in vessel width estimation for the first time. The effectiveness of a segmentation algorithm in this second task is important since metrics based on vessel widths are considered biomarkers of systemic diseases. Therefore automatic segmentation algorithms producing inaccurate measures of widths could lead to erroneous conclusions in biomarker studies.

The proposed method achieves the best results in our comparison tests in vessel segmentation accuracy (Acc = 0.965 ± 0.006) and AUC (0.97). The low value of SD of the segmentation accuracy suggests that the method performs consistently on the entire set of windows. Windows located close to the OD are where largest vessels are the most visible. Thin vessels, instead, are more abundant in windows taken from the periphery of the image. A low SD in segmentation accuracy is therefore an indication of the goodness of the proposed technique in segmenting all possible scales of vessels. These results represent a considerable improvement with respect to our previous approach [14] and have proven to be significantly better than the performance achieved by the best of the techniques [15, 16] developed for fundus camera images that we adapted to UWFoV SLO images.

At the same time, the proposed method presents the lowest overall bias (0.22 pixels), which is comparable to those between human observers, and the lowest SD (1.11 pixels) in width estimation errors among the automatic algorithms [14–17] used for comparison. The results achieved by the proposed method are the only ones that do not show a statistically significant difference from the ground truth. Lastly, the values of Pearson's r coefficients indicate that the widths estimated from the binary vessel maps automatically segmented with the proposed method are the most correlated ($r = 0.82$) to the ground truth.

It is worth noting that a good value of vessel segmentation accuracy does not necessarily imply good results in vessel width estimation. This is made explicit by the performance in the two tasks (see Table 1 and Table 2) of [14] and [15]. Both techniques show the second highest value of segmentation accuracy (Acc = 0.957) but at the same time the two lowest correlations (r respectively equal to 0.42 and 0.49) to the vessel width ground truth.

One known limitation of the proposed algorithm is its supervised nature that requires a tedious and time consuming step of manual segmentation of retinal images, necessary to train the neural network classifier. After the training phase, the time needed to process a whole UWFoV SLO image by our method is comparable (approximately 200 seconds) to the time required by the other supervised method [15] that has been tested. The unsupervised technique by Bankhead et al. [16] is considerably faster (10 seconds) given the same computer configuration (i5-3450 CPU @ 3.10 GHz, 8.00 GB of RAM).

A limitation of this study is that the OD dimension is assumed to be constant among participants as previously reported by other authors [7]. The study of the refraction of each subject is also beyond the scope of this work.

A more comprehensive investigation of the performance of the proposed method in conventional fundus camera images and the possible differences with respect to UWFoV SLO ones acquired from the same subject is currently being carried out.

Acknowledgements