

A Review on Medical Image Registration Techniques

Shadrack Mambo, Karim Djouani, Yskandar Hamam, Barend van Wyk, Patrick Siarry

Abstract—This paper discusses the current trends in medical image registration techniques and addresses the need to provide a solid theoretical foundation for research endeavours. Methodological analysis and synthesis of quality literature was done, providing a platform for developing a good foundation for research study in this field which is crucial in understanding the existing levels of knowledge. Research on medical image registration techniques assists clinical and medical practitioners in diagnosis of tumours and lesion in anatomical organs, thereby enhancing fast and accurate curative treatment of patients. Literature review aims to provide a solid theoretical foundation for research endeavours in image registration techniques. Developing a solid foundation for a research study is possible through a methodological analysis and synthesis of existing contributions. Out of these considerations, the aim of this paper is to enhance the scientific community's understanding of the current status of research in medical image registration techniques and also communicate to them, the contribution of this research in the field of image processing. The gaps identified in current techniques can be closed by use of artificial neural networks that form learning systems designed to minimise error function. The paper also suggests several areas of future research in the image registration.

Keywords—Image registration techniques, medical images, neural networks, optimisation, transformation.

I. INTRODUCTION

IMAGE processing is a highly researched field due to its many areas of application such as medical imaging, Geographical Information System (GIS) and mapping, satellite communications, biomedical engineering, robotics, remote sensing, among others. It encompasses image registration, image segmentation and edge detection, image enhancement and restoration, image compression and pattern recognition. The importance of medical imaging as a core component of several medical application and healthcare diagnosis cannot be over emphasised. Integration of useful data acquired from different images is vital for proper analysis of information contained in the images under observation. For the integration process to be successful, a procedure referred to as image

registration is necessary. Image registration process compares a source image with a reference image in order to best find a geometric transformation that portrays good spatial correspondence between them by optimising a registration criterion. The parameters used during image registration to find a geometric transformation can be computed directly or searched for. Image registration process has four distinctive steps. First, feature extraction is carried out to identify features in two images. Secondly, pairing process is done to determine which feature in one image should be aligned with which feature in the other image. Thirdly, calculation of transformation is done, which is the step where mathematical operation that would be necessary to align the sets of paired features is found. Finally, application of transformation is done, where the results of the calculation are applied to all pixels or voxels in one image set in order to align to the other image. This paper carried out literature review on 2D-3D and 4D image registration techniques, where the merits and demerits of these techniques are analysed. Literature review on various transformation models and optimisation methods are also discussed. The paper comprises six sections. The first section covers the introduction. The second section addresses literature review on image registration techniques, while the third and fourth sections cover literature review on transformation models and optimisation methods, respectively. The fifth section covers literature review on performance evaluation. The sixth section deals with conclusion which identifies the gap in image registration techniques and suggests the way forward.

II. MEDICAL IMAGE REGISTRATION TECHNIQUES

Medical image registration algorithm is classified into three major areas namely, the similarity measure, the transformation model and the optimisation process. Recent research work on review of image registration techniques was done by [1]-[4]. Survey of medical image registration on graphics hardware was been carried out by [2], where an analysis of different approaches to programming on graphics processing units (GPU), programming models and interfaces were presented. Another survey of deformable image registration (DIR) for lung stereotactic body radiotherapy (SBRT) was carried out by [5]. These researchers also discussed two forms of evaluation, namely commissioning and daily practice or daily clinical use of DIR. An interactive multigrid refinement using digital B-Splines for DIR has been presented by [6] that models an interactive refinement for both auto and manual processes. B-Splines are applied because they

S. M. Mambo is with the French South Africa Technology Institute (F'SATI), Electrical Engineering Department, Tshwane University of Technology (TUT), Pretoria, South Africa (e-mail: mambosf@tut.ac.za or mainmambo@gmail.com).

K. Djouani is Full Professor and SARChI Chair at University Paris Est-Creteil (UPEC), France and French South Africa Technology Institute (F'SATI), Electrical Engineering Department, Tshwane University of Technology, Pretoria, South Africa.

Y. Hamam is Emeritus Professor at ESIEE, Paris, France and French South Africa Technology Institute (F'SATI), Electrical Engineering Department, Tshwane University of Technology, Pretoria, South Africa.

B. J. van Wyk is Full Professor at French South Africa Technology Institute (F'SATI), Electrical Engineering Department, Tshwane University of Technology, Pretoria, South Africa.

P. Siarry is Full Professor at University Paris Est-Creteil (UPEC), France.

are computationally efficient even under changing data points. Image registration techniques are categorized according to the following approaches: geometric-based approaches, intensity-based approaches or the combination of both known as hybrid approaches as discussed by [7]. Geometric-based approaches have explicit models, fast optimisation procedures and are used for rigid or affine transformations that require user intervention to identify landmarks. Feature extraction steps determine the accuracy of registration. By use of a mathematical or statistical criteria, intensity patterns are matched using intensity-based approaches as shown by [7], which define the measure of intensity similarity between source and reference images. Determination of the transformation that optimises the voxel similarity measure is then carried out. Hybrid approaches are a combination of both the geometric and the intensity based approaches. The combined advantages of both geometric-based and intensity-based approaches are utilized in hybrid approach to achieve more accurate registration. Several methods have been proposed for medical image registration. According to [3], they are classified depending on the following criteria: image dimensionality, nature of registration basis, nature of transformation, domain of transformation, degree of interaction, optimisation procedure, modality, subject and object. These classifications have further subdivisions such as 2D, 3D, and 4D in image dimensionality; intensity-based, feature-based or control point-based registration in nature of registration; rigid, affine, projective, perspective and curved in nature of transformation; global and local in domain of transformation; interactive, semi-automatic or automatic in degree of interaction; continuous and discrete in optimisation procedure; mono-modal and multi-modal in modality; intra-subject, inter-subject and atlas in subject, and brain, lung, breast etc. in object. Enormous amount of research has been dedicated in the field of image registration which has generated many innovative ideas regarding the algorithmic registration steps. Comprehensive scientific reviews in this field have been proposed by [1], [2], [8], [9].

A. Intensity-Based Registration

An exhaustive discussion for intensity-based image registration was done by [4], [10] where simplicity and memory capacity, high accuracy and growth of computational speed were the main findings. 2D-3D image registration methods do not require user interaction as discussed by [11]. The author recommended Powell-Brent search strategy for intensity-based 2D-3D image registration in cerebral interventions due to its good performance and concluded his work by showing that further research on the influence of optimisation method based on intensity approach on 2D-3D image registration needed to be done. Intensity-based registration methods have wide areas of application ranging from registering images with the same or different dimensionalities, intra-modality or inter-modality images to rigid transformation or deformable images. The similarity measures or cost functions used with intensity-based registration methods include: Sum of Squares Differences

(SSD); Correlation Coefficient (CC); Ratio-Image Uniformity (RIU); Partition Intensity Uniformity (PIU); Joint Histogram and Joint Probability Distribution (JPDF); Joint Entropy (JE); Mutual Information (MI) and Normalised Mutual Information (NMI). Research on intensity-based 3D image registration using local smoothing statistical procedures was proposed by [12], where the geometric transformation does not require any parametric form nor other global regularisation conditions.

B. Feature-Based Registration

Researchers [13] discussed use of unsupervised deep feature learning independent bases for medical image registration. They sought to address limitations for supervised deep learning-based methods by considering the feature spaces present in image patches. 3D/2D registration with superabundant vessel reconstruction is introduced by [14] to address the standard problem of reconstruction in establishing one-to-one correspondence. Control point-based registration provides for manual selection of common features in an image to map to the same pixel location. This method is best suited for images with distinct features. Correspondence establishment between detected set of candidate points in the source image and reference image is done using a search procedure that minimises dissimilarity metric, as discussed by [15]. Feature-based image registration detects feature points in both the source and reference images. It finds corresponding pairs and computes image transformation. Detectors such as Harris corner detector, Scale Invariant Feature Transform (SIFT) detector and Random Sample Consensus (RANSAC) are used in this registration. Researcher works by [16], [17] presented use of RANSAC algorithm and SIFT features for feature-based image registration. A method for fitting digital line and plane to a consensus sets of points in 2D and 3D images susceptible to noise was proposed by [18], where a comparison of the proposed algorithm was done with RANSAC method. Feature-based image registration methods are used when local structure image data is much higher than data carried by image intensity, can handle complex distortions between images and are faster. They rely on relatively small number of features and do not evaluate a matching criteria for every single pixel. The general process includes identifying features in two images which are then paired to determine which feature in one image should be aligned to the other image. A calculation step then follows where the mathematical operation necessary to align sets of paired images is done. Finally application of transformation is done where the results of the calculations are applied to all pixels or voxels in one image that will be aligned with another image. Researchers [19] presented automatic multimodal 2D-3D breast image registration using biomechanical models and intensity-based optimisation. Research based on elastic image registration was proposed by [20], who developed Elastix, a toolbox for intensity-based medical image registration. Another linear elastic model-based image registration algorithm was proposed by [21], where robustness of the registration accuracy was the key finding. In the work of [22], an automatic algorithm for registration of multimodal images was outlined, which

demonstrated the ability to identify optimum registration, nonlinear transformations of tie points as well as a high degree of accuracy as compared to the manual algorithm. This algorithm produced results which showed that the automatic operator worked much better than the manual operator. In order to increase the speed of registration, researchers [22] suggested use of known complex search methods as areas of investigation for future research. In their research, [23] presented robust image registration based on mutual information measure and showed that it was a highly effective method for registration of multi-modal medical images.

Research carried out by [24] recommended future use of artificial neural networks (ANN) in medical image registration during pre-processing and post-processing stages. Computational intelligence with neural networks cover applications in medical imaging such as medical image registration, medical image content analysis used in edge detection, segmentation, breast cancer screening, and computer-aided detection and diagnosis as shown by [25]. Neural networks are designed to find varying solutions through competitive learning, self-organising maps (SOM) and grouping method or clustering to provide and process input features, as well as give the best possible alignment during registration between different images or datasets.

Recently discovered 4D imaging techniques such as 4D-computed tomography (CT), 4D-cone beam computed tomography (CBCT), 4D-magnetic resonance imaging (MRI), and 4D-positron emission tomography (PET) are effective tools used in spatial and temporal definition of tumor target volume in human anatomy. 4D-4D image registration as presented by [26] sort to establish a spatio-temporal correspondence between a set of input images, determine the transformation matrix $T(x, t)$ that maps an arbitrary point (x, t) from the source image to the corresponding point (x', t') on the reference image or vice versa. During the iterative optimisation of the metric function, the following basic operations on the moving image set are involved: translation in the x, y, and z directions and in the temporal axis; nonuniform scaling in the x, y, and z directions and in the temporal axis, and rotation in 3D space. Automated 4D-4D image registration as shown by research findings of [26] can find the best possible spatio-temporal match between two 4D data sets and is useful in all the 4D applications mentioned above. Image registration procedures for spatio-temporal alignment of image sequences using time series calculations were discussed by [27]. Researchers [28] presented 3D surface-based deformable models for nonrigid medical image registration. Geometric-based method for nonrigid 3D medical image registration and fusion was discussed and evaluation of registration using Dice Similarity Coefficient and Hausdorff distance was performed. An approach that uses surface information to carry out elastic image registration was also presented by the same researchers. Non-rigid registration of 3D medical images using some special techniques of the grid deformation and multi-grid optimisation methods was presented by [29]. In their research on non-rigid registration of images for medical applications, researchers [29] gave two drawbacks for non-rigid registration as speed and

non-existence of a general standard method for assessing and evaluating the success of the registration technique. A non-rigid medical image registration method based on improved linear elastic model discussed by [21] proved that not only high registration accuracy was achieved, but also enhanced robustness and anti-noise properties of the registration algorithm. A volume based multi-modal medical image registration using partial volume interpolation and sum of conditional variance as a similarity metric was proposed by [30]. The development of non-rigid registration techniques is an open area for further research and most algorithms are under different stages of evaluation and validation.

A method utilising of local invariant features for accurate and quick registration of cardiac images were presented by [31], which outperforms traditional sift invariant feature transform. Researchers [32] proposed invariant feature matching for image registration application using novel dissimilarity of spatial features that relies on dissimilarity values between two distinct features. The dissimilarity metrics applied improved matching technique accuracy. In their research on image registration via combining local features and geometric invariants, [33] employed computer vision oriented fast and rotated brief algorithms, in which features are extracted using Hamming distance criterion together with K nearest neighbour for bidirectional matching constraint. Research by [34] proposed retinal image registration via feature-guided Gaussian Mixture Model (GMM), which addressed the issue of lack of true correspondence in low-quality retinal images. A two step registration framework for multimodal retinal images was proposed by [35], which outperformed state-of-art traditional methods after quantitative and qualitative evaluations were carried out. In order to obtain good multiresolution registration that ensures convergence is not trapped in local minima, [36] proposed group-wise similarity registration using t-mixture model, which is a special form of GMM. Another multimodal retinal image registration using edge map and GMM was proposed by [37], where maximum likelihood framework was used to solve the problem. Novel research by [38] proposed image registration based on autocorrelation of local image structures. This research helped alleviate the confounding effect of signal intensity fluctuation caused by large deformation due to structural movement in images. In their research, [39] presented feature-based non-uniform meshing algorithm for deformable image registration, that gave better registration results when a larger normalized cross correlation value is obtained.

III. TRANSFORMATION MODELS

Transformation in image registration is defined as the coordinate mapping from the reference image domain to the source image domain. Precise image registration is a crucial preprocessing step for many tasks in image registration techniques as discussed by [40]. The fundamental characteristic of any image registration technique is the type of spatial transformations or mapping used to properly overlay two images, details of which are given by [41]. Several of these

transformations exist such as rigid, affine, global, projective, and perspective. The following are the types of transforms and their mathematical formulations commonly used in image registration:

Translation:

$$T_{\mu}(x) = x + t \quad (1)$$

Rigid or Euler Transform:

$$T_{\mu}(x) = R(x - c) + t + c \quad (2)$$

Similarity:

$$T_{\mu}(x) = sR(x - c) + t + c \quad (3)$$

Affine:

$$T_{\mu}(x) = A(x - c) + t + c \quad (4)$$

B-Spline:

$$T_{\mu}(x) = x + \sum_{x_k \in N_x} \rho_k \beta^3 \frac{x - x_k}{\sigma} \quad (5)$$

where,

$T_{\mu}(x)$ - is the transform;

t - is translation;

c - is a constant;

s - is similarity;

R - is rotational matrix;

A is matrix without restrictions;

x_k are control points;

p_k is B-Spline coefficient vector (control points displacement);

σ is B-Spline control point spacing;

N_x is set of all control points with the compact support of the B-Spline at x ;

$\beta^3(x)$ is the cubic multidimensional B-Spline polynomial.

Transformation model can be subdivided into rigid and non-rigid as illustrated in the work of [42]. Rigid registration finds the various degrees of freedom, namely three rotational and three translational forms of transformation that map any point in the source image into the corresponding points in the reference image. They are best in applications where there is virtually little or no change in shape or location of the structure. Transformation parameters in 2D rigid transformation are discussed by [43] in detail. In their research, [44] developed a rigid point set registration method based on the application of genetic algorithms and Hausdorff distance. The proposed method, unlike other methods that match two intensity images, can match a set of data extracted from an image. Non-rigid registrations are usually applied on imaged body organs which undergo soft-tissue type of deformation. Researchers [20] made a comparison of accelerated techniques in medical image registration and introduced a fast non-rigid registration that allows on-line updating of treatment plan.

Diffeomorphism is defined as one-to-one, differentiable, invertible and smoothing mapping. Large deformation diffeomorphic metric mapping (LDDMM) is a framework in which the optimal velocity fields are time-dependent and geodesic, which are discussed in detail by [45], [46]. It statistically compares images and shapes as well as creation of atlases. LDDMM is a nonlinear registration technique

that defines diffeomorphic transformations between images in which anatomical structures and sub-structures are maintained, as shown by [47]. This algorithm enhances registration accuracy and, by minimising the function of velocity field vector in deformation flow, it resolves registration between two images in an Euler-Lagrange framework by applying gradient descent as discussed by [45]. Research by [48] presented step-wise inverse consistent Euler's scheme for diffeomorphic image registration. The challenges of LDDMM include memory and time consumption as well as practical use limited to small deformations even though designed for large deformations. Log-Demons or spectral Log-Demons uses spectral correspondence to find similarity between reference image and source image. The general Log-Demon framework comprises an input which has reference image, source image and an initial velocity field, and an output consisting of a transformation from the reference image to the source image as detailed by [49]. Thin plate spline, as shown by [50], also referred to as surface spline is commonly used in non-rigid medical image registration as a transformation function, which is presented by [51] and [52] in their research. Together with Gaussian and multi-quadric functions, thin-plate spline form radial basis functions. Their common properties include providing optimally smooth deformations, are generally stable for weight estimation for different configurations of points, and are expensive to re-evaluate whole image match because a change of location on any landmark changes the whole deformation field.

Similarity measure is the second part of a registration process that computes the degree of alignment of the images. It can be categorised into two approaches, namely feature-based and voxel-based similarity measures. Feature-based approach, shown by researchers [53] requires a feature extraction step which can bring an error that can generally affect the registration algorithm and cannot be reversed later, as indicated by [29]. Voxel-based approach aims at determining the degree of similarity in the image intensities. Voxel similarity measures are generally preferred methods for measuring image similarity because of being robust and accurate. According to [11], the three similarity measures that give good accuracy and robust results are gradient descent, gradient correlation and pattern intensity. In their research, [54] concluded that the choice of the characteristic of the cost function and the search strategy used determines how successful the registration process will become. Single modality image registration is best done using invariant moments while multi-modality image registration is best done using mutual information similarity measure. For images with rotational differences, cross correlation coefficients and invariant moments types of similarity measures are the best to apply. Mutual information similarity measure has highest sensitivity to image similarity, as presented by [55] because it is not calculated based on pixel by pixel value but by use of histogram of the gray scale values of two images. Similarity measures are also considered during image registration process. The two commonly used types of similarity measures are difference measures and statistical measures. Difference measures are the simplest and belong to a class of similarity measures known

as point-wise measures as indicated in research done by [56]. They are based on differences of intensities between the source and reference images. The most popular statistical measures include Correlation Coefficient (CC), Mutual Information (MI) and Entropy Correlation Coefficient (ECC) shown in the research by [56].

IV. OPTIMISATION TECHNIQUES

The optimisation process is the last component of image registration algorithm. Optimisation method is a procedure that finds various parameters that optimise a given similarity measure. A dependable optimiser will reliably and quickly find the best possible transformation. The dependency of the registration result on the optimisation strategy follows from the fact that image registration is inherently ill-posed as proposed by [57]. Registration via optimisation is a variational-based approach as shown by [57], which allows a sound mathematical treatment, characterization, formulation as well as classification of the most used procedures. Optimisation-based registration is classified according to the area to which deformations belong, either rigid or non-rigid. Rigid, sometimes referred to as affine, registration process depends on some selected few parameters, while spline-based approaches usually have very high-dimensional transformation area. During image registration, issues such as ill-conditioning, instability of solutions and non-convexity of the cost functions occur which can be alleviated by introduction in the optimisation problem, of a regularisation and additional penalty term. Researchers [58] presented robust rigid registration of retinal angiogram images through systematic comparison of different optimisation techniques such as Nelder-Mead local search and ant colony metaheuristic.

The most commonly used optimisation algorithms are gradient descent as presented by [1], Powell [11], non-conjugate gradient descent, stochastic gradient descent and Marquardt-Levenberg methods presented by [1]. Recent research produced other approaches like local perturbation as illustrated by [59], global optimisation approaches such as stochastic global optimisation, convex optimisation, stochastic approximation, exploration or selection, sequential Monte Carlo technique and library-based optimisation. Optimisation problems can be classified as deterministic and non-deterministic. In deterministic optimisation problems, neither randomness nor uncertainty are taken into account as shown by [60], and they are very simple to solve. However, in non-deterministic optimisation problems, which reflect actual optimisation problems, noise or uncertainties occur in the form of randomness. Stochastic optimisation is very useful during design, analysis, and operation of modern systems. Optimisation problems seek to determine a configuration or design that minimises the cost function as shown by [60].

$$\min_{\theta \in \Theta} J(\theta) \quad (6)$$

where, θ is a p-dimensional vector of all decision variables, commonly represented by x in mathematical programming, and Θ is the feasible region.

If the cost function $J()$ is linear in θ and Θ can be expressed as a set of linear equations in θ , then we have a linear program. Similarly, if $J()$ is convex in θ and Θ is a convex set, then we have a convex optimisation problem. Another definition of the optimisation problem can be presented as follows:

$$\text{minimise}_{x \in R^n} := g(x) + h(x) \quad (7)$$

where, g is a convex, continuously differentiable function, and h is a convex but not necessarily differentiable penalty function or regulariser. Proximal Newton-type procedures inherit the desirable convergence behaviour for minimising smooth functions. The minimisation of the cost function follows line search methods as per

$$x_{k+1} = x_k + t_k \Delta x_k \quad (8)$$

where, t_k denotes a scalar gain factor that controls the step size in the search direction;

Δx_k is the search direction at iteration k and means that several iterations of an algorithm are carried out.

The search direction and the gain factors are chosen such that the sequence x_k converges to a local minimum of the cost function. Approaches towards stochastic simulation optimisation were discussed by [60]. Model-based approaches and meta-heuristics can improve image registration processes because with reference to simulation optimisation, the handles associated with the search have been eliminated, and therefore allocation of simulation replications to different or alternative designs can be carried out efficiently. Meta-heuristics start with an initial population of designs. These approaches can be used for performance evaluation when the design area is being searched for. This is because generation of a good population of designs requires that iteration to iteration in the search process be carried out. Several research works on optimisation on image registration can be found in [11], [43], [61]-[63]. In their research work, [64] designed a powerful tool whose framework uses an engine that compares different registration approaches and hence makes the tool suitable for easy integration, optimisation and evaluation. This tool contributes immensely in establishment and optimisation of image registration techniques due to its ability to be automated. As a result a lot of time is saved in clinical application procedures. The research work by [65] in its contribution explains that the choice of optimisation procedure adopted significantly impacts on the computation time, accuracy and robustness of the registration method used, which in turn influences the clinical procedures and the turnaround time for diagnosis and therapy treatment. In the research by [66], [67], a stochastic adaptive descent optimisation method for image registration with adaptive step size prediction was presented, which provided a solution to Robbin-Monro scheme's shortcoming of the need for a predetermined step size function. The main advantage of adaptive stochastic gradient descent optimiser stemmed from the fact that random sampling of the data in the computation of the derivatives was utilized, which translated into a meaningful reduction of computation time. A comprehensive review of

2D-3D registration based on optimisation procedure has been proposed by [1] for image-guided interventions.

V. PERFORMANCE EVALUATION

Several performance evaluation methods for medical image registration techniques have been discussed in literature. A comparative evaluation study of target tumor volumes acquired from deformable image registration of PET/CT scans was presented by [68], where the properties of tumor volumes were compared. Significant improvements in target volumes were observed compared to gross tumor volumes contoured on planning CT. Researchers [69] proposed evaluation of deformable image registration using free form deformation and demons' methods for dose monitoring. Mutual information and mean square error metrics were applied. A comprehensive evaluation using B-Spline free form deformation, different variants of demons and optical flow methods were proposed by [70] in their research on improving oncological breast tumor bed localisation using image registration algorithms. The results of their research showed that symmetric demons method provided the most accurate alignment in reconstruction of deformable field. Research done by [71] discussed performance evaluation of different systems on a common database. An investigation on detection performance combining individual systems and objective evaluation framework were carried out and the observer study proved that the best nodule detectors were by expert readers. Medical image registration evaluation using qualitative meta analysis review was presented by [72], which was based on analysis of qualitative research data from other studies of similar or related findings. Researchers [73] evaluated several medical image registration techniques for generality, accuracy, robustness using public software tools and databases to ensure reproducibility. They found deformable registration via attribute matching and mutual-saliency (DRAMMS) and advanced normalised tools (ANTS) to be among the best algorithms. Comparative study and evaluation of estimation of lung motion fields using intensity-based image registration was proposed by [74]. Their study sort to complement existing multi-institutional comparison studies. An evaluation method to quantify the quality of a similarity metric in medical image registration of brain images was proposed by [75]. The similarity measure applied in their research was normalised spatial mutual information which was found to have high robustness compared to other metrics. A systematic evaluation of interpolation effect on upsampling and accuracy in automatic image registration was carried out by [76]. Comparison was carried out using qualitative interpolation error measurement, visual expert assessment and run time determination. Performance evaluation of several deformable image registration algorithms for thoracic 4D CT images was carried out by [77]. Various commercially or publicly available DIR algorithms were applied and the results showed that better accuracy was achieved in optical flow, Demons and B-Splines algorithms. Research done by [78] proposed performance evaluation of 3D local surface descriptors with low as well as high resolution range image data. Range imaging registration

is applied in digitising shapes for 3D objects and provides accurate and low cost means of processing.

VI. CONCLUSION

A literature review for medical image registration techniques was carried out, where a methodological analysis and synthesis of literature on earlier research was outlined. Advantages and shortcomings of various image registration methods were identified. Ways of closing the identified gaps have been suggested and areas of future research development suggested. Current optimisation techniques used in medical image registration tend to have high computational and memory demands because of dense sampling of displacement space. The other draw back is lack of iterative solution and image interpolation coupled with no known standard procedure. These gaps can be closed by use of artificial neural networks, which are computational systems consisting of simple processing units that form learning networks designed to minimise error function in an iterative gradient descent algorithm. The impact of optimisation method on intensity-based 2D-3D image registration has not been investigated fully. There is need to use the theoretical convergence properties of optimisation to derive an image driven selection mechanism for the required parameters. The derivation can be based on known characteristics of the objective functions that generally occur in intensity-based image registration problems. Use of complex search methods such as artificial neural networks (ANN) as areas of investigation for future research is highly recommended. Another area of future research exploitation is the development of non-rigid registration techniques. Adaptation of approaches towards simulation optimisation where model-based approaches and meta-heuristics are applied is another area recommended for future research.

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Shadrack Mambo is an engineer and a lecturer at Kenyatta University. He received his Masters degree in Radio and TV Engineering from Odessa National State Polytechnic University in Odessa, Ukraine. He worked for various telecommunications companies as an engineer rising to the position of General Manager in engineering services. In 2006, he joined academia as a lecturer at Kenyatta University and held various key positions such as Founding Chairman of Electrical Engineering Department and later as Dean, School of Engineering and Technology. Shadrack is a member of: Institute of Electrical and Electronic Engineers (IEEE), Engineers Registration Board of Kenya (EBK) and Institute of Engineers of Kenya (IEK). He is currently a fulltime Doctorate of Technology (DTech) student undertaking research on Optimisation and Performance Evaluation in Image Registration Techniques under the supervision of Prof. Karim Djouani, Prof. Yskandar Hamam, Prof. Ben Van Wyk, all from the Electrical Engineering Department, Tshwane University of Technology (TUT), and Prof. Patrick Siarry from University Paris Est Creteil (UPEC) under the Cotutelle PhD programme. The research is funded through a grant by Tshwane University of Technology.