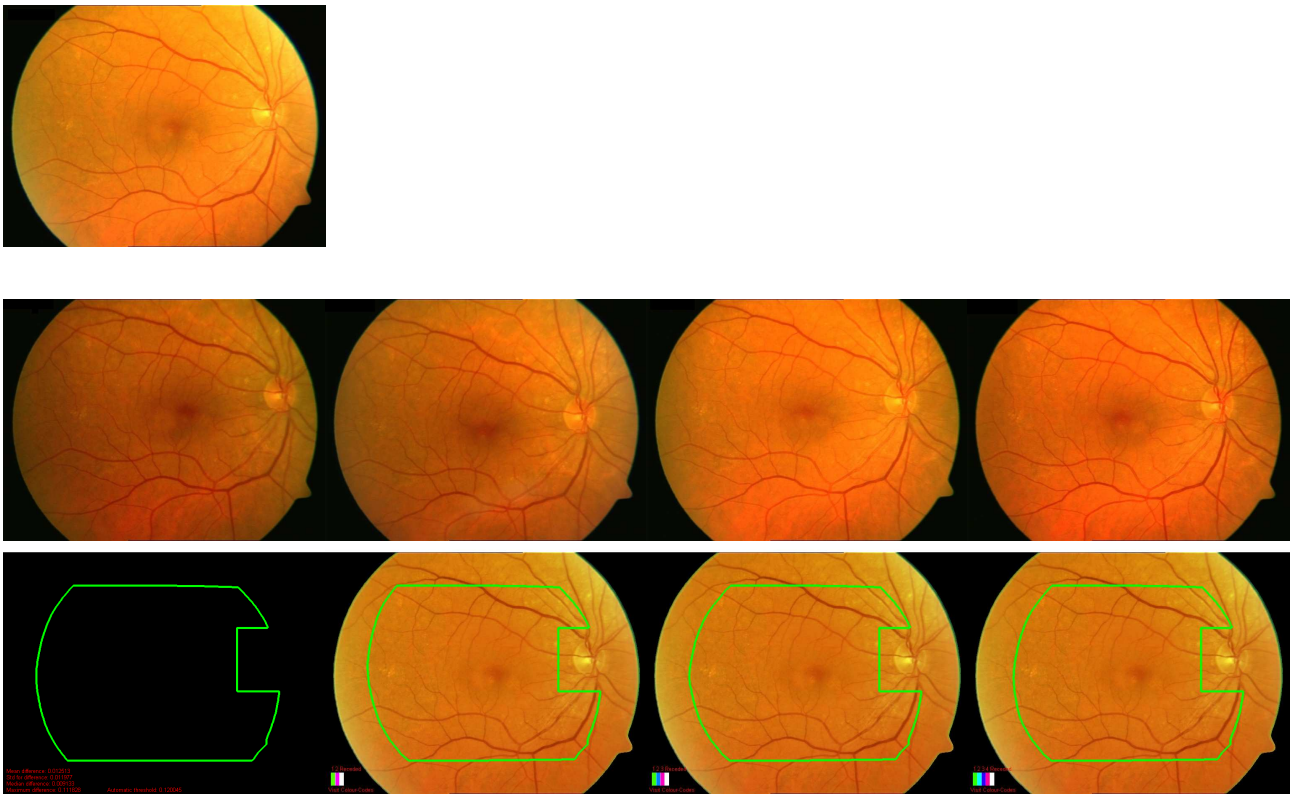

Figure 4: Results for the first case-study two-year follow-up, which pertains to an eye of a healthy subject. Top: baseline (visit 1) fundus photograph. Middle: fundus photographs for visits 2 to 5. Bottom: from left to right, the first difference-image followed by the difference evolution sequence; as expected, no changes were detected. Areas bounded by a green border are the processing regions-of-interest.

respective original images, difference-images and difference evolution sequences are presented for analysis.

The color-coded scheme used for earmarking retinal changes (also depicted on figure 3) works as follows:

General Rule: Each area where retinal changes have been detected is earmarked with a specific color depending on the visit when those alterations occurred.

Refinement 1: The earliest earmarking color of areas which have been detected in multiple instances in the follow-up timeline is kept.

Refinement 2: Areas which have suffered changes but have returned to their original appearance are earmarked with a specific color-code (white).

Except on areas earmarked as described on **Refinement 2**, all other changes are earmarked using different intensity values of their corresponding color, which are linearly proportional to the relative importance of the change corresponding to each pixel, as a result of the PCA. Note that the linearity of this proportion only holds for a particular instant in the follow-up timeline.

Discussion

Using PCA, the greatest variance of the difference data comes to lie on the primary axes of projection (i.e., the first principal components), effectively showing the location and relative importances of the most significant differences detected throughout the follow-up study, as described above.

Two major problems that hinder the earmarking performance have been stated earlier:

(1) Registration accuracy;
(2) Focusing errors.

Effectively solving these problems would allow the suppression of the blurring filter and consequently favor the use of less conservative threshold values for the difference-images, thus improving the overall performance and allowing for better detection of low-profile changes, such as microaneurysms.

As for the first problem, it is hoped that future improvements of the registration procedures will lead to increased accuracy [4]. However, focusing errors may be difficult to deal with after the imaging process has taken place.

As a final remark, please note that the purpose of this earmarking procedure is not to classify changes, which remains the grader's role, but only, as mentioned before, to assist the grader in his/her classification duties.

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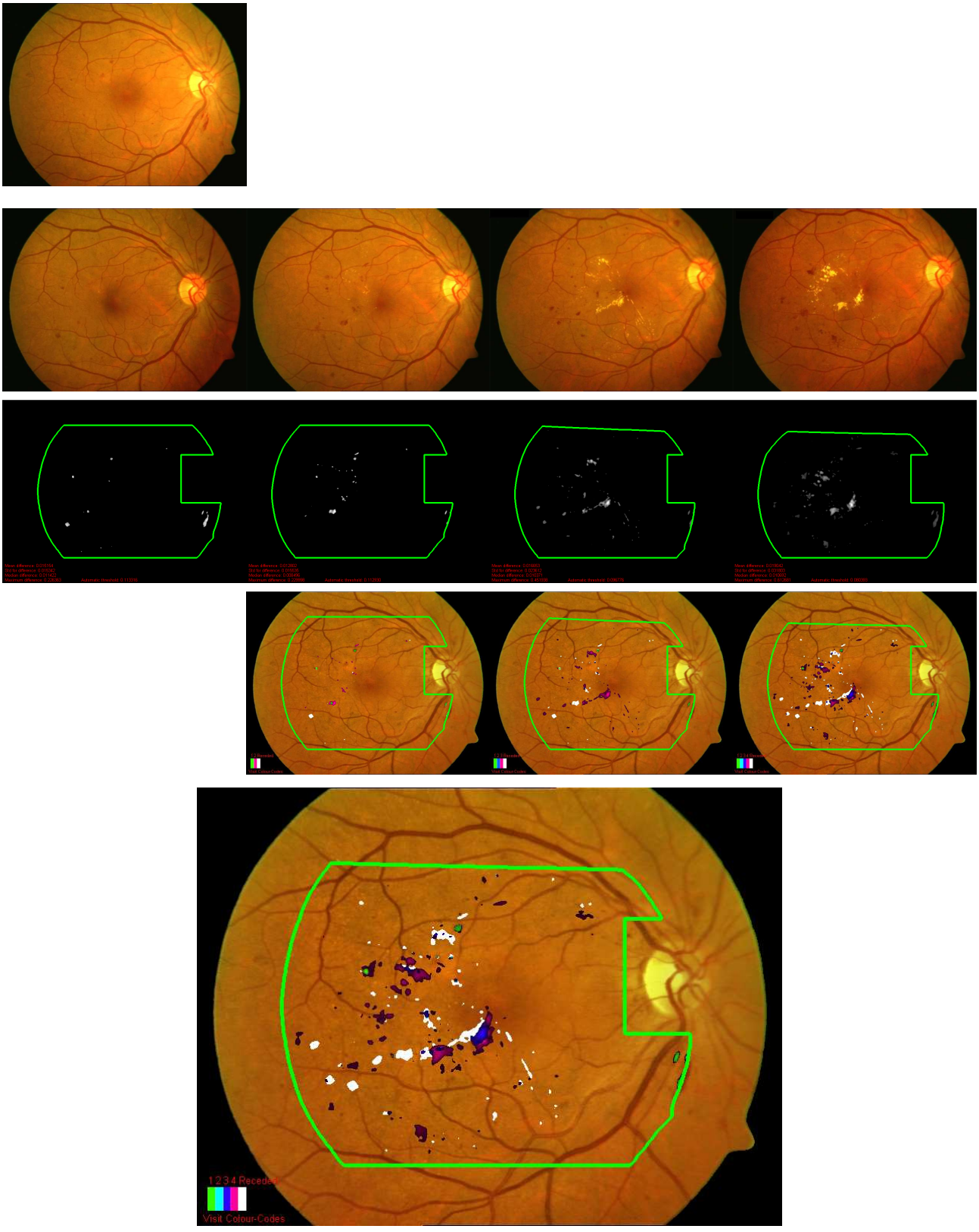

Figure 5: Results for the second case-study two-year follow-up, which relates to a subject presenting a clinically significant macular oedema resulting from diabetic retinopathy. Far top: baseline image (visit 1) used for reference. Far bottom: evolution image for last follow-up instant. Rest of the images, from top to bottom: images of remaining visits, difference-images corresponding to each of the visits above them, and difference evolution sequence projected onto the baseline image — all of these are aligned column-wise to represent a particular instant in time. Areas bounded by a green border are the processing regions-of-interest.

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Conclusions

Changes detected in retinographic color images have been successfully earmarked through an automatic procedure using a temporal color-coded scheme, driving the grader's attention to where meaningful retinal changes might have been present.

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