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Increased Resolution Macular Thickness Mapping by OCT

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Abstract— **Optical coherence tomography (OCT) poor mapping resolution has been pointed out as the biggest disadvantage of this technique when compared to others, e.g., retinal thickness analyzer.**

In this work we were able to solve this problem by developing an atlas of macular thickness of the human retina into which OCT scans were thereafter registered. This atlas is used to allow registering OCT scans from the *Fast Macular Protocol*, thus bringing OCT scans into the atlas coordinates, therefore correcting for misfixations, while simultaneously allowing to perform OCT inter-scan registration.

From this initial registration, we were able to compute a thickness map into which *Fast RNFL Protocol* scans were merged, thus allowing for increased OCT mapping resolution.

I. INTRODUCTION

THE human macula is the area of the human retina centered on the fovea and bound by major vessel arcades, and contain most of the photoreceptors, i.e., cones and rods. Any change occurring in this area has, therefore, a potential impact on visual acuity, hence the special attention given to this area of the retina when monitoring any changes over time. In this way, any increase in macular mapping accuracy is welcome.

Retinal thickness assessment has been traditionally performed by stereofundus photography (SFP) and more recently by Optical Coherence Tomography (OCT – Carl Zeiss Meditec, Dublin, California, USA) and Retinal Thickness Analyzer (RTA – Talia Technology, Lod Indst Area, Israel) [1], [2], [3], [4], [5], [6].

While SFP represents a qualitative assessment of retinal thickness, both the OCT and RTA represent quantitative assessments therefore expressing an objectively measured retinal thickness. These quantitative approaches remove any subjectivity inherent to the SFP technique and allow for a quantitative follow-up of a patient retina from the thickness viewpoint.

Although being the OCT and RTA both quantitative techniques, there are advantages and disadvantages of the OCT over the RTA and vice-versa, being the OCT biggest disadvantage its poor retinal thickness mapping resolution, which was not addressed even in the latest OCT version and thus remains to be resolved. Therefore, OCT retinal thickness maps can only be built based on six-radial line scans, 30° apart, that are expected to cross in the center of fovea. In this paper we will address this problem by developing a technique to increase the macula thickness mapping resolution by merging different scan types.

II. MATERIAL AND METHODS

In the work presented in this paper we will make use of both fast scan protocols available in the *Stratus OCT*, the *Fast Macular Protocol* and the *Fast RNFL Protocol*, by merging retinal thickness information from these two scans. So to correctly locate, in the retina, scans performed by OCT, these will be registered into an atlas of the human retina. For this purpose, a retinal thickness atlas (*RT-Atlas*) was built based on RTA II retinal thickness maps from a control healthy population [$n = 32$].

A. Instrumentation

The OCT makes use of a Michelson interferometer. Low coherence light, from a superluminescent diode light source in near-infrared wavelength at $\sim 800\ nm$ and wavelength bandwidth of $20\ nm$, is coupled into the fiber-optic Michelson interferometer and is split into a reference and sample paths, respectively the reference mirror and the eye. Light reflected from the reference mirror is then recombined with light backscattered from the eye. An *A-scan*, an axial profile of optical reflectivity versus distance, is obtained by moving the reference mirror while recording the magnitude of the resulting interference signal. This process can be repeated many times while scanning the beam through the eye fundus, thus allowing to obtain an optical cross-section image, a *B-scan*. Details can be found in [7], [8].

The distance computed from the ILM (Inner Limiting Membrane) to the RPE (Retinal Pigment Epithelium), at each *A-scan*, is the OCT measured retinal thickness at that specific location in the eye.

OCT macula thickness mapping is based on six-radial lines (*B-scans*) taken in 1.92 seconds using the *Fast Macular Protocol*. The angle between consecutive scans is therefore of 30° this meaning that a large interpolation is performed when mapping retinal thickness, with the interpolation factor increasing with the distance to the center of the map. Moreover, all the six-radial line scans are expected to cross in the center of the map and at the center of the fovea, thus not taking into consideration eventual misfixations, saccades and/or difficulties on focusing the target area.

So to increase OCT mapping resolution, two protocols will be used to collect retinal thickness information using the *Stratus OCT*, the aforementioned *Fast Macular Protocol* and

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Fast RNFL Protocol. While the former consists on six-radial line scans, 30° apart and $6000\ \mu m$ in diameter (default), the latter consists on six concentric circle scans of 1440, 1690, 1900, 2250, 2730 and $3400\ \mu m$ radii. Each component of the *Fast Macular Protocol* and each component of the *Fast RNFL Protocol* are made of 128 *A-scans* and thus of 128 retinal thickness measures.

B. OCT to Atlas Registration

An atlas of the healthy human macula thickness was establish making use of a RTA II to scan retinas from healthy volunteers and in this way allowing to establish the *RT-Atlas* through principal component analysis (PCA). In this atlas, the center of the fovea is at the origin of the axes, while the horizontal axis is defined as the line connecting the center of the fovea to the center of the optic disc, with increasing values in the direction fovea-optic disc.

Each OCT *B-scan* from the *Fast Macular Protocol* may therefore be registered into the *RT-Atlas* space by estimating Γ such that

$$\widehat{\Gamma} = \arg\min_{\Gamma} E\left\{\Omega \cdot (O - R(\Gamma))^2\right\} \ , \qquad (1)$$

where O is the low-pass filtered thickness OCT measurement to be registered, $E\{\cdot\}$ is the expectation of the dot product between Ω (a vector of weights) and the squared differences between O and $R(\Gamma)$ on their overlapping areas. Ω can be defined for each specific pathology to have relative higher weights on less changed retinal areas. For example, should the fovea be spared and Ω can be made from sampling a $2D$ Gaussian function, centered on the fovea, along the path defined by $R(\Gamma)$.

$R(\Gamma)$ represents the sampling in the *RT-Atlas* along a path similar to the *B-scan*, i.e., the OCT scan to be registered, being it driven by a set of parameters (Γ) that allow to specify the location and orientation for each individual scan, as well as to accommodate for the differences in instrumentation (DC component (dc), sampling rate (sr) and a gain factor (g)). Moreover, Γ also takes into account the relation between the set of radial scan lines. Therefore, Γ is composed of 6 parameters defining the *Fast Macular Protocol* set plus 3 additional parameters per *B-scan*, i.e.,

$$\Gamma = (x, y, \theta, dc, sr, g, \Delta x_1, \Delta y_1, \Delta\theta_1, \cdots \\ \cdots, \Delta x_6, \Delta y_6, \Delta\theta_6) \ . \qquad (2)$$

While x, y and θ in (2) represent parameters defining the location and orientation of the set of scans composing the *Fast Macular Protocol*, Δx_i, Δy_i and $\Delta\theta_i$ represent individual degrees of freedom for the i scan relatively to x, y and θ, respectively.

Fig. 1 shows the achieved registration of the six-radial line scans from a *Fast Macular Protocol* into the *RT-Atlas*.

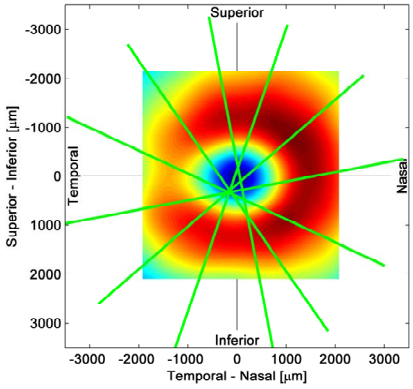

Fig. 1. This figure shows in $2D$ the *RT-Atlas* plus the computed location of each of the six line scans composing the *Fast Macular Protocol* from patient A right eye. Please note that line scans do not intersect at a single point. Also, the origin of the coordinate system corresponds to the center of the fovea and the horizontal axis is the line connecting the center of the fovea to the center of the optic disc with increasing $x-$values in the direction fovea-optic disc. No color scale is given as the *RT-Atlas*, computed by PCA, captures the shape but does not preserve scale, hence the parameters dc and g in (2). Line scans of $6000\ \mu m$ in length are shown here with increased length due to the sr parameter (2).

C. OCT Mapping

Having estimated Γ defined as in (2), one may compute the macular thickness map using thin-plate spline (TPS) [9].

TPS allows to define a surface, passing through or close to every control point (depending on a regularization parameter), while presenting the minimum *bending energy* for the entire space. The interpolation function f is defined as

$$f(P) = \sum_{i=1}^{K} w_i g(P - P_i) + a_0 + a_x x + a_y y \ , \qquad (3)$$

where $P_i = (x_i, y_i)$ $(i = 1 \ldots K)$ are the control points in *RT-Atlas* coordinates, with thickness values z_i, P a point with coordinates (x, y) where the OCT map is to be interpolated, and w_i, a_0, a_x, and a_y are parameters, computed based on the set of control points, defining the interpolation surface.

The TPS *basic function* is defined as

$$g(\rho) = \begin{cases} 0 & if\, \rho = 0 \\ \rho^2 \log(\rho) & otherwise \end{cases} \qquad (4)$$

with ρ the L_2-norm $\left(\rho = \sqrt{x^2 + y^2}\right)$ [9].

Having computed the entire OCT macular thickness map using (3), represents having corrected both the location of the fovea, due to having registered OCT scans into the *RT-Atlas*, as well as performing inter-scan registration, i.e., registration of the set of *B-scan* composing the *Fast Macular Protocol* among themselves. This allows to achieve a better defined macular thickness map compared to the original OCT map, where no corrections are made neither for the location of the fovea or inter-scan registration.

Fig. 2 shows the macular thickness map, as computed by (3), based on *Fast Macular Protocol* scans only.

D. Merging Fast Macular and Fast RNFL Protocols

Having computed the macular thickness map as above (section II-C), one can now register *Fast RNFL Protocol* scans into the computed thickness map, following a similar approach to the one of section II-B.

Although in the *Fast RNFL Protocol* six circular scans are performed, with radii of 1440, 1690, 1900, 2250, 2730 and 3400 μm, the latter one is not considered as it corresponds to macular thickness measurements beyond the limits of the previous macular thickness map as, by default, *Fast Macular Protocol* scans are of 6000 μm in length. We will then register 5 of the 6 circular scans into the OCT thickness map built in section II-C.

Each OCT *B-scan* from the *Fast RNFL Protocol* may therefore be registered into the built macular thickness map by estimating Ψ such that

$$\widehat{\Psi} = \arg\min_{\Psi} E\left\{(O - R(\Psi))^2\right\} \ , \tag{5}$$

where O is the low-pass filtered thickness OCT measurement to be registered and $E\{\cdot\}$ is the expectation of the squared differences between O and $R(\Psi)$ on their overlapping areas.

$R(\Psi)$ represents the sampling in the interpolated map along a path similar to the *B-scan*, i.e., the OCT scan to be registered, being it driven by a set a parameters (Ψ) that allow to specify the location and a set of extra parameters allowing for deformation for each individual scan. Moreover, Ψ also takes into account the relation between the set of these circular scans. Therefore, Ψ is composed of 3 parameters defining the *Fast RNFL Protocol* set plus 7 additional parameters per *B-scan*, i.e., 3 parameters for position and orientation, plus 4 parameters to allow for deformations, being Ψ defined by

$$\Psi = (x, y, \theta, \Delta x_1, \Delta y_1, \Delta\theta_1, s_{x_1}, s_{y_1}, s_{hx_1}, s_{hy_1}, \cdots \\ \cdots, \Delta x_5, \Delta y_5, \Delta\theta_5, s_{x_5}, s_{y_5}, s_{hx_5}, s_{hy_5}) \ . \tag{6}$$

In (6), x, y and θ represent parameters defining the location and orientation of the set of scans composing the *Fast RNFL Protocol*, while Δx_i, Δy_i and $\Delta\theta_i$ represent individual degrees of freedom for the i scan relatively to x, y and θ, respectively. Parameters s_{x_i}, s_{y_i}, s_{hx_i}, s_{hy_i} allow for individual deformations of circle scan i.

E. Increased Resolution Mapping

Having registered OCT scans from the *Fast Macular Protocol* (section II-B) and *Fast RNFL Protocol* (section II-D), we have in fact registered the two OCT fast protocols not only between themselves, but registered all the 11 *B-scans* (6 from the *Fast Macular Protocol* and 5 from the *Fast RNFL Protocol*) among themselves. Moreover, having used the *RT-Atlas* to register the *Fast Macular Protocol* and having registered the *Fast RNFL Protocol* into to the first macular thickness map (section II-C) means that the final macular thickness map will be given in *RT-Atlas* coordinates, i.e., absolute macular coordinates.

Repeating the approach followed in section II-C by computing a new set of parameters for (3) – w_i, a_0, a_x and a_y – allows to build the final macular thickness map based on both OCT fast scan modes. Fig. 3 shows the final macular thickness map made of 1408 control points (retinal thickness samples), while the original OCT map is based on 768 control points only. Also of particular importance is the fact that the extra 640 control points, coming from the *Fast RNFL Protocol*, are distributed on areas corresponding to less sampled regions of the *Fast Macular Protocol*, thus clearly improving the sampling distribution over the macular area.

Moreover, while this new macular thickness map corrects for the location of the fovea, for eye tilt and for individual

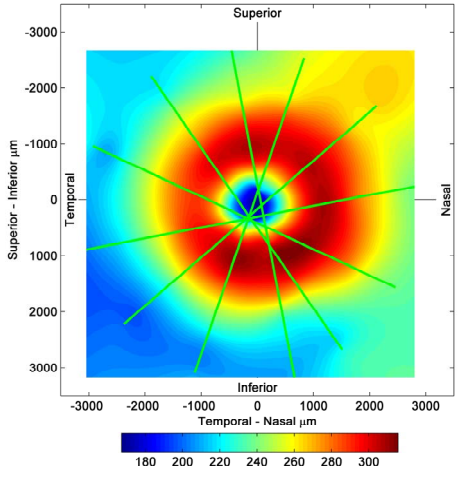

Fig. 2. OCT macular thickness map from patient A right eye, computed based on *Fast Macular Protocol* scans only (green lines on top of the map shows line scan locations). Please note the foveal depression clearly centered on the origin of the coordinate system. The thickness color map can be deciphered with the help of the color bar.

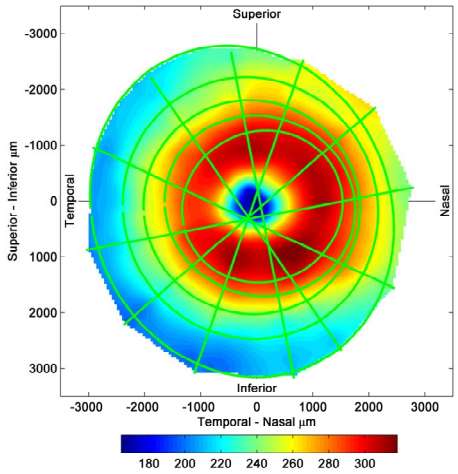

Fig. 3. OCT macular thickness map from patient A right eye, computed based on *Fast Macular Protocol* and *Fast RNFL Protocol* scans. Green lines on top of the map shows line scan locations from both protocols. The thickness color map can be deciphered with the help of the color bar.

scan location and orientation, the OCT mapping does not. This new map therefore represents an important step for the improved accuracy of macular thickness mapping.

Fig. 4 allows to compare macular thickness values for the nine mapping areas established for the OCT. Besides the changes in thickness values for each area, please note the correction made for the fovea, correctly located on the center of the map using our proprietary software (right), compared to the original OCT map (left), as well as the smoothed foveal area due to individually registering OCT *B-scans* into the *RT-Atlas* (no *Fast RNFL Protocol* circles exist for this central area as shown in fig. 3).

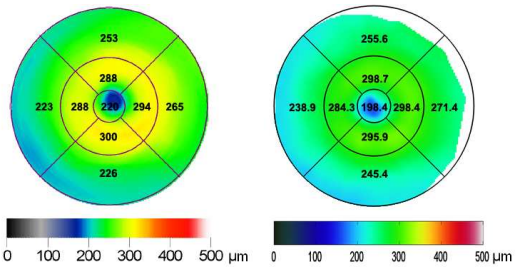

Fig. 4. Patient A right eye. Comparison between the original (left) and the new built OCT type map (right) where the clear distinction between the foveal position in both maps can be seen. Also shown is how thickness values are changed accordingly, with differences from -4.2% in the central area, to $+4.7\%$ in the outer temporal (left) ring area.

III. CONCLUSIONS

A. Conclusions

In this work we were able to increase the *Stratus OCT* mapping resolution by merging the two fast scan protocols available. In order to do so, we have established an atlas of the thickness of the human macula using a RTA II to scan retinas of healthy volunteers. This allowed to establish macular coordinates and to register the *Fast Macular Protocol* into the atlas.

An initial macular thickness map was built, using the registered OCT thickness values as control points to define a thickness surface, into which the *Fast RNFL Protocol* scans were registered. Here, deformations were allowed to a certain degree of freedom so to compensate for saccades.

Results obtained using the developed technique allows us to state that an important improvement was achieved, not only by almost doubling the number of data points used to build the thickness map, from 768 to 1408 control points, but to correctly locate the center of the fovea in the center of the map and to compensate for saccades, allowing for deformations on the *Fast RNFL Protocol* scans and allowing for translation/rotation on *Fast Macular Protocol* scans.

IV. DISCUSSION

Optical coherence tomography has evolved into an important technique in ophthalmology in recent years, not only for macular thickness mapping but also by allowing to perform optical-histology of the human retina. The biggest disadvantage on mapping macular thickness was, since the beginning, its poor mapping resolution as compared to different techniques, e.g., the RTA.

Due to its indication for cases with some media opacities, where the OCT has clear advantages over other techniques, and the growing need for mapping diabetic macular edema, as new drugs are becoming available for this major cause of vision loss, OCT mapping was still needed. The increasing number of OCT new devices with very fast mode capabilities now appearing in the market, the so called ultra-fast OCT devices, may respond to this need. However, these are expensive compared to the existent one – they will be used mainly for research for the next decade due to their limited availability and cost –, plus the fact that there is already an installed capacity all over the world that can be used to its maximum capabilities.

By developing such a tool, we believe that we are contributing to an improved diagnosis of retinal macular diseases.

V. ACKNOWLEDGMENTS

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