3.8 An actual clinical application

The results presented at the previous sections were achieved mainly in our site; the research partners at Galicia would send the images, and our task had been to adapt the single-pair registration schemes to video sequences. This section reports the collaboration research during a stage in our group of Cástor Pérez Mariño. He was successful at refining our algorithms to work for a larger number of video sequences (rather than the three sequences forming our database), and finally he fully developed an application suited to the medical requeriments at his site. Following we present the report of the results.

The normal procedure at the Ophthalmologic Service sited in *Complejo Hospitalario Universitario de Santiago de Compostela* to acquire sequences of *SLO* images starts with the injection of 3 ml of fluorescein sodium into the antecubital vein of the right arm of the patient. Next, the ophthalmoscope device (SLO-101, Rodenstock with Argon laser, 488 nm), set at fluerescein mode, starts to acquire the images. These are digitized with a frame grabber (Matrox RT2000) on a conventional PC at a rate of 25 frames per second during 90 seconds, with a resolution of 720×576 pixels and 256 gray levels. Images were captured with an angular field of view of 40°.

In order to evaluate the results obtained, the dilution graphs have been compared to those manually obtained by an expert clinician according to his regular procedure, i.e., choosing two points in the reference frame (one in an artery, the other in a vein) and trying to pick the same points over the rest of the sequence, while annotating the gray value of these points to draw the dilution graph (see figure 3.30).

Once obtained these curves, hemodynamic parameters can be measured. One of them is the transient time artery-vein (AV time) [115], which measures the time it takes to the dye to cover the distance between the point in the artery and the point in the vein.

This time can be estimated by fitting a straight line to the points in the ascendant slope of each of the data sets. Then, the so-called **contrast arrival time** to a vessel is defined as the time it takes to the adjusted line to achieve the maximum luminance, and the **AV time** as the difference between the contrast arrival time for an artery and a vein.

It must be pointed out that the AV time is usually employed by clinicians not in a precise manner but rather as an indicator of the response of a patient to a treatment. For a patient having an abnormal AV time, any improvement produced by the treatment would be reflected at posterior analysis.

Figure 3.30 illustrates this procedure with one of the sequences. The artery (A) and vein (V) landmark points at the reference image (top) have taken along the sequence the values indicated as points in the two graphs below, which also depict the lines fitting the ascendant slope. Although the automatic method was applied to the whole set of frames, in order to resemble the sampling of the manual procedure only one out of five frames is actually employed.

The AV time obtained by the expert, 2.8 seconds, is similar to that obtained by the algorithm, 3.14 seconds, but the comparison must be fully validated with a large number of cases.

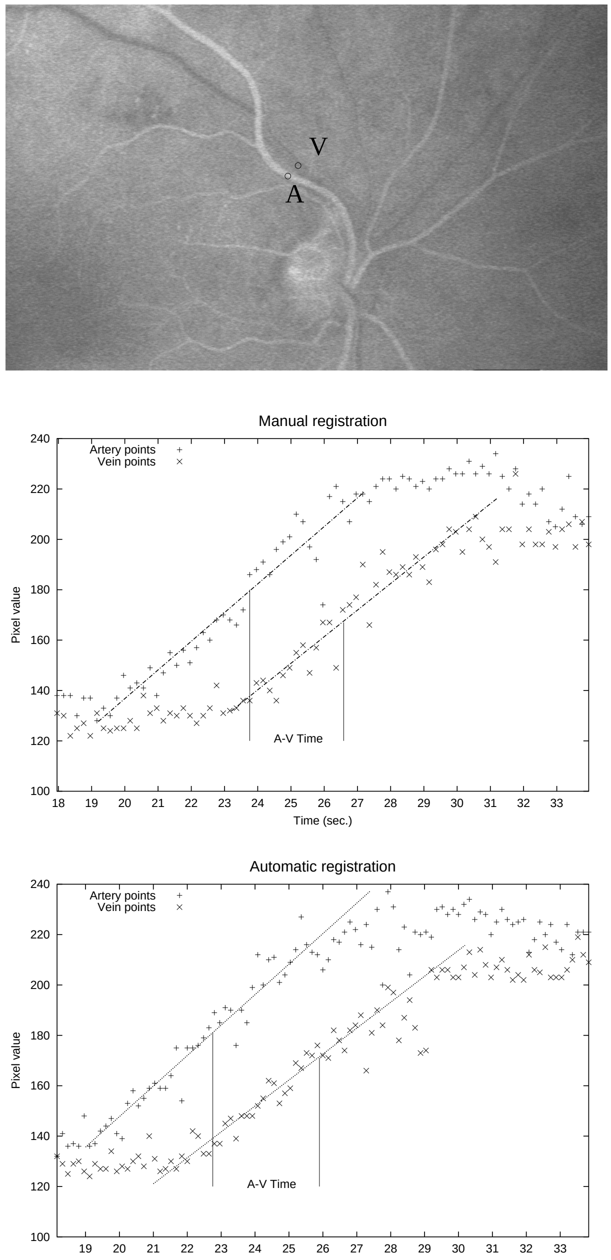

Figure 3.30: Top: Image with the landmark point for an artery (A) and a vein (V). Middle: dilution graph obtained by an expert, together with the lines approximating the ascendant slopes. Bottom: Same, with our method.

3.9 Future work

We have demonstrated that the local-based registration achieves an improvement on the accuracy, which is reflected in the smoothness of the accumulation curves. The reason why this type of registration was needed was explained through the chapter and in figure 3.17 as caused by the special curved geometry of the imaged surface, the fundus, and the optical distortion of the eye lens.

We have presented a solution for the deformation which divides the images into grids, which are registered individually. This method raises several objections:

- Regions without creaseness information in any of the two images cannot be registered.
- Some rectangles remain unmatched because the target regions are too far and thus do not appear in the corresponding candidate rectangle.
- Some regions do not converge properly, because they contain too little information. The transformation found must be then accepted or rejected following some criterium, in general difficult to state.
- Large missregistration, which have been for some reason accepted, influence neighbouring regions when the tranformed image is built.
- All rectangles are registered independently, while some global coherence exists and is not being used.

In short, the main problem is caused by using local transformation when a global model exists. We have started some research with the aim of emplying this global model, but unfortunately we can not present any result yet. In our opinion, the full research for this point would probably need a whole chapter on its own.

Therefore, here we will simply sketch the few steps we have done, and propose the scheme of an alternative method for registration.

The first item we investigated was to find the proper deformation model, this is, to find the reason why our transformation did not permit global convergence. The paper from [7] was very helpful for this purpose; however, the method they propose can not be applied to our images because they acquire the images with a camera that had been previously calibrated.

Therefore we browsed literature, and the search key was in a field related to transformations: satellite image deformations. Literature under this scope is extremely wide and demands studying a complete new field. Still, we tried some deformations, inspired by a book [20]. Note that formulae can not be identical because satellite image a convex surface, while the fundus is concave and there is an extra lens set. We have included initial developement of the formulae and preliminar results in appendix E.

3.10 Conclusions

We have presented a novel method to register retinal images, with several advantages compared to others:

- reliable landmarks extraction using a creaseness operator.
- cross-correlation for robustness against superfluous or missing landmarks.
- hierarchical approach to speed up the results and improve robustness.
- local registration to include geometric distortions.
- experiments include severe miss-registration conditions.

Also, in the evaluation step we have taken into account the accuracy needed by final medical requirements. Figures obtained were consistent and satisfactory.

Our method works fast and reliably for long sequences of *SLO* images, and also for pairs of images of other retinal modalities. Because of its reliability, the method has become the core of a real opthalmologic application, currently developed by Cástor Mariño at the Universidade de A Coruña. A paper with the initial work has been accepted in [46], and another with the final figures has been submited in [45]. We have made original and registered sequences available for researches in our web, [43].