Superimposition of eye fundus images for longitudinal analysis from large public health databases

G Noyel, R Thomas, G Bhakta, A Crowder, D Owens and P Boyle

1 International Prevention Research Institute, 95 Cours Lafayette, Lyon, F-69006, France
2 Diabetes Research Group, Institute of Life Sciences, College of Medicine, Swansea University, SA2 8PP, United Kingdom
3 Diabetic Eye Screening Wales, 1 Fairway Court, Tonteg Road, Upper Boat, Treforest, Pontypridd CF37 5UA, United Kingdom
4 Strathclyde Institute of Global Public Health, University of Strathclyde, Glasgow, United Kingdom
5 Author to whom any correspondence should be addressed.
E-mail: guillaume.noyel@i-pri.org, r.l.thomas@swansea.ac.uk, gavin.bhakta@drssw.wales.nhs.uk, andrew.crowder@drssw.wales.nhs.uk, owensDR@cardiff.ac.uk and peter.boyle@i-pri.org

Keywords: eye fundus images, image registration, invertible model, longitudinal analysis, public health databases, radial distortion, diabetic retinopathy

Abstract

In this paper, a method is presented for superimposition (i.e. registration) of eye fundus images from persons with diabetes screened over many years for diabetic retinopathy. The method is fully automatic and robust to camera changes and colour variations across the images both in space and time. All the stages of the process are designed for longitudinal analysis of cohort public health databases where retinal examinations are made at approximately yearly intervals. The method relies on a model correcting two radial distortions and an affine transformation between pairs of images which is robustly fitted on salient points. Each stage involves linear estimators followed by non-linear optimisation. The model of image warping is also invertible for fast computation. The method has been validated (1) on a simulated montage and (2) on public health databases with 69 patients with high quality images (271 pairs acquired mostly with different types of camera and 268 pairs acquired mostly with the same type of camera) with success rates of 92% and 98%, and five patients (20 pairs) with low quality images with a success rate of 100%. Compared to two state-of-the-art methods, ours gives better results.

1. Introduction

Diabetic retinopathy (DR), as one of the major causes of visual impairment in the world, represents a major public health challenge. It is a complication of both types of diabetes mellitus, which affects the light perception part of the eye (retina). DR may lead to the development of sight threatening lesions and without adequate and timely treatment patients could lose their sight and eventually become blind (Scanlon et al. 2009, International Diabetes Federation and The Fred Hollows Foundation 2015). DR is often asymptomatic until an advanced stage, thereby screening to detect sight threatening DR at an early stage is essential, which has resulted in the introduction of DR screening services in many countries such as the UK (Harding et al. 2003), USA, the Netherlands, France, etc. The commonest screening method involves acquiring eye fundus images on an annual or biennial basis.

As these DR screening programs have been in existence over several years, performing longitudinal analysis of the eye fundus images of the same patient is now possible. However, in order to accurately compare the evolution of DR over time, the images must be perfectly superimposed.

The direct superimposition of two images of the same patient never gives good results (see figure 1). Indeed, for two separate photographic-eye examinations the patient is never in exactly the same position and also the camera may differ. Therefore, the superimposition method has to take into account the different causes of the deformation such as: (i) the position of the patient by taking into account rotation, translation and scaling, (ii) the change of the camera using scaling and radial correction, (iii) the projection of a 3D scene assimilated to a sphere (the retina of the eye) onto the 2D plane of the sensor of the camera using radial correction, (iv) the radial deformation due to

© 2017 IOP Publishing Ltd
the optics of the camera using radial correction and (v) the colour variability between images due to the light intensity and sensor.

To perform a superimposition—also named registration—two stages are regarded as necessary: a model of deformation and a matching criterion to fit the model. Registration of medical images has been a very active field for research during recent decades, especially in the field of radiology. For an overview of medical image registration methods see e.g. Maintz and Viergever (1998), Oliveira and Tavares (2014), and Viergever et al (2016). Pluim et al (2003) have also written a survey about mutual-information-based registration of medical images and Sotiras et al (2013) about deformable registration. In this paper, we will focus on the registration of eye fundus images.

Several models of superimposition between pairs of eye fundus images are in existence. The earliest methods relied on fluorescein images and were based on a composition of translation, rotation and scaling—i.e. an affine transformation model (Zana and Klein 1999a, 1999b). The bifurcations of the vessels were used to match the points and fit the model. Another matching criterion consists in the minimisation of image intensity differences (Gideciyan 1995, Matsopoulos et al 1999, Ritter et al 1999, Adal et al 2014). Matching by salient points using the SURF—Speeded Up Robust Features—detector, was used in Cattin et al (2006).

Other methods are based on similarity (i.e. rotation and translation) (Matsopoulos et al 1999, Lloret et al 2000) and an elastic model of deformation (You et al 2005, Fang and Tang 2006). In Jian et al (2010) and Ghassabi et al (2013), new descriptors, PIIFD (partial intensity invariant feature descriptors), have been introduced for multimodal image superimposition between auto-fluorescence, infrared and red-free images (i.e. the green component of colour eye fundus images) using an affine and a quadratic model of deformation. This method, powerful for multimodal image registration, has not been designed and tested for the superimposition of colour eye fundus images.

More recently, it has been shown that a quadratic model gives better registration results (Can et al 2002, Stewart et al 2003, Ryan et al 2004, Chanwimaluang et al 2006, Adal et al 2014). The difficulty inherent in these models is estimating their parameters. To overcome such a limitation, a radial distortion model has been introduced by Lee et al (2007) and compared to previous methods in Lee et al (2010). It consists of adding a radial model to the affine transformation in order to correct the effects of radial distortion due to the geometry of the camera and of the eye. Superimposition of eye fundus images has also been performed in the tri-dimensional space using a model of near planar surface (Lin and Medioni 2008) or an ellipsoid model (Hernandez-Matas et al 2016).

However, for all these methods the superimposition of eye fundus images is performed with colour images acquired by the same camera during the same examination. Superimposing colour images acquired by different cameras with at least a year-long interval and stored in large screening databases still remains a challenging problem. Two new issues are appearing: (i) the radial distortion must be corrected for the two different lenses because the camera has changed, and (ii) the colour of the eye may have changed due to a different source of light and to an evolution of the anatomy of the eye (e.g. cataract removal, evolution of the retinopathy to a more severe stage, etc).

Currently, for colour eye fundus images, no existing method has been designed to address the problem of the change of camera lenses, camera and light for retinal examination used for DR screening (i.e. at a yearly interval). In addition, in the existing methods, even when one radial distortion is corrected by a radial distortion correction or by a second order model, the

Figure 1. Superimposition of eye fundus images acquired with different cameras and image resolution. (a) Naive superimposition of images. (b) Perfect superimposition of images using a model. For display purposes, in each panel (a) and (b), one image of the pair is falsely coloured (i.e. bluish colour).
A registration criterion requires a similar and uniform intensity (i.e. colour) of the images, particularly if the extraction of anatomical features such as the vessels is needed. These methods are working in laboratory conditions (several acquisitions on the same day with the same equipment) but failed when they are used on public health databases constituted by routine screening across years of patients with diabetes.

In this paper, our contribution has been to address this challenge by presenting a robust superimposition method designed for longitudinal screening of large public health image based databases. After having taken into account the variation of colour, we introduce a new model of image registration based on two radial distortions and a homography. Importantly, this model is invertible which is useful for image deformation (i.e. image warping) and makes it suitable for fast computation, a key factor for efficient analysis of large databases. We also introduce linear equations to estimate the parameters of the model in a fast and simple way. Finally, we provide a complete framework for robust image superimposition. The registration criterion is based on a standard salient point extraction, which does not rely on the extraction of anatomical features.

The paper is organised as follows: after presenting our method to superimpose pairs of images, it will be validated on a simulated montage and using different patient databases. It will be compared with two well-established methods of image registration. Then, the results will be interpreted and discussed before the conclusion.

2. Methods

During a photographic eye examination, two eye fundus (retina) images of both eyes are acquired in two positions i.e. a 45 degree ‘nasal’ and ‘macular’ field (figure 2). As patients with diabetes are annually screened this gives a series of images available for longitudinal analysis. This is a different problem from large mosaics of eye fundus images acquired during the same examination with the same camera (Chanwimaluang et al 2006). Consequently, the aim of this study was to develop a method to superimpose images in the same positions, even if they were captured during two different exams or often with different cameras and resolutions.

A schematic description of the study is represented in figure 3. The different stages have been designed to
provide efficient solutions to the superimposition of images acquired for practical screening. Between two examinations, the camera and lighting might have been changed, producing differences in colour requiring a pre-processing stage consisting of (1) normalizing the colour of the eye fundus image (Noyel et al 2015). In addition, the position, resolution and radial distortion between the images might be different requiring an image transformation estimated thanks to the (2) extraction of characteristic points in the pairs of images, (3) a matching procedure, (4) the use of a model correcting radial distortion of both images, and (5) the estimation of the parameters of the model by a robust optimisation. Eventually, the method is validated (6) on a simulated montage and the super-impositions of the image of the database are verified (7) and compared to state of the art methods.

In this paper, the image pairs of the same eye in the same position, ‘nasal’ or ‘macular’, are registered independently.

2.1. Pre-processing

The brightness of eye fundus images is non-uniform for various reasons: disease such as cataracts, motion of the patient, acquisition conditions and differences in absorptions of the light in the eye (Walter 2003, Walter and Klein 2005). Some parts of the images appear as bright while others are dark. Moreover, the possible change of the eye fundus camera between two separate examinations may contribute to a change in the colour between two images of the same eye (figure 4). We have used a method (Noyel et al 2015) to correct the variations of colour contrast between the images. The method is based on a colour model consistent with the physical principles of image formation. The contrast of the dark or the bright elements are adjusted in a way that provides a similar colour aspect to lesions such as micro-aneurysms or to anatomical structures such as vessels or veins. Results can be seen in figure 4. Our colour methods goes further than previous existing grey-level methods using polynomial adjustment (Walter et al 2007), mathematical morphology (Zhang et al 2014) or histogram equalisation (Zuiderveld 1994).

2.2. Extraction of characteristic points

The pre-processing is followed by the extraction of several salient points (figure 5) using the scale-invariant feature transform—SIFT—algorithm (Lowe 2004, Vedaldi and Fulkerson 2008). The SIFT algorithm has been designed to be robust to the variation of observation angle and to some variations in lighting. Briefly, SIFT consists of extracting key points based on a multiscale analysis. Then, a series of descriptors are computed for each salient point. These descriptors are used for point matching.

2.3. Point matching with a preliminary estimate of the image deformation

Point matching is a necessary step before the estimation of the model of deformation. With the SIFT method to extract characteristic points, Lowe (2004) has proposed a matching method. However, it was not robust enough to estimate the model of deformation in the database. Therefore, a three-step procedure of matching has been proposed.
Figure 4. (a), (b) Eye fundus images of the same patient acquired with the same camera during two exams with 1.5 years interval. These low quality images have been acquired in harsh conditions. (c), (d) Colour stabilisation of eye fundus images (a) and (b).

Figure 5. Point extraction and matching between images. (a) Initial matching (green arrows). (b) Matching after simplification (red arrows).
(a) A first matching by Lowe’s method followed by a refined selection of the correspondence vectors according to their size and orientation (see hereinafter).

(b) A preliminary estimate of the image deformation by a homography. The position of the characteristic points is transformed using a homography (see hereinafter).

(c) Step (a) is run a second time using the transformed points.

2.3.1. Selection of the correspondence vectors
First of all, the region of interest of both images are extracted and joined together after resizing and padding to have the same vertical size (figure 5). As the image deformation is closed to a similarity (i.e. rotation, translation and scaling), the length of ratios and angles are invariant by similarity (Hartley and Zisserman 2004). This property is used to remove the correspondence vectors \( v \) between inconsistent matched points. With the two images joined together, a two-step selection is performed on the lengths \( l \) and orientations \( \theta \) of the correspondence vectors.

(i) Only the vectors \( v \) whose length \( l_v \) and orientation \( \theta_v \) are in the interval \( \{ |l_v - E\{l_v\}| \leq \sigma \{l_v\} \} \) are kept. \( E\{\} \) is the mean and \( \sigma\{\} \) the standard deviation of a variable.

(ii) Among the selected vectors \( \tilde{v} \), only the vectors whose length \( l_\tilde{v} \) and orientation \( \theta_\tilde{v} \) are in the interval \( \{ |l_\tilde{v} - E\{l_\tilde{v}\}| \leq \max(3\sigma\{l_\tilde{v}\},5\% \times \text{size}) \} \) and \( \{ |\theta_\tilde{v} - E\{\theta_\tilde{v}\}| \leq \max(5\%, \sigma\{\theta_\tilde{v}\}) \} \) are kept. \( \text{size} \) is the number of lines in the image.

Note. The value 5\% has been empirically selected and works perfectly for all the processed images.

2.3.2. Estimation of a homography
The affine homography (or affine transformation) \( H \) is defined as:

\[
H = \begin{bmatrix} A & T \\ \text{O}^T & 1 \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & t_x \\ a_{21} & a_{22} & t_y \\ 0 & 0 & 1 \end{bmatrix},
\]

\( A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}, \forall i, j \in \{ 1,2 \}, a_{ij} \in \mathbb{R}, \) is a 2 \( \times \) 2 non-singular matrix (i.e. with a nonzero determinant) and represents the linear applications.

\( T = \begin{bmatrix} t_x \\ t_y \end{bmatrix}, t_x, t_y \in \mathbb{R}, \) is a translation.

The estimation of a homography is performed using a robust maximum likelihood estimation with the random sample consensus (RANSAC) algorithm applied on the ‘linear normalised DLT’ (direct linear transform) algorithm (Hartley and Zisserman 2004).

This is the initialisation step of the ‘gold standard algorithm’ of Hartley and Zisserman (2004). This initialisation algorithm estimates around 100 homographies on four randomly selected pairs of points. Then, the homography with the minimum error, when transforming the matched points, is selected. This allows the removal of the incorrect matchings. However, as there is also a radial distortion in the image, the deformation is not entirely modelled by a homography. Therefore, some homographies must be discarded. In particular, those with a scaling factor on the \( x \) and \( y \) axis with a relative difference greater than 1\%, because the sensor resolution is almost the same in \( x \) and in \( y \). For this purpose, several estimates (until 50) using the initialisation algorithm are performed if the relative difference between the scaling factors is greater than 1\%. If the value of 1\% is never reached, then the homography with the smallest relative difference between the scaling factors is kept. Finally, a non-linear estimation is performed with the algorithm of Levenberg–Marquardt (More 1978, Bonnans et al 2006). It serves as a good initialisation of the estimation of the complete deformation model.

2.4. Model of deformation
The model of deformation ensures a correct superimposition between the images. Several deformations are taken into account: (i) the difference in terms of positions of the eye between a pair of images will be corrected by an affine transformation (i.e. and a homography) and (ii) the radial deformations due to the projection of the eye into the camera and due to the optics of the camera (Hartley and Zisserman 2004) will be corrected using a radial transformation. For this purpose, Lee et al (2007, 2008), have proposed a model coupling a unique radial transformation for both images and a homography. Lee et al (2010) have made the comparison with two other second order models.

Their approach was extended by defining a model with one homography \( H \) and two radial distortions, i.e. one for each image. Indeed, the camera may have changed between screening exams on a large number of patients.

The radial distortion due the background of the sphere surface of the eye and of the radial distortion of the camera was modelled by a division model (Fitzgibbon 2001) in the following way:

\[
P^d = (1 + k(r^d)^2) \cdot P^u.
\]

\( P^d \in \mathbb{R}^2 \) are the distorted coordinates in the original (i.e. distorted) image. \( P^u \in \mathbb{R}^2 \) are the undistorted coordinates in the undistorted image. \( P^d \in \mathbb{R}^2 \) are the distorted coordinates centred on the image centre \( C \): \( P^d = P^d - C \). \( P^u \in \mathbb{R}^2 \) are the undistorted coordinates centred on the image centre \( C \): \( P^u = P^u - C \). \( r^d = ||P^d - C|| \) = \( ||P^u|| \in \mathbb{R}, \) is the distance of the deformed coordinates \( P^d \) from the optic centre \( C \) (i.e. the image centre). \( k \) is a real parameter of distortion.
Its normalised version, $\tilde{k} = k(1 + \|C\|^2)$, is in the interval $[-0.2; 0.2]$.

This model was named the division model because the distorted coordinates were divided by the radial distortion $P_2^d/(1 + k(r_2^d)^2) = P^u_2$. The distorted image corresponds to the original image and the undistorted image is the image after the correction of radial distortion.

Given $P_1^d$ and $P_2^d$, the coordinates of the points in the original (i.e. deformed) images 1 and 2, $k_1$ and $k_2$ are the distortion parameters, $C_1$ and $C_2$ are the image centres, and the model mapping image 1 into image 2 is defined as follows:

$$P_2^d = \frac{P_1^d}{H} + C_2,$$

(3)

where $H = \frac{P_1^d}{1 + k_1(r_1^d)^2} + C_1$.

If the same camera is used to acquire both images, the distortion parameters are equal, $k_1 = k_2 = k$, and the model corresponds to the model of Lee et al. (2007). However, in our approach, the model is estimated after having extracted and matched the points in the pair of original images (target and reference). Therefore, the radial distortion correction is performed after the detection of the feature correspondence points in the original (i.e. distorted) image. It has been programmed in the subsequent way.

After point matching, the model is estimated by minimising the deformation error $\varepsilon$ between the undistorted points in image 2 estimated by the model, $(P_2^u)^{est} = H\left[\frac{P_1^d}{1 + k(r_1^d)^2} + C_1\right] - C_2$, and the undistorted points extracted in image 2, $P_2^u = P_2^d/(1 + k_2(r_2^d)^2)$. The deformation error is $\varepsilon = \| (P_2^u)^{est} - P_2^u \|$. Note. Even if linear equations are introduced to estimate the model parameters, a final non-linear estimator is used for two reasons. Firstly, an estimate of the model is performed using the (non-linear) parameterisation of the matrix $A$ into a set of two angles and two scaling factors (Hartley and Zisserman 2004, p 40), which have a direct physical interpretation. Secondly, the location of the correspondence points may be re-estimated jointly with the model parameters using the 'Sampson error' or the 'gold standard error' (Hartley and Zisserman 2004, p 114). In this paper, the

2.5. Estimation of the model parameters

The model parameters are estimated in figure 6 by a different method of Lee et al (2007) and Abramoff et al (2012). In particular, during the initialisation step, the type of model is selected: either a single distortion model, if the images are acquired by the same camera, or a two distortion model if two cameras are used. In addition, the radial distortion is estimated after homography without needing any preliminary initialisation by a calibration of the camera (Hartley and Zisserman 2004). Moreover, we have introduced linear estimators at each step of the process.

The estimation process is as follows (figure 6). The homography and radial distortions are initialised using linear estimators. Then, an iterative estimation is performed independently for the homography and the radial distortions until the deformation error has converged. In order to ensure that the error has converged, at each step a linear estimator is used as an initialiser of a non-linear (iterative) optimiser such as Levenberg–Marquardt (More 1977, Bonnans et al 2006). Indeed, without initialisation, the non-linear estimator may converge towards a local minimum of the error (Hartley and Zisserman 2004, p 110). The convergence criterion is defined by:

$$\text{convergence} = [\varepsilon < \varepsilon_0 \text{ and } \frac{\varepsilon_n - \varepsilon_{n-1}}{\varepsilon_{n-1}} < \text{tol}]$$

and $[\tilde{k} \text{ or } [\tilde{k}_1 \text{ and } \tilde{k}_2] \in [-0.2; 0.2]]$ and $[n < \text{MaxIter}]$.

err is the mean error at iteration $n$, $\varepsilon_0 = 0.01$ is the tolerance on the error, $\text{tol} = 0.01$ is a tolerance on the relative error between iterations and $\text{MaxIter} = 100$ is the maximum number of iterations. For each iteration, the normalised radial distortion parameters $\tilde{k}$ must be in the interval $[-0.2; 0.2]$. If not, the algorithm stops and the model estimate with the smallest error is selected.

The final optimisation is performed jointly on the homography and the radial distortion with a linear estimator followed by a non-linear optimiser such as Levenberg–Marquardt (More 1977, Bonnans et al 2006) for a single distortion or for two distortions the ‘trust region method’ (Moré 1983, Bonnans et al 2006) with the bounds $[-0.2; 0.2]$ for the radial distortion parameters.
position of the correspondence points has not been reestimated. It will be studied in a future paper.

2.5.1. Estimation of the model with two radial distortions
When a different camera is used for each image of a pair, two radial distortions must be estimated, \( k_1 \) and \( k_2 \). Let us define linear estimators to initialise the nonlinear estimators of the model parameters.

2.5.1.1. Linear estimator of the radial distortion parameters \( k_1 \) and \( k_2 \)
Equations (1) and (3) imply that:
\[
\begin{align*}
&k_1k_2[(r_1^2 r_2^2)^2 + D] + k_1[r_1^{d2} \cdot D + r_1^{d2} \cdot P_1^d] \\
&+ k_2[r_2^{d2} \cdot D - r_2^{d2} \cdot AP_1^d] = -[P_1^d + D - AP_1^d]
\end{align*}
\]
with \( D = C_2 - AC_1 - T \). Equation (4) is a quadratic equation with its unknowns \( k_1 \) and \( k_2 \), \( k_1k_2[M_{12}] + k_1[M_i] + k_2[M_j] + [M_0] = 0 \). The variables \( M_i, i = \{0, 1, 2, 12\} \), have two components \( M_i = [M_{1i}, M_{2i}, M_{12}, M_0] \) in \( \mathbb{R}^4 \). For each component, the equation is verified for each of the \( N \) pairs of matched points. This leads to a set of two systems of quadratic equations. The set of equations corresponds to the intersection of two conics, which has a unique pair of solutions according to Bernstein’s theorem for bivariate polynomials (Sturmfels 2002, p 37). This result can be explained in a more intuitive way; between a pair of matched points, there is one pair of solutions per equation (i.e. two pairs). As the solution must be valid for both systems of equations, there is only a unique solution pair \( (k_1, k_2) \) valid for all the matched points. The other solutions are only valid for a single pair of matched points. The unique solution pair \( (k_1, k_2) \) satisfies both systems of equations together and can be obtained by elimination of the second order term:
\[
\begin{align*}
&k_1k_2 + \frac{M_{12}^2}{M_{12}^2}k_1 + \frac{M_{12}^2}{M_{12}^2}k_2 + \frac{M_0^2}{M_{12}^2} = 0 \\
&k_1k_2 + \frac{M_{12}^2}{M_{12}^2}k_1 + \frac{M_0}{M_{12}^2}k_2 + \frac{M_0}{M_{12}^2} = 0 \\
&\Rightarrow k_1 \left[ \frac{M_{12}^2}{M_{12}^2} - \frac{M_0}{M_{12}^2} \right] + k_2 \left[ \frac{M_{12}^2}{M_{12}^2} - \frac{M_0}{M_{12}^2} \right] = 0 \\
&\Rightarrow \frac{M_{12}^2}{M_{12}^2} - \frac{M_0}{M_{12}^2}.
\end{align*}
\]

The unique solution pair \( (k_1, k_2) \) of equation (5) is determined using the method of least squares. When the camera is the same for both images, only one radial distortion, \( k = k_1 = k_2 \), needs to be estimated in equation (5).

2.5.1.2. Linear estimator of the radial distortion parameters \( k_1 \) and \( k_2 \) and the homography
From equations (1) and (3), we obtain:
\[
\begin{align*}
&k_1k_2D[(r_1^d r_1^d)^2] + k_1D[r_1^{d2}] + k_2[r_2^{d2} \cdot P_1^d] \\
&+ k_2D[r_2^{d2}] - k_2A[r_2^{d2} \cdot P_1^d] - A[P_1^d] + D[1] = -[P_1^d].
\end{align*}
\]
Equation (6) is a linear equation with its variables in the bracket. It is valid for each component \( x \) and \( y \) of the vectors \( P_1^d = [P_1^{dx}, P_1^{dy}]^T \) and \( D = [D^x, D^y]^T \), leading to a system of two equations:
\[
\begin{align*}
&\begin{cases}
&k_1k_2D^x[(r_1^{d2})^2] + k_1D^x[r_1^{d2}] + k_2[r_2^{d2} \cdot P_1^{dx}] \\
&+ k_2D^y[r_2^{d2}] - k_2a_1[r_2^{d2} P_1^{dx}] - k_2a_2[r_2^{d2} P_1^{dy}] - a_1[P_1^{dx}] - a_2[P_1^{dy}] + D^x[1] = -[P_1^{dx}] \\
&\end{cases}
\end{align*}
\]
\[
\begin{align*}
&\begin{cases}
&k_1k_2D^y[(r_1^{d2})^2] + k_1D^y[r_1^{d2}] + k_2[r_2^{d2} \cdot P_1^{dy}] - k_2D^y[r_2^{d2}] - k_2a_1[r_2^{d2} P_1^{dx}] - k_2a_2[r_2^{d2} P_1^{dy}] - a_1[P_1^{dx}] - a_2[P_1^{dy}] + D^y[1] = -[P_1^{dy}].
\end{cases}
\end{align*}
\]
The 20 variables—in the brackets—correspond to the data. The 18 parameters of the set of both equations are estimated using the method of least squares applied to the set of both equations. As there are multiple relations between the 18 estimator parameters, only the 8 parameters of the model—\( k_1, k_2 \) and \( H \) (through the intermediary of \( A \) and \( D \)—are unknown. An admissible solution for \( k_1, k_2 \) and \( H \) is deduced from the 18 parameters of the linear estimator. The value of \( k_1 \) is directly obtained (3rd term of the 1st equation) as well as those of \( D^x \) and \( D^y \) (9th terms of both equations) and \( a_{ij} \) (7th and 8th terms of both equations). The value of \( k_2 \) is deduced, e.g. from the 4th term of the 1st equation. Then, this admissible solution is introduced as the initialisation of the nonlinear estimation.

2.6. Image warping
In order to analyse a large database, a fast algorithm of image warping is needed. Forward warping is time consuming and so we therefore use inverse warping. However, the registration model needs to be invertible (Wolberg 1990). The radial distortion is modelled in equation (3) by a division model (Fitzgibbon 2001). Wonpil (2003) and Park et al (2009) have computed an approximate transformation for a standard distortion method. Here, the exact inversion of the division model is computed.

Given \( r^w = ||P^w - C|| = ||P^w|| \in \mathbb{R} \), the distance of the undistorted coordinates \( P^w \) from the optic centre \( C \), using equation (2) gives:
\[
r^d = (1 + k(r^w)^2)r^w.
\]
Equations (2) and (8) imply that:

\[ P^u = r^d P^d = W(P^d), \]  

Equation (8) is equivalent to \( kr^d + r^d = 0 \), where \( r^d \) is the discriminant and \( W \) is the inverse transform.

In order to use inverse warping, it is necessary to determine \( W^{-1} \) transforming the undistorted points \( P^u \) into the distorted points \( P^d \). From equation (9), it is equivalent to determine \( r^d \) knowing \( r^u \).

Equation (8) is equivalent to \( kr^d + r^d = 0 \), where \( r^d \) is the discriminant, and \( W^{-1} \) corresponds to the root:

\[ r^d = W^{-1}(r^u) = \frac{1 - \sqrt{1 - 4kr^2}}{2kr^u}. \]

Demonstration: let us demonstrate (i) the positivity of the discriminant and (ii) the choice of the selected root.

We have:

\[ \frac{1}{2} |k| |r^u|^2 > \frac{1}{4} |C| \frac{1}{4.10^{-7}} \]  

which implies that \( 4|k| |r^u|^2 < 8.10^{-1} < 1 \).

Therefore, we have: \( \Delta = 1 - 4kr^2 > 0 \) (i.e. \( q.e.d. \)).

When the discriminant is positive, there exist two roots: (a) \( \frac{1}{2} \frac{\sqrt{\Delta}}{2kr^2} \geq \frac{1}{4} |C| \frac{1}{4.10^{-7}} = 2.5|C| \), which corresponds to a solution where the pixel locations are rejected outside a given radius, 2.5|C|. This is an aberrant solution. (b) \( \frac{1}{2} \frac{\sqrt{\Delta}}{2kr^2} \leq \frac{1}{4} |C| \frac{1}{4.10^{-7}} = 2.5|C| \), which corresponds to a solution where the pixel locations are inside a given radius, 2.5|C|. This is the correct solution (ii).

Therefore, the transformation used is invertible (equation (10)). An invertible image warping method compared to a non-invertible method dramatically reduces the computation time (Wolberg 19990). We experimented a reduction from about 10 min to a few seconds (about 5 s) on a standard computer using Matlab (16 GB RAM, processor Intel i7-4702HQ, 2.20 GHz).

2.7.2. Validation with a public health database
Our method needs to be visually evaluated and compared to other state-of-the-art methods in public health databases used for retinopathy screening. In order to assess the evolution of diabetic retinopathy several screening programs in the world are in existence. Trials have been performed in a database of 69 randomly selected patients coming from the Diabetic Eye Screening Wales (DESW) program in the United Kingdom (Thomas et al 2012). All patients had diabetes and different severity stages, including no signs of retinopathy or maculopathy. All the selected patients have been screened annually for several years, for seven years on average. For each of them we have kept two series of two examinations with an approximate screening interval of one year between the examination events. For each event exam, four images are available, two positions (nasal and macular) per eye. There were two series of images acquired for different years, with the first series made up of 271 pairs of sufficient image quality (63% are acquired with different cameras) and the second series including 268 pairs (9% are acquired with different cameras). In the first series, 11 pairs have a small overlapping area (about 30% of the surface of the registered pair). For each position, we have performed the superimposition of the images between the two different examinations. All the retinal photographs were high quality images made according to a protocol including pupillary dilation.

In addition, in order to show that our method is not only useful on high quality images acquired following pupillary dilation but also on low quality images without dilation of the pupils prior to photography, a second validation test is performed to superimpose the images of low/poor quality for five patients with diabetes. The quality of image superimposition is checked for the 20 pairs of images (i.e. four per patient). The acquisition conditions were significantly harsher compared to the high quality images and the quality of images was quite heterogeneous, in part due to the lack of pupillary dilation prior to
photography. In this database, the patients with diabetes have two retinal examination with at least a year interval using the same camera.

As there is no reference registration for the databases (i.e. no ground truth), for all pairs of images the superimposition has been visually checked by the same expert. The complete overlapping area of each pair has been carefully checked. The classification has been done in two categories: (1) no noticeable difference (i.e. correct) and (2) noticeable difference (i.e. incorrect). The category ‘incorrect’ includes three subcategories: (i) differences of the size of a small diameter vessel, (ii) differences of the size of a large diameter vessel or (iii) even larger. In this paper, the three subcategories have been grouped into a single category ‘incorrect’. For each set of about 270 images, the duration of one check for one model is longer than an hour and a half. For each method and each pair of each set a first check has been done and a second check has been performed for verification by the same person. For almost all the pairs the results have been in accordance between both checks. In the rare cases of discrepancy, an adjudication has always been taken in the most restrictive way (i.e. ‘incorrect’). Therefore, the total duration of the check process was longer than thirty hours for the five methods tested hereinafter.

A visual evaluation has been performed on the two series of high quality images and on the series of low quality images in order to compare our approach to two other well established state-of-the-art whose code is publicly available: ‘gdbicp’ (Stewart et al 2003, Yang et al 2007) or that we have reprogrammed (Lee et al 2007). In particular, we have tested five methods (see table 3):

(i) our method on the normalised images with an automatic choice of one or two radial distortions according to the number of cameras used,
(ii) our model with a single radial distortion for all the original image pairs without colour stabilisation, in order to be similar to the state-of-the-art method of Lee et al (2007),
(iii) the state-of-the-art method ‘gdbicp’ with a quadratic model (Stewart et al 2003) on the original images,
(iv) ‘gdbicp’ with a radial model on the original images (Yang et al 2007),
(v) and ‘gdbicp’ with a quadratic model (Stewart et al 2003) on the normalised images.

Note. To facilitate the comparison between (i) our model and (ii) the model similar to Lee et al (2007), we have performed the model fitting with our method for both models, using the characteristic points extracted by SIFT, whereas Lee et al (2007) use the centreline of the vessels and the branch centres for their model.

3. Results

3.1. Validation by a simulated montage

Using our method, with a single distortion, the mean registration error is of 0.86 pixels (standard deviation 1.75 pixels) in images of size 1568 × 2352 pixels (figure 7) with vessels of maximum diameter of 30 pixels. The relative error with respect to the image diagonal is 0.03%, and with respect to the vessels is 2.9%. With two distortions, the mean registration error is of 0.92 pixels (standard deviation 1.94 pixels) and the relative error is 0.03% with respect to the image and 3.1% with respect to the vessels (see table 1). In figure 7, the error is mainly located on the external part of the superimposed pair of images.

Our method is compared to another state-of-the-art method ‘gdbicp’ which superimposes eye fundus images with a quadratic model (Stewart et al 2003). Using the simulated montage, the mean registration error is 2.44 pixels (standard deviation 1.64 pixels). As a reminder, the model of deformation proposed in this paper with a single radial distortion corresponds to the model of Lee et al (2007), however, with a different method to estimate the parameters.

As a speed test, the duration of the different superimposition methods is measured with the images of the simulated montage (see table 2). The experiments have been done on a new computer (16 GB RAM, processor Intel i7-4702HQ, 2.20 GHz). The inverse warping method with one or two distortions lasts approximately 5.5 s using Matlab.

3.2. Validation with a public health database and comparison to other state-of-the-art methods

A visual evaluation is essential on the public health databases for the five methods previously described.
| Model                                          | Mean (pixels) | Standard Deviation (pixels) | Mean relative error respective to the image (%) | Mean relative error respective to the vessels (%) |
|-----------------------------------------------|---------------|-----------------------------|------------------------------------------------|------------------------------------------------|
| Homography and one radial distortion (normalised images) (our method) | 0.86          | 1.75                        | 0.03%                                           | 2.9%                                           |
| Homography and two radial distortions (normalised images) (our method) | 0.92          | 1.94                        | 0.03%                                           | 3.1%                                           |
| 'gdbicp' quadratic (initial images)            | 2.44          | 1.64                        | 0.08%                                           | 8.1%                                           |
Figure 8. Superimposition of three pairs of eye fundus images with correction of one or two radial distortions. (a) Superimposition of the pair in figures 3(a) and (b), with two radial distortions $\hat{k}_1 = -0.0546, \hat{k}_2 = -0.0646$. (b) Superimposition of the pair in figures 3(c) and (d), with two radial distortions $\hat{k}_1 = -0.0695, \hat{k}_2 = -0.0536$. (c) Superimposition of the pair in figures 4(a) and (b), with a single radial distortion $\hat{k} = -0.0819$.

Table 2. Duration of each method of superimposition.

| Model                                      | Duration (seconds) |
|--------------------------------------------|--------------------|
| Homography and one radial distortion       | 64.5               |
| Homography and two radial distortions      | 71.7               |
| 'gdbicp' quadratic (normalised images)     | 169                |

Table 3. Percentage of correct superimpositions of image pairs of eye fundus in public health databases for different methods and models.

| Model                                           | 1st series—271 pairs (63% different cameras) (high quality images) | 2nd series—268 pairs (9% different cameras) (high quality images) | 3rd series—20 pairs (similar cameras) (low quality images) |
|-------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|------------------------------------------------------------------|
| (i) Homography and one or two radial distortions (normalised images) (our method) | 92%                                                               | 98%                                                               | 100%                                                             |
| (ii) Homography and one radial distortion (original images) (similar to Lee et al (2007)) | 88%                                                               | 95%                                                               | 95%                                                             |
| (iii) 'gdbicp' quadratic (original images) (Yang et al 2007)                | 74%                                                               | 58%                                                               | 40%                                                             |
| (iv) 'gdbicp' radial (original images)                      | 48%                                                               | 33%                                                               | 25%                                                             |
| (v) 'gdbicp' quadratic (normalised images)                  | 88%                                                               | 87%                                                               | 100%                                                            |

Preliminary results have been presented in Noyel et al (2017).

(i) First of all, our superimposition method is applied on standardised images. If the same camera acquired both images of a pair, our model is used with a single radial distortion. If two cameras were used, the model with two radial distortions is applied. In figures 1 and 8, four examples of superimpositions with the radial distortion model are shown. One can notice the good quality of the superimposition. In figures 8(a) and (b), two radial distortions have been used to correct the deformation of two different cameras, whereas in figure 8(c) a single radial distortion corrects the deformation of a single camera. The validation results for the complete database are presented in table 3. In the first series of 271 pairs, two pairs have small differences in the external part of the superimposition. These differences are of the size of the diameter of a vessel (figure 10). When the percentage of overlapping surface is low (around 30%) compared to the surface of the superimposed image, the superimpositions are correct in 92% of the pairs and 96% if we consider the pairs in the same position. In the second series of 268 pairs of images acquired a few years later, the superimposition was successful for 98% of the pairs. Within the pairs incorrectly superimposed, the external part was presenting differences whereas the central part was perfectly superimposed. For both series, for the pairs with sufficient overlap (greater than 50%), no noticeable difference has been perceived between them.

(ii) Our approach is compared to the one similar to Lee et al (2007) (table 3). In the first series with 271 pairs (respectively second series with 268 pairs),
the method similar to Lee et al (2007) finds a superimposition solution for 88% of pairs (respectively 95%), while ours gives a correct result for 92% of the pairs (respectively 98%). In figure 9, with their approach, a noticeable difference appears near a vessel located on the external part of the image, where the effect of the radial deformation is most important, while there is no noticeable difference using our method.

(iii) Our method is compared to the state of the art method ‘gdbicp’ (Stewart et al 2003, Yang et al 2007), which superimposes images with a quadratic model (table 3). In the first series with 271 pairs (respectively second series with 268 pairs), their method has found a superimposition solution for 74% of pairs (resp. 58%) while our method gives a correct result for 92% of the pairs (resp. 98%).

(iv) In addition, when using the ‘gdbicp’ homography and two radial distortions using a multiplicative model—which is therefore not invertible—fewer pairs are registered (48% in the first series and 33% in the second series). The method of ‘gdbicp’ with a quadratic model gives better results for eye fundus images than ‘gdbicp’ with radial distortions. Because ‘gdbicp’ with a quadratic model was specifically designed to superimpose eye fundus images in Stewart et al (2003).

In order to illustrate the robustness of our method, superimposition is performed on the database of five patients with 20 pairs of low quality images. In each case, there was no noticeable difference in the superimposition (i) with our method, even on the border of the images. (ii) The method similar to the one of Lee et al (2007) gives a correct superimposition for 95% of the pairs. (iii) ‘gdbicp’ with a quadratic model 40% and (iv) ‘gdbicp’ with a homography and two radial distortions 25%. In this second validation, our method gives better results than the others.

4. Interpretation and discussion

The accuracy of the superimposition methods has been validated on a simulated montage (table 1). The superimposition error is smaller for our model including one or two radial distortions than with a quadratic model of superimposition such as the one used in the ‘gdbicp’ quadratic (Stewart et al 2003, Yang et al 2007, Jian et al 2010, Adal et al 2014). This confirms the results of Lee et al (2010) who previously showed that quadratic models have a greater error than a homography and a radial distortion model. Such results demonstrate that our method gives a superimposition without noticeable difference by a human observer. Therefore, this approach is suitable to perform analysis of a large public health database.

In terms of speed, our method is 2.4 times faster than the ‘gdbicp’ quadratic (table 2), even using a slower computer language (Matlab versus a compiled language). The duration results show that our method is computationally efficient when analysing large databases. The good speed results are due to the linear estimators of the model parameters and the use of an invertible model of deformation. In future, we will look for an even more efficient implementation using a compiled language, which is faster.

In order to assess the efficiency for public health purposes, our superimposition method has been validated on public health databases with high quality images of 69 patients (two series including 271 pairs and 268 different pairs) and five patients (20 pairs) with low quality images. In the first series, the majority of the pairs were acquired with two cameras while in the second series the majority were acquired with the same camera. Whatever the number of cameras, there is no noticeable difference in the superimposed images if the overlap is sufficient (more than about 50%) (table 3—(i)). For pairs with a small overlapping area, we have developed another algorithm using, in addition to the matched points, the distance between the retinal vessels. This algorithm is similar to those described by Can et al (2002) and Lee et al (2010). These findings will be presented in a future paper.
However, the interest of the superimposition is to compare the evolutions in public health databases over many years, which is only useful when the image overlap is large enough. This means that our method, efficient when the image overlap is sufficient, is suitable to be applied to analyse large databases.

(v) Finally, in order to show the influence of the colour stabilisation on the superimposition, the ‘gdbicp’ method with a quadratic model is applied on images with colour stabilisation (i.e. normalised). The results obtained with colour stabilisation are much better than without: in the first series with 271 pairs, 88% versus 48%, in the second series with 268 pairs, 87% versus 33% and in the third series with 20 low quality pairs of 100% versus 25%.

Compared to the other state-of-the-art method of Lee et al (2007) made of homography and a single distortion (ii), for all three series of images, our method (i) systematically improves the obtained results (table 3). This result is due to the use of two radial distortions, instead of one, when images of different size are acquired by different cameras. This shows the importance of using an adapted model to the type of cameras.
used to acquire a pair of images. Therefore, our model goes further than the previous one (Lee et al 2007) that did not take into account the change of camera. We underline that in Lee et al (2007, 2010) the authors were interested in large mosaicking with images acquired using the same camera during the same patient examination, and therefore they were using a corresponding database (i.e. images of similar colour and same distortion parameter). Our database is made of images from patients acquired with at least a year interval by different cameras and they may be of low quality.

Compared to the method ‘gdbicp’ quadratic (Yang et al 2007) (iii), which uses a quadratic model, our method (i) better registers the eye fundus images. Our method better still superimposes the images than the method ‘gdbicp’ quadratic with normalised images (v). However, when the image overlapping area is small (i.e. less than 50%), the ‘gdbicp’ quadratic (v) better registers than our method. This is due to the detection of vessel landmarks, which makes the model fitting more efficient with a small overlap. However, in this image configuration, the superimposition solution given by the ‘gdbicp’ quadratic ((iii), (v)) often presents a strong shearing deformation that has no physical justification. This means that the quadratic model is not well adapted when the overlapping area is small. This confirms the results obtained by Lee et al (2010) who have shown that quadratic models introduce more errors than models based on a homography and a radial distortion. Indeed, with 12 parameters to be fitted (versus 8 parameters for our model—6 for the homography and 2 for the radial distortions) quadratic models have a greater degree of freedom, which is a source of additional errors. Therefore, our model goes further than the previous approaches with quadratic models (Can et al 2002, Lee et al 2010, Jian et al 2010, Adal et al 2014). When the overlapping area is small (less than 50%), the method ‘gdbicp’ quadratic with normalised images (v) is complementary to our method (i) due to the detection of vessel landmarks.

To summarise the comparison, our method (i) better superimposes the images of our public health databases (table 3). The second model is the one of Lee et al (2007) (ii), whose results are systematically improved by our method. The third method is the ‘gdbicp’ quadratic (Yang et al 2007) (iii) which is improved when normalising the images (v). The method gdbicp’ quadratic, and also the method described in Lee et al (2007), is based on the detection of vessel landmarks. Therefore, when they are used on images with a small overlap, the vessel detection makes them more efficient and complementary to our method. We will present such an improvement for our method in a future paper.

The results obtained with the validation montage and with the public health databases demonstrate that our model better corrects the errors coming from the different positions of the patient during image acquisition, the change in the camera employed (resolution and optical lenses) and the projection of a 3D scene onto a plane and the variability of colour between images.

In addition, the colour stabilisation step is useful when images have strong contrast variations. The results obtained with the ‘gdbicp’ quadratic with the colour stabilisation (v), which are better than and without (iii), show the importance of using normalised images for colour in public health databases (table 3). In our method (i), the SIFT points are extracted and matched on the normalised images for colour contrast before estimating the registration model. Experiments have shown that using normalised images gives more robust results when extracting and matching the SIFT points, even if these points are known to be robust to colour variations (Lowe 2004, Vedaldi and Fulkerson 2008). Importantly, even when using normalised images with ‘gdbicp’, our method remains better.

Moreover, our method has been tested for images acquired with a field of view (FOV) of 45° which are used for DR screening by single-field fundus photography (Williams et al 2004). In addition, our approach could be useful for automatic detection of referral patients due to diabetic retinopathy (Fleming et al 2010, Decencièrre et al 2013, Abramoff et al 2013, Quellec et al 2016).

Despite the good results obtained, our method does have a limitation. For images with a smaller overlap (e.g. 30% of the surface of the mosaic image), the superimposition may present small differences on the external part. To address this issue, we have developed another algorithm using, in addition to the matched points, the distance between the vessels. It will be presented in a future paper.

5. Conclusions

We have therefore successfully achieved a new method to answer the main challenges to superimpose eye fundus images coming from large public health databases. In addition to the previously existing methods, ours has been designed to deal with changes in terms of camera, lens, image resolution and strong colour variations between two retinal exams. The presented method consists of fitting a registration model composed of a homography and one or two radial distortions on salient points extracted in images after colour stabilisation. The choice between the number of radial distortions is made automatically depending of the number of cameras used to acquire the pair of images. Then, the image warping is performed using a division model, which is invertible, which makes it fast to compute. Linear equations are introduced to estimate the parameters of the model in a fast way, followed by non-linear estimators. Importantly, the method is easy to use and does not require
one to extract intrinsic characteristics such as the vessels or their branch points.

The efficiency of our method has been validated on a simulated montage with a superimposition error, which is less than the error of a quadratic model. Its efficiency has also been demonstrated on public health databases with high quality images and images of lower quality, due to differences in the conditions of acquisition, and pairs of images acquired with the same or different cameras. Nevertheless, the results show that there is no noticeable difference between the images from two examinations with the eye in the same position (nasal or macular). The superimposition is correct in more than 92% of cases (96% with an overlapping area greater than 50%). In these databases, our method better superimposes the images than the two state-of-the-art methods of Lee et al (2007) and of ‘gbipc’ (Stewart et al 2003, Yang et al 2007).

Conflict of interest

No conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ORCID

G Noel https://orcid.org/0000-0002-7374-548X

References

Abramoff M, Niemeijer M, Lee S and Reinhardt J 2012 Optimal registration of multiple deformed images using a physical model of the imaging distortion Google Patents University of Iowa Research Foundation

Abramoff M D et al 2013 Automated analysis of retinal images for detection of referable diabetic retinopathy JAMA Ophthalmol. 131 351-7

Adal K M, Ening R M, Couvert R, van Etten P, Martinez J P, Vermeer K A and van Vliet L J 2014 A hierarchical coarse-to-fine approach for fundus image registration Biomedical Image Registration (London: Springer) pp 93–102

Bonnans J F, Gilbert C, Lemaréchal C and Sagastizabal C A 2006 Numerical Optimization. Theoretical and Practical Aspects (Berlin: Springer) (https://doi.org/10.1007/978-3-540-34447-9)

Can A, Stewart CV, Rosyn B and Tanenbaum H L 2002 A feature-based, robust, hierarchical algorithm for registering pairs of images of the curved human retina IEEE Trans. Pattern Anal. Mach. Intell. 24 674–67

Cattin P C, Bay H, Van Gool L and Székely G 2006 Retina mosaicking using local features Medical Image Computing and Computer-Assisted Intervention—MICCAI 2006 ed R Larsen et al (Berlin: Springer) pp 185–92

Chanwimaluang T, Fan G and Fransen S R 2006 Hybrid retinal image registration IEEE Trans. Inf. Technol. Biomed. 10 129–42

Cideciyan A V 1995 Registration of ocular fundus images: an algorithm using cross-correlation of triple invariant image descriptors IEEE Eng. Med. Biol. Mag. 14 52–8

Decencière E et al 2013 TeleOphtha: machine learning and image processing methods for teleophthalmology IRBM 34 196–203

Fang B and Tang Y Y 2006 Elastic registration for retinal images based on reconstructed vascular trees IEEE Trans. Biomed. Eng. 53 1183–7

Fitzgibbon A W 2001 Simultaneous linear estimation of multiple view geometry and lens distortion Proc. IEEE Computer Society Conf. Computer Vision and Pattern Recognition (https://doi.org/10.1109/cvpr.2001.993465)

Fleming A D, Gostman K A, Philip S, Prescott G J, Sharp P F and Olson J A 2010 Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts Br. J. Ophthalmol. 94 1606–10

Ghassabi Z, Shanbehzadeh J, Sedaghat A and Fatemizadeh E 2013 An efficient approach for robust multimodal retinal image registration based on UR-SIFT features and PIHFD descriptors EURASIP J. Image Video Process 2013 25

Harding S, Greenwood R, Aldington S, Gibson J, Owens D, Taylor R, Kohnert E, Scanlon P and Lee J 2003 Grading and disease management in national screening for diabetic retinopathy in England and Wales Diabet. Med. 20 965–71

Harley R and Zisserman A 2004 Multiple View Geometry in Computer Vision (Cambridge: Cambridge University Press) (https://doi.org/10.1017/cbo9780511811685)

Hernandez-Matas C, Zabulis X and Argyros A A 2016 Retinal image registration through simultaneous camera pose and eye shape estimation IEEE 38th Annual Int. Conf. of the Engineering in Medicine and Biology Society (EMBC) (https://doi.org/10.1109/EMBC.2016.7594121)

International Diabetes Federation and The Fred Hollows Foundation 2015 Diabetes Eye Health. A Guide for Health Professionals (Brussels: International Diabetes Federation and The Fred Hollows Foundation)

Jian C, Jie T, Lee N, Jian Z, Smith R T and Laine A F 2010 A partial intensity invariant feature descriptor for multimodal retinal image registration IEEE Trans. Biomed. Eng. 57 1707–18

Lee S, Abramoff M D and Reinhardt J M 2007 Feature-based pairwise retinal image registration by radial distortion correction Proc. SPIE 6512 651220

Lee S, Abramoff M D and Reinhardt J M 2008 Retinal image mosaicing using the radial distortion correction model Proc. SPIE 6914 691435

Lee S, Reinhardt J M, Cattin P C and Abramoff M D 2010 Objective and expert-independent validation of retinal image registration algorithms by a projective imaging distortion model Med. Image Anal. 14 539–49

Lin Y and Medioni G 2008 Retinal image registration from 2D to 3D Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognition (IEEE) pp 1–8

Llort D, Serrat J, Lopez A M, Soler A and Villanueva J J 2009 Retinal image registration using creases as anatomical landmarks IEEE 15th Int. Conf. on Pattern Recognition pp 203–6

Lowe D G 2004 Distinctive image features from scale-invariant keypoints Int. J. Comput. Vis. 60 91–110

Maintz J B A and Viergever M A 1998 A survey of medical image registration through simultaneous camera pose and eye shape estimation IEEE 38th Annual Int. Conf. of the Engineering in Medicine and Biology Society (EMBC) (https://doi.org/10.1109/EMBC.2016.7594121)

Matsopoulos G K, Mouravliansky N A, Delibasis K K and Nikita K S 1999 Automatic retinal image registration scheme using global optimization techniques IEEE Trans. Inf. Technol. Biomed. 3 47–60

More J J 1978 The Levenberg–Marquardt algorithm: implementation and theory Numerical Analysis: Proceedings of the Biennial Conference Held at Dundee (28 June – 1 July 1977) ed G A Watson (Berlin: Springer) pp 105–16

More J J 1983 Recent developments in algorithms and software for trust region methods Mathematical Programming: The State of the Art ed A Bachem et al (Berlin: Springer) pp 258–87

Noyel G, Jourlin M, Smans M, Thomas R, Iles S, Bhakta G, Crowder A, Owens D and Boyle P 2017 American Diabetes Association 77th Scientific Sessions—ADA2017 (San Diego, CA) (http://abstractsonline.com/p8/#/4297/presentation/45074 and https://hal.archives-ouvertes.fr/hal-01539980)
Oliveira F P and Tavares J M 2014 Medical image registration: a review Comptes Rendus Biomech. Biomed. Engin. 17 73–93
Park J, Byun S-C and Lee B-U 2009 Lens distortion correction using ideal image coordinates IEEE Trans. Consumer Electronics 55 987–91
Pluim J P, Maintz J B and Viergever M A 2003 Mutual-information-based registration of medical images: a survey IEEE Trans. Med. Imaging 22 986–1004
Quellec G, Lamard M, Erginay A, Chabouis A, Massin P, Cochener B and Cazuguel G 2016 Automatic detection of referral patients due to retinal pathologies through data mining Med. Image Anal. 29 47–64
Ritter N, Owens R, Cooper J, Eikelboom R H and van Saarloos P P 1999 Registration of stereo and temporal images of the retina IEEE Trans. Med. Imaging 18 404–18
Ryan N, Heneghan C and de Chazal P 2004 Registration of digital retinal images using landmark correspondence by expectation maximization Image Vis. Comput. 22 883–98
Sotiras A, Davatzikos C and Paragios N 2013 Deformable medical image registration: a survey IEEE Trans. Med. Imaging 32 1153–90
Stewart C V, Tsai C L and Roysam B 2003 The dual-bootstrap iterative closest point algorithm with application to retinal image registration IEEE Trans. Med. Imaging 22 1379–94
Sturmfels B 2002 Solving Polynomial Equations (CBMS Regional Conference Series in Mathematics vol 97) (Providence, RI: American Mathematical Society)
Thomas R L, Dunstan F, Luzio S D, Roy Chowdury S, Hale S L, North R V, Gibbins R L and Owens D R 2012 Incidence of diabetic retinopathy in people with type 2 diabetes mellitus attending the diabetic retinopathy screening service for wales: retrospective analysis Br. Med. J. 344 e874
Vedaldi A and Fulkerson B 2008 VLFeat: an open and portable library of computer vision algorithms (http://vlfeat.org/)