Retrospective Motion Correction in Digital Subtraction Angiography: A Review

Erik H. W. Meijering, Wiro J. Niessen, Max A. Viergever

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Abstract—Digital subtraction angiography (DSA) is a well-established modality for the visualization of blood vessels in the human body. A serious disadvantage of this technique, inherent to the subtraction operation, is its sensitivity to patient motion. The resulting artifacts frequently reduce the diagnostic value of the images. Over the past two decades, many solutions to this problem have been put forward. In this paper, we give an overview of the possible types of motion artifacts and the techniques that have been proposed to avoid them. The main purpose of this paper is to provide a detailed review and discussion of retrospective motion correction techniques that have been described in the literature, to summarize the conclusions that can be drawn from these studies, and to provide suggestions for future research.

Keywords—Digital subtraction angiography, motion correction, registration, matching.

Abbreviations

nD	n-dimensional, $n \in \{1, 2, 3\}$
CBC	coincident bit counting
CC	correlation coefficient
DSA	digital subtraction angiography
DSC	deterministic sign change
DSR	digital subtraction radiography
ECG	electrocardiogram
ENT	entropy of the histogram of differences
EHD	energy of the histogram of differences
FOV	field of view
MAC	minimal artifacts criterion
NCC	normalized cross-correlation
PC	phase correlation
SAVD	sum of the absolute values of differences
SPD	sum of positive differences
SSC	stochastic sign change
SSD	sum of squared differences
SDT	sum of the absolute values of differences above a threshold
VOD	variance of differences

I Introduction

Over the past two decades, DSA has become a well-established modality for the visualization of blood vessels in the human body [10, 34, 59, 71, 73, 84, 92, 109, 114, 115, 131, 160]. With this technique, a sequence of 2D digital X-ray projection images is acquired to show the passage of a bolus of injected contrast material through the vessels of interest. In the images that show opacified vessels (often referred to as *contrast images* or *live images*), background structures are largely removed by subtracting an image acquired prior to injection (usually called the *mask image*).[1]

It is obvious that in the resulting subtraction images, background structures will have been completely eliminated only in those situations where these structures are exactly aligned and have equal grey-level distributions. Clinical evaluations of DSA, following its introduction in the early 1980s, revealed that this is not the case for a substantial number of examinations. Images taken at different time instances will always differ in some respect, due to fluctuations in the power of the X-ray source, or noise in the image intensifier and the subsequent imaging chain. However, the main cause of differences is *patient motion*. In the literature on DSA imaging one can find many examples of cases in which the artifacts caused by patient motion reduced the quality of the images to the extent that they became diagnostically useless.

In order to cope with this problem one may endeavor to prevent patient motion, by taking special precautions concerning either the patient or the acquisition system, or both. However, in many cases artifacts can not be entirely avoided and one is forced to resort to retrospective motion correction techniques, which constitute the main subject of this paper. Although there exists quite some literature on the subject, it appeared to us that frequently "new" ideas are published, without reference to similar work previously done by other researchers. In view of future research, it is very useful and advantageous to have an overview of the techniques and evaluations published so far, and of the conclusions that can be drawn from them. It is the purpose of this paper to provide such an overview.

This paper is organized as follows. In Section II, we will summarize the types of motion artifacts most frequently reported in the literature, as well as the solutions that have been proposed to prevent them. In the subsequent sections we will focus on retrospective motion correction. In Section III, full account will be given of the validity of such an approach in the particular case of DSA. In Section IV we will elaborate on the various aspects of retrospective motion correction by image registration and grey-level distortion correction. The advantages and disadvantages of the various techniques will be discussed in Section V. Concluding remarks are made in Section VI.

II Motion Artifacts and Possible Solutions

Before going into details about retrospective motion correction, we will first give an impression of the types of motion artifacts that may be encountered. We will also summarize the techniques that have been proposed to avoid motion artifacts.[2] A brief introduction into retrospective motion correction will conclude this section.

[1] The idea of subtraction of angiographic images for the enhanced visualization of vascular structures was first described by Ziedses des Plantes, in the 1930s [168,169]. For a brief historical review on the development of subtraction techniques in angiography the reader is referred to Verhoeven [160], or Jeans [71].

[2] We note that the literature overview presented in this section is by no means complete. In nearly every paper on examinations using DSA one can find some discussion on problems concerning motion artifacts.

II.A Examples of Motion Artifacts

Although gross movement during the acquisition of X-ray image sequences can usually be avoided with a cooperative patient, involuntary local motion of particular organs is practically inevitable. For example, most patients cannot resist an urge to swallow or cough, the resulting artifacts of which may cause difficulties in the interpretation of DSA images of the carotid arteries [12,28,65,103,114,137,149]. The pulsatile motion of arteries in combination with the presence of calcifications may cause problems in studies of the carotid bifurcation [12,33,39,149].

Artifacts caused by bowel gas and the peristaltic motion of intestines may cause difficulties in studies of the splenic and portal veins [51], or of renal vascular abnormalities [63,64]. Respiratory and cardiac motion may cause misregistration artifacts in images of the thoracic and abdominal regions [7], in particular the pulmonary [96,126] and cardiovascular systems [103,162].

Sudden motion of arms and legs degrades the visualization of peripheral arteries [56, 144]. When using automated stepping, the time span between the acquisitions of mask and contrast images is relatively large, and therefore patient motion frequently occurs [41]. Especially in examinations of the lower peripheral vasculature, artifacts can be very misleading, since the lateral displacement of a leg may produce artifacts along bone-tissue transitions that very much resemble vessels [160].

II.B Patient-Related Solutions

Early attempts to reduce motion artifacts in DSA images focused on techniques to avoid patient motion during exposure. In many cases patient motion is initiated by the sudden sensation of heat caused by the contrast material [141, 160]. To reduce these reactional flexes it has been suggested to use non-ionic instead of ionic contrast media [33, 77], although other studies showed no difference in imaging quality [141,149].

Immobilization of the head prevents motion artifacts in DSA images of the neck and head [40,138]. This technique can also be applied to peripheral DSA [41]. To some extent, artifacts caused by respiratory motion can be avoided by applying generous amounts of oxygen before injection, thereby allowing patients to hold their breath for a longer period of time [77]. Deep inspiration pulls the diaphragm down and eliminates the inhomogeneity of dense abdomen, *e.g.* when imaging the thoracic aorta [7]. In other cases, *e.g.* hepatic or carotid DSA, it has been shown that motion artifacts are better reduced by an expiration holding method [72,164].

Several methods have been proposed to avoid or reduce artifacts caused by peristalsis. For example, administration of glucagon prior to contrast material injection temporarily diminishes peristaltic activity [14, 58, 64, 108, 125]. Alternative solutions are the use of a compression band in order to displace overlying stomach and bowel [7, 63, 64], or to turn the patient in prone position in order to displace bowel gas [58, 140].

II.C Acquisition-Related Solutions

Another line of research has focused on modifications of the acquisition system, by exploiting *a priori* knowledge about the nature of patient motion or the properties of the contrast material (iodinated solutions) and the tissues to be imaged. An example of this is the use of sophisticated filtering techniques. Temporal band-pass or band-reject filters may offer a higher degree of immunity to some types of patient motion than mask-mode subtraction [78]. Especially with rapid periodic motion, *e.g.* caused by cardiac pulsation, grey-level variations often contribute to specific parts of the temporal frequency spectrum, which can subsequently be filtered out using a band-pass filter.[3] This has shown to be successful in a number of cases [80, 112]. Given the contrast dilution curve, even better results can be obtained by using a *matched filter*, which maximizes iodine signal to noise and dose efficiency [79, 95, 128–130].

Another means of exploiting *a priori* knowledge is subtraction of images acquired at different energy levels. The energy dependent linear X-ray attenuation coefficient of iodine shows a discontinuity at 33keV, whereas the attenuation coefficients of bone and soft-tissue vary only gradually as a function of energy. This implies that the iodine contrast in images obtained using X-rays above this edge is larger than in images obtained with X-rays below this edge. Subtraction will result in a reduction of background structures, while the iodine contrast is greatly enhanced [66, 81].[4] Since the time span between the acquisitions can be made very small (a few milliseconds), patient motion is limited. However, this technique is successful only if the X-rays are nearly monoenergetic, which puts high demands on the X-ray generator.

Alternative energy subtraction techniques make use of X-ray spectra with average energies above the absorption edge of iodine. Since the contributions to X-ray attenuation of photoelectric absorption and Compton scatter are different for bone and soft-tissue, a linear combination of images obtained at different average energy levels allows for selective cancellation of either bone or soft-tissue [11, 89].[5] Such techniques may be incorporated into a so-called *hybrid subtraction* scheme [9], comprising both energy and temporal subtraction. With cooperative patients, artifacts are mainly due to involuntary motion of soft-tissue, *e.g.* in examinations of the carotid arteries or the abdominal areas. Dual energy subtraction can be used to remove soft-tissue structures from both mask and contrast images, while temporal subtraction eliminates residual bone structures. Although hybrid subtraction may be successful in patient motion reduction, the improvements are obtained at the cost of an increase in patient exposure and a decrease in the signal-to-noise ratio [9, 15, 50, 55, 97, 145].[6]

Depth information may be useful in regions that show independently moving superimposed structures, such as in abdominal images, or in regions with superimposed iodinated structures, such as the coronary arteries and the chambers of the heart [10]. Therefore, it has been proposed to use tomographic DSA to isolate arteries within a single anatomic plane. Kruger *et al.* [3, 83] described an approach in which the image intensifier and the plane of projection are moved in such a way that only a single plane of the exposed 3D scene is in-focus. The contributions of out-of-focus planes can be diminished by applying the aforementioned temporal band-pass filtering techniques. It is also possible to reconstruct multiple planes of focus from a single set of projection images, without additional X-ray exposure [36, 57, 85, 94, 100, 101].[7]

In some cases motion artifacts may be reduced by choosing a different mask image. A system for automatic remasking during acquisition was mentioned by Oung & Smith [113]. Using a real-time motion detector, based on computing the variance of the histogram of grey-values in successive subtraction images, which can be considered a measure of

[3]Note that low-pass filters are not adequate for this purpose because they do not remove stationary background anatomy [80].

[4]Since the discontinuity at 33keV corresponds to the K-shell absorption energy level of iodine, this technique is often referred to as K-edge energy subtraction.

[5]This is known as *dual energy subtraction*.

[6]To some extent, this may be compensated for by applying matched filtering [127].

[7]This is known as *tomosynthesis*.

similarity between mask and contrast images (see also Section V.B), a new mask image was selected as soon as the measure exceeded a predefined threshold.

Finally, we mention the possibility of motion-synchronized gating of X-ray exposure. For example, artifacts due to the pulsatile motion of vascular structures, as caused by cardiac pulsation, may partially be avoided by using images acquired during the same cardiac phase.[8] The gating pulses of ECG-equipment are related to the QRS-complex in the ECG-curve, and may be exploited to trigger X-ray exposure. ECG-gating has been successfully applied in studies of the aortic arch and carotid arteries and bifurcations [5, 33, 52, 53, 74, 116]. Alternatively, gating may be triggered by internal densitometric measurements of cardiac and respiratory motion [139].

II.D Retrospective Image Processing Solutions

Although the techniques mentioned in Sections II.B and II.C may provide a remedy in specific cases, to some extent patient motion always occurs, causing the subtraction images to show artifacts that may hamper the interpretation of the images and, consequently, proper diagnosis. In such situations, motion artifacts may be corrected for retrospectively, by means of image registration and grey-level distortion correction techniques. With these techniques the images in a sequence are analyzed so as to retrieve a geometrical transformation that accounts for the changes caused by patient motion, and to bring the mask image in optimal correspondence with the contrast image prior to subtraction.

The simplest approach in this respect is probably the manually controlled translation of the mask image with respect to the contrast image, a technique often referred to as *pixel shifting.* Since in DSA systems images are acquired, stored, and processed digitally, this technique is quite easy to implement and it has been applied since the early 1980s [59, 93]. In fact, it is still the only available motion correction technique on current clinical DSA systems. Obviously, pixel shifting provides a solution only in those situations where artifacts have been caused by gross translational motion. In most cases, patient motion is more complex and can not be modeled by such a basic transformation. Although pixel shifting may reduce artifacts in some parts of the image, in the remainder of the image artifacts will inevitably be reinforced or even newly created, as already pointed out by Levin *et al.* [93].

In order to correct for more complex patient motion, registration techniques should be designed so as to have more local control. An example of this is the approach described by Pickens *et al.* [119], in which second order polynomials were used to define the geometric transformation of the mask. The 12 parameters of the transformation were determined by manually selecting six points in the mask image, as well as the six corresponding points in the contrast image, and by solving the system of equations that resulted after substitution of these points into the transformation. Higher-order polynomials can be used to define the transformation, simply by incorporating more control points.

However, as also pointed out by Pickens *et al.*, manual selection of corresponding points introduces the possibility of operator error. In order to avoid operator-induced problems, the registration operation should be automated to the highest possible degree. Many techniques have been developed for this purpose. In the subsequent sections we will analyze the validity of retrospective motion correction by image registration and grey-level distortion correction, and review the techniques that have been proposed to perform these tasks in DSA.

[8] Since vessels spend most of their time at or near positions corresponding to the end-diastolic phase, images are preferably acquired during this phase [160].

III Retrospective Motion Correction: Preliminaries

It is important to note that the individual X-ray images in digital angiography are in fact 2D projections of 3D anatomical structures. This implies that in the case of patient motion, differences between the 2D mask and contrast images are the result of a 3D transformation of these structures. In an attempt to correct for the artifacts in the resulting subtraction images retrospectively, the use of 2D registration techniques is justified only when it can be shown, at least theoretically, that it is possible to construct a 2D geometrical transformation that completely accounts for the projective effects of a 3D transformation. In this section it will be argued that, although this is indeed the case, in practice the extraction of such a transformation from the projection images is limited.

III.A The Existence of a 2D Geometrical Transformation

In X-ray projection imaging, the grey-value of an arbitrary pixel in an image is determined by the energy flux, or intensity, Φ, of the X-rays incident on the corresponding detector element. In principle, $\Phi(\mathbf{x}),\ \mathbf{x} \in \mathbb{R}^2$, is constituted by the contributions of all particles in the 3D scene, according to the relationship:

$$\Phi(\mathbf{x}) = \int_0^\infty \mathcal{S}(\mathbf{x}, E)\mathrm{e}^{-\mathcal{L}(\mathbf{x},E)}dE, \tag{1}$$

where E denotes energy, $\mathcal{S}(\mathbf{x}, E)$ is the energy spectral density, at the source, of the X-rays incident on the detector matrix at position $\mathbf{x}$, and $\mathcal{L}(\mathbf{x}, E)$ is the line-integral given by:

$$\mathcal{L}(\mathbf{x}, E) = \int_0^1 \mu(\lambda_{\mathbf{x}}(\xi), E)d\xi. \tag{2}$$

Here, μ denotes the linear X-ray attenuation coefficient, which is dependent on the type of material (accounted for by a position dependency), as well as on the energy E of the rays. Integration of μ is carried out along the linear path as traversed by the ray, *i.e.*, from the source to the element at position $\mathbf{x}$ on the detector matrix, of which $\lambda_{\mathbf{x}} : [0, 1] \to \mathbb{R}^3,\ [0, 1] \subset \mathbb{R}$ is a parametric representation.

Although, in practice, X-rays will be polyenergetic, *i.e.*, $\mathcal{S}$ is non-zero for a certain range of energies, it is common use to assume the rays to be *mono*energetic, *i.e.*, $\mathcal{S}(\mathbf{x}, E) = \Phi_\varnothing(\mathbf{x})\delta(E - E_q)$, where E_q is the energy level of the X-ray quanta and $\Phi_\varnothing(\mathbf{x})$ is the energy flux that is measured when the traversed path $\lambda_{\mathbf{x}}$ is completely in vacuum (no material encountered by the rays). In this case, Φ is given by Lambert-Beer's law:[9]

$$\Phi(\mathbf{x}) = \Phi_\varnothing(\mathbf{x})\mathrm{e}^{-\mathcal{L}(\mathbf{x},E_q)}. \tag{3}$$

After logarithmic post-processing and calibration with respect to $\Phi_\varnothing$, the grey-value I at position $\mathbf{x}$ in the resulting image is given by:[10]

$$I(\mathbf{x}) \propto \mathcal{L}(\mathbf{x}). \tag{4}$$

Starting from (4), the problem of the existence of a 2D geometrical transformation that accounts for the projective effects of a 3D transformation was studied by Fitzpatrick [42].

[9] After the Swiss-German mathematician and physicist J. H. Lambert (1728–1777) and the German physicist A. Beer (1825–1863). It is a combination of Lambert's law (also known as Bouguer's law) from optics, which relates the amount of light absorbed and the distance it travels through an absorbing medium, and Beer's law, which relates absorption and the concentration of the absorbing substance.

[10] Since E_q is fixed, it is left out for convenience hereafter.

He argued that, since the total amount of attenuation of X-rays, as caused by the material in a confined volume, can be changed only by transport of particles across the boundaries of that volume, the attenuation coefficient μ behaves as the density of a conserved quantity, for which the continuity equation from continuum mechanics and fluid dynamics holds.[11] Using the continuity equation he proved that, given two X-ray projection images $I_0(\mathbf{x}) = I(\mathbf{x}, t_0)$ and $I(\mathbf{x}) = I(\mathbf{x}, t)$, taken at times t_0 and $t \neq t_0$ respectively, there always exists a one-to-one 2D mapping $\Psi : \mathbb{R}^2 \rightarrow \mathbb{R}^2$ that transforms points $\mathbf{x}_0 \in \mathbb{R}^2$ in I_0 into their corresponding points $\mathbf{x} = \Psi(\mathbf{x}_0)$ in I, and that the associated change in grey-value is given by the following relation:[12]

$$I(\mathbf{x}) = J_{\Psi}^{-1}(\mathbf{x}_0) I_0(\mathbf{x}_0), \tag{5}$$

where J_{Ψ}^{-1} is the inverse Jacobian of the mapping Ψ. As argued by Fitzpatrick [44], the factor J_{Ψ}^{-1} will be finite and larger than zero for all transformations describing physical motion. In regions where Ψ describes local expansions of tissues, $J_{\Psi}^{-1} < 1$, and in regions where Ψ describes local contractions, $J_{\Psi}^{-1} > 1$. For in-plane rigid motion of tissues in the 3D scene, this factor will be equal to one.[13]

III.B Limitations in Transformation Recovery

As emphasized by Fitzpatrick [42], his proof shows only that at least one such image transformation *exists*.[14] It does not yield a recipe for retrieving a transformation from the two images. In fact, in most practical cases it will be impossible to retrieve a transformation that exactly satisfies (5). There are at least three reasons for this:

(i) Since we are dealing with discrete images, measurement of the displacement at a certain pixel in the image inevitably involves incorporation of neighboring pixels into the computations: in all practical situations, comparison of individual pixels is useless and some form of regularization in required. In the case that the changes in a neighborhood have been caused by the uncorrelated motion of several superimposed objects, the result of the measurement can be expected to be entangled.[15]

(ii) Due to the limited FOV of the image intensifier, the images I_0 and I are defined only on a confined domain, $\mathbf{D} \subset \mathbb{R}^2$, and do not contain any information about the displacement of particles that entered or left the FOV. In the particular case of angiography, the presence of additional contrast in one of the images, as caused by the introduction of contrast material into the scene, may pose a serious problem.

(iii) At pixels that lie on isophotes in the image, it is impossible to retrieve the tangential component of the displacement vector, since motion in the tangential direction does

[11] See *e.g.* Condon & Odishaw [31].

[12] The proof was subject to a few constraints that are easily met in X-ray projection imaging. Although it was based on the assumption of orthogonal projections, it was argued that a similar proof, though more complex, can be constructed in the case of perspective projections.

[13] Note that (4) implies that $I(\mathbf{x}) = a\mathcal{L}(\mathbf{x})$, where a is a constant. If $a > 0$, local expansions will result in a decrease of local grey-values in the resulting projection images, whereas local contractions will result in an increase of local grey-values. On the other hand, if $a < 0$, local expansions or contractions will cause the grey-values to increase or decrease, respectively. In either case, (5) holds.

[14] In fact, given the two images I_0 and I that differ as a result of a single 3D transformation, there exist infinitely many mappings Ψ for which (5) holds.

[15] This problem was also alluded to by Kruger *et al.* [80].

not cause a change in the local appearance of the image.[16] In the field of (computer) vision this ambiguity problem is generally known as the *aperture problem* [62, 102].

In addition to these fundamental problems, there are other factors that may complicate the process of finding the optimal correspondence between successive images. These are due to imperfections of the acquisition system, such as limited spatial resolution, grey-level quantization, noise, or the effects of time-varying scatter, X-rays being non-monoenergetic, or beam hardening, which causes the assumption of proportionality (4) between the line-integral of the attenuation coefficient and the actual grey-values to be valid only approximately. However, these effects have been shown to be negligible [44, 47, 49, 118].

IV Retrospective Motion Correction: Techniques

The problem of finding the correspondence between images appears in many situations. Surveys of registration techniques have been described by Aggerwal & Nandhakumar [1] and Brown [13], and in the field of medical imaging by Van den Elsen *et al.* [150] and Maintz & Viergever [98]. However, as these papers aim at providing a general review of the subject, they tend to be rather superficial with respect to specific applications. In this section we present a detailed overview of the techniques that have been proposed to perform the registration task in the particular field of DSA.

In principle, techniques for the automatic computation of local motion, or displacement of certain objects or structures, can be divided into two categories: (i) (gradient-based) *optic-flow* techniques, and (ii) *template-matching* based techniques. In order to allow for the application of any of these techniques to the problem of registration of digital X-ray projection images, account must be given of the validity of their basic assumptions for this particular type of images. In a previous paper [106], we have discussed the issue of optic flow versus template matching. It was concluded that the basic assumptions of optic flow techniques do not apply to digital X-ray projection imaging, except in the case of parallel projection and in-plane rigid body motion in the original 3D scene. In addition, these techniques suffer from all of the problems mentioned in Section III.B. Although optic-flow techniques have been applied to X-ray angiographic images for motion analysis of the heart [107], and for the determination of blood flow [2], they have, to our knowledge, never been used to solve the registration problem for these type of images. Therefore, they are not considered further in this paper.

Template-matching techniques are based on the assumption that a local displacement, $\mathbf{d} = (d_x, d_y)$, of a structure in one image I_0 can be estimated by defining a certain window $\mathcal{W}$ (say $K \times L$ pixels in size) containing this structure, and by finding the corresponding window in a second image I in the sequence by means of correlation.[17] Although these techniques also suffer from the aperture problem and the problem of superimposed and independently moving structures, they can be made much more robust against the presence of additional contrast in some parts of the live images, *viz.*, by applying a similarity measure that is relatively insensitive to local grey-level changes.[18] Since, in angiographic images, the contrasted blood vessels are the objects of interest, this is an important property. In the following subsections we will elaborate on the various aspects of template-matching based motion correction in DSA.

[16] Note that this holds true only for certain types of rigid motion, *viz.*, for which $J_\Psi^{-1} = 1$ in (5).
[17] Not necessarily in the mathematical sense of the word.
[18] We will return to this issue in Sections IV.B and V.B.

IV.A Complexity of the Transformation

Since template-matching algorithms can be computationally very expensive, it is usually not a viable approach to use them to compute the displacement explicitly for every pixel in the image. Therefore, most template-matching based motion correction techniques compute the optimal correspondence only for a limited number of windows, or regions of interest. This imposes limitations on the complexity of the geometrical transformation that can be constructed and therefore on the complexity of the patient motion that can be corrected for.

In the simplest case, the entire mask image is used as a template, which amounts to taking a single window of size $M \times N$, where M and N are, respectively, the x and y dimension of the image.[19] This has been used, *e.g.*, by Potel & Gustafson [120]. Since it is not possible with this approach to correct for patient motion other than gross translation and rotation, it boils down to automated pixel shifting. In order to correct for more local translational and rotational motion, the window should be reduced to a confined part of the image. Examples have been described by Venot *et al.* [154, 157, 158], Wu *et al.* [166], Hua & Fram [67] and Tianxu *et al.* [147], where the windows were user-defined regions of interest. Registration in a larger part of the image can then be obtained simply by defining more regions of interest, that may differ in size. Pickens *et al.* [118] and Fitzpatrick *et al.* [43, 44, 46–49] described a more flexible approach, where the transformation of a quadrilateral region of interest is not determined by translation and rotation of the entire window, but rather by the independent displacement of the four constituent corner points. This allows for the construction of more complex geometrical transformations, in particular the one-to-one polynomial mappings from the class proposed by Fitzpatrick & Leuze [45]. This approach has also been used by Mandava *et al.* [99].

More sophisticated algorithms are those in which the displacement vectors at a larger number of so called *control points* are considered samples of the original displacement vector field, and from which a global geometrical transformation is constructed by means of interpolation. The displacement vectors at the control points are, again, computed by applying template matching to small windows around these points. With this approach, the size of the windows is not determined by the dimensions of the region of interest as indicated by the user, but rather by the minimum amount of information required to obtain reliable estimates for the displacements of the corresponding control points. This, in turn, depends highly on the criterion that is employed to determine similarity (see Section IV.B), and may also depend on image content. Control points may be chosen on a regular grid, from which a global displacement vector field can easily be computed, *e.g.*, by defining a quadrilateral mesh, and by using bilinear interpolation within every individual quadrilateral, as has been described by *e.g.* Takahashi *et al.* [146], Morishita & Yokoyama [110], Wilson *et al.* [163], Zuiderveld *et al.* [170, 171], Roos & Viergever [133–135], Van Tran & Sklansky [152, 153], Cox & De Jager [32] and Ko *et al.* [76]. Hayashi *et al.* [61] used cubic B-splines to construct the complete displacement vector field.

By using a regular grid, control points are chosen without taking into account the image content within the corresponding windows. However, it is well-known that, regardless of the employed similarity measure, template-matching techniques tend to yield unreliable results in or near homogeneous regions. To correct for this, Zuiderveld *et al.* [170, 171] proposed to track down unreliable displacement vectors *a posteriori* and to bring them into agreement with the displacement vectors of neighboring control points by means of

[19] In digital angiographic images $M = N$, where M is usually 512 or 1024 pixels.

iterative relaxation.[20] Buzug *et al.* [16, 17, 19, 21, 24, 25] proposed to use an exclusion technique, by which grid points in regions with insufficient contrast variation are excluded *a priori* from the set of control points.[21] Although, with this approach, the remaining control points are still on the regular grid, it is no longer possible to define a quadrilateral mesh. In order to obtain a complete displacement vector field, they used the displacement vectors at the control points to compute an affine transformation [17,19–21,23–25].[22] They also experimented with elastic transformations [16,22,25], using radial basis functions, in particular thin-plate splines [6].

The exclusion concept can be taken one step further by dismissing the regular grid paradigm and by extracting regions with sufficient contrast variation *prior* to control-point selection. The first steps in this direction can be attributed to Yanagisawa *et al.* [167]. They proposed to use the displacement vectors at a limited number of control points (being the centers of user-defined regions containing interesting structures) to determine the global translation and rotation in a least-squares sense, and to interpolate the residual local displacement vectors onto the remainder of the image by means of radial basis functions. In recent publications [104, 106] we have argued that, since in the subtraction images artifacts will appear only in those regions where strong object edges are present in the unsubtracted images, the selection of control points should be based on an edge detection scheme. We have used Canny's operator [26] to detect edges in the mask image, and to extract control points by means of a three-parameter algorithm based on assumptions about the coherence of image structures. To obtain the complete displacement vector field we used linear interpolation within the individual polygons of the Delaunay tessellation that can be constructed from the resulting set of irregularly distributed control points.

IV.B Similarity Measures

Even if the constructed mesh of control points is capable of accurately modeling the geometric transformation induced by patient motion, the algorithm will be useless if the template-matching operation fails to yield the correct displacement vectors. The most important aspect of template matching is therefore the similarity measure that is used to determine the amount of correspondence between windows in successive frames. Many measures have been devised and applied to X-ray angiographic data. Here we will briefly describe each of them.

IV.B.1 Correlation-Based Measures

In digital image processing, the use of correlation for the purpose of image registration has been proposed since the 1970s [54,122,123,136]. The *normalized cross-correlation* (NCC) similarity measure is computed as:

$$\mathcal{M}_{\text{NCC}}(\mathbf{d}) = \frac{\sum_{\mathbf{x}\in\mathcal{W}} I_0(\mathbf{x}) I(\mathbf{x}+\mathbf{d})}{\sqrt{\sum_{\mathbf{x}\in\mathcal{W}} I_0^2(\mathbf{x}) \sum_{\mathbf{x}\in\mathcal{W}} I^2(\mathbf{x}+\mathbf{d})}}, \tag{6}$$

[20] Displacement vectors were considered unreliable if either the curvature of the match surface around the optimum was too low, or the vector's deviation from neighboring vectors was too large.

[21] Determined by computing the entropy of the grey-value distributions in the windows in the mask image around these points, and by applying a threshold.

[22] Since this is an over-constrained problem, they used singular value decomposition to obtain the best result in the least-squares sense.

which is the zero-mean version of the *correlation coefficient* (CC) measure:[23]

$$\mathcal{M}_{\mathrm{CC}}(\mathbf{d}) = \frac{\sum_{\mathbf{x}\in\mathcal{W}}[I_0(\mathbf{x}) - \langle I_0\rangle_{\mathcal{W}}][I(\mathbf{x}+\mathbf{d}) - \langle I\rangle_{\mathcal{W},\mathbf{d}}]}{\sqrt{\sum_{\mathbf{x}\in\mathcal{W}}[I_0(\mathbf{x}) - \langle I_0\rangle_{\mathcal{W}}]^2 \sum_{\mathbf{x}\in\mathcal{W}}[I(\mathbf{x}+\mathbf{d}) - \langle I\rangle_{\mathcal{W},\mathbf{d}}]^2}}, \tag{7}$$

where $\mathbf{d} = (d_x, d_y)$ denotes the local displacement vector and

$$\langle I_0\rangle_{\mathcal{W}} = \frac{1}{KL}\sum_{\mathbf{x}\in\mathcal{W}} I_0(\mathbf{x}) \quad \text{and} \quad \langle I\rangle_{\mathcal{W},\mathbf{d}} = \frac{1}{KL}\sum_{\mathbf{x}\in\mathcal{W}} I(\mathbf{x}+\mathbf{d}) \tag{8}$$

denote the mean values of the image intensities in the respective windows. Both measures are to be maximized. Since in digital angiographic images the grey-values are positive integers, in the range $[0, G]$ say,[24] it follows that $\mathcal{M}_{\mathrm{NCC}} \in [0,1] \subset \mathbb{R}$ and $\mathcal{M}_{\mathrm{CC}} \in [-1,1] \subset \mathbb{R}$. Note that $\mathcal{M}_{\mathrm{NCC}}$ assumes its maximum value only when $I_0(\mathbf{x}) = \kappa I(\mathbf{x}+\mathbf{d})$, while $\mathcal{M}_{\mathrm{CC}}$ assumes its maximum when $I_0(\mathbf{x}) = \kappa_1 I(\mathbf{x}+\mathbf{d}) + \kappa_2$, where κ, κ_1 and κ_2 are constants.[25]

These measures have been applied to the registration problem in DSA by Potel & Gustafson [120], Yanagisawa *et al.* [167], and Takahashi *et al.* [146], and have later been mentioned by many others in discussions on comparative evaluations of similarity measures (see further Section V.B).

Correlation-based measures can also be constructed in the frequency domain. If two images, or windows within the images, I_0 and I, are assumed to differ as a result of only pure translational motion, *i.e.*, $I_0(\mathbf{x}) = I(\mathbf{x}+\mathbf{d})$, it can easily be derived that their Fourier transforms, $\tilde{I}_0$ and $\tilde{I}$, respectively, are related by

$$\tilde{I}_0(\mathbf{f}) = \mathrm{e}^{\mathrm{i}2\pi\mathbf{f}\cdot\mathbf{d}}\tilde{I}(\mathbf{f}), \tag{9}$$

where $\mathbf{f} \in \mathbb{R}^2$ denotes 2D frequency and $\mathrm{i} = \sqrt{-1}$ is the imaginary unit number. That is, the images, or windows, have identical Fourier spectra up to a phase difference that corresponds to the relative displacement.

Using (9), one readily derives the cross-power spectrum, $\mathcal{S}$, of I_0 and I:

$$\mathcal{S}(\mathbf{f}) \triangleq \frac{\tilde{I}_0(\mathbf{f})\tilde{I}^*(\mathbf{f})}{|\tilde{I}_0(\mathbf{f})\tilde{I}^*(\mathbf{f})|} = \mathrm{e}^{\mathrm{i}2\pi\mathbf{f}\cdot\mathbf{d}}, \tag{10}$$

where $\tilde{I}^*$ is the complex conjugate of $\tilde{I}$. The inverse Fourier transform of the complex conjugate of $\mathcal{S}(\mathbf{f})$ will yield a Dirac delta pulse, $\delta(\mathbf{x}-\mathbf{d})$, with the position of the pulse corresponding to the displacement $\mathbf{d}$. This observation has led to the introduction of the *phase-correlation* (PC) measure, defined as:

$$\mathcal{M}_{\mathrm{PC}}(\mathbf{d}) = \mathcal{F}^{-1}[\mathcal{S}^*(\mathbf{f})], \tag{11}$$

[23] Note that although (6) and (7) are the formal definitions of these measures, the normalized cross-correlation and correlation coefficient are usually not exactly computed this way. Several components of these measures, such as $\langle I_0\rangle_{\mathcal{W}}$, $\sum_{\mathbf{x}\in\mathcal{W}} I_0^2(\mathbf{x})$, and $\sum_{\mathbf{x}\in\mathcal{W}}[I_0(\mathbf{x}) - \langle I_0\rangle_{\mathcal{W}}]^2$, are independent of $\mathbf{d}$ and can therefore be precomputed. Normalization with respect to I_0 can even be omitted, without altering the final result (*i.e.*, the displacement vector $\mathbf{d}$ that yields the largest correlation value). Also, in order to be able to apply these measures (and the ones described hereafter), one will have to decide on how to treat windows that extend beyond the image borders. In the sequel of this section we will present only the basic principles and definitions, without going into implementation-related details.

[24] With current DSA devices, the quantization precision is usually 10 bits, which implies that $G = 1023$.

[25] Unless explicitly noted otherwise, the other similarity measures described in this section assume their extreme value only when $I_0(\mathbf{x}) = I(\mathbf{x}+\mathbf{d})$.

where $\mathcal{F}^{-1}[\cdot]$ denotes the inverse Fourier transform. Note that $\mathcal{M}_{\text{PC}}$ is insensitive to grey-level scaling. That is, if $I_0(\mathbf{x}) = \kappa I(\mathbf{x} + \mathbf{d})$, where κ is any constant, the extremum of $\mathcal{M}$ will have the same value for all κ. Note also that, in practice, due to the use of discrete Fourier transforms, this extreme value will be finite.

The phase-correlation measure was originally proposed by Kuglin & Hines [86] and has since then been applied to DSA by Leclerc & Benchimol [87] and Wu *et al.* [166]. A related approach, based on the power-cepstrum[26] representations of the images, was used by Englmeier *et al.* [38].

IV.B.2 Sum of the Absolute Values of Differences

In contrast with correlation-based measures, most similarity measures are defined in terms of the grey-values in the difference images $I_{\mathbf{d}}(\mathbf{x}) = I_0(\mathbf{x}) - I(\mathbf{x}+\mathbf{d})$. The most well-known measure is the *sum of the absolute values of differences* (SAVD):

$$\mathcal{M}_{\text{SAVD}}(\mathbf{d}) = \sum_{\mathbf{x}\in\mathcal{W}} |I_{\mathbf{d}}(\mathbf{x})|, \tag{12}$$

which is to be minimized, and assumes values in the range $[0, GKL] \subset \mathbb{Z}$.

This measure was first used by Svedlow *et al.* [143] for alignment of land-sat images, and has later been applied to the registration problem in DSA by several authors, *viz.*, Wilson *et al.* [163], Van Tran & Sklansky [152, 153] and Ko *et al.* [76]. A similar measure, the *mean of the absolute values of the differences*, was used by Pickens *et al.* [117, 118], Fitzpatrick *et al.* [43, 44, 46–49] and Mandava *et al.* [99].

IV.B.3 Sum of Squared Differences

Another measure based on absolute differences is the *sum of squared differences* (SSD):

$$\mathcal{M}_{\text{SSD}}(\mathbf{d}) = \sum_{\mathbf{x}\in\mathcal{W}} [I_{\mathbf{d}}(\mathbf{x})]^2. \tag{13}$$

The displacement vector that minimizes $\mathcal{M}_{\text{SSD}}$ corresponds to the window in the contrast image that is most similar to the window in the mask image, in a least-squares sense. Note that $\mathcal{M}_{\text{SSD}} \in [0, G^2KL] \subset \mathbb{Z}$.

Hayashi *et al.* [61] applied this measure to Laplacean-filtered versions of the mask and contrast images. Although the SSD measure has been mentioned by many others as a potential criterion for image registration in DSA [68, 120, 147, 152, 153, 163], in most cases alternative measures were used.

IV.B.4 Variance of Differences

The standard deviation of differences has been used by Van der Stelt *et al.* [151] as a similarity measure for determining the optimal projections for subtraction, and by Dunn *et al.* [37] as a quality measure for comparing different registration techniques in dental DSR. A related measure, based on the *variance of differences* (VOD), was proposed by

[26] An anagram of the word "spectrum". See *e.g.* Lee *et al.* [88] for details on the use of power-cepstrum and -spectrum techniques for image registration.

Cox & De Jager [32] for registration in DSA:[27]

$$\mathcal{M}_{\text{VOD}}(\mathbf{d}) = \frac{1}{KL} \sum_{\mathbf{x} \in \mathcal{W}} [I_{\mathbf{d}}(\mathbf{x}) - \langle I_{\mathbf{d}} \rangle_{\mathcal{W}}]^2, \tag{14}$$

with the operator $\langle \cdot \rangle_{\mathcal{W}}$ as defined in (8). This measure assumes values in the range $[0, G^2] \subset \mathbb{R}$, and is to be minimized. Note that $\mathcal{M}_{\text{VOD}}$ assumes its extreme (minimum) value only when $I_0(\mathbf{x}) = I(\mathbf{x} + \mathbf{d}) + \kappa$, where κ is any constant.

IV.B.5 Sign-Change Measures

If two images $I_0(\mathbf{x})$ and $I(\mathbf{x})$ are assumed to differ only as a result of noise, the difference image $I_{\mathbf{d}}(\mathbf{x})$ will exhibit random fluctuations according to the noise properties in case $\mathbf{d} = \mathbf{0}$, and will contain additional distortions in case $\mathbf{d} \neq \mathbf{0}$ (provided that the original images are not entirely homogeneous). This implies that if the noise is additive, with zero mean and a symmetrical probability density function, the difference image will have many sign changes when scanned row-wise or column-wise, the number of sign changes being maximum when $\mathbf{d} = \mathbf{0}$. This observation by Venot *et al.* has led to the construction of the *stochastic sign change* (SSC) measure [154, 157].

Although the SSC measure had been successfully applied to normalization and registration of scintigraphic images [155, 156], it did not appear to be an adequate measure for registration of X-ray images, because of the relatively low noise level as compared to the quantization precision [154, 157].[28] In order to cope with this "problem", Venot *et al.* adjusted the SSC measure to form the *deterministic sign change* (DSC) measure:

$$\mathcal{M}_{\text{DSC}}(\mathbf{d}) = \sum_{\mathbf{x} \in \mathcal{W}'} \text{sgn}(I_{\mathbf{d}}^{\mathcal{P}}(x, y) I_{\mathbf{d}}^{\mathcal{P}}(x - 1, y)), \tag{15}$$

where $\mathcal{W}' = \{\mathbf{x} | (x - 1, y) \in \mathcal{W}\}$ (the window $\mathcal{W}$ is assumed to be scanned row-wise), $I_{\mathbf{d}}^{\mathcal{P}}(\mathbf{x}) = I_0(\mathbf{x}) - I(\mathbf{x} + \mathbf{d}) + \mathcal{P}(\mathbf{x})$, and the functions $\text{sgn}(x)$ and $\mathcal{P}(\mathbf{x})$ are defined as, respectively:

$$\text{sgn}(x) \triangleq \begin{cases} 0, & \text{if } x \geqslant 0, \\ 1, & \text{if } x < 0 \end{cases} \tag{16}$$

and

$$\mathcal{P}(\mathbf{x}) \triangleq \begin{cases} +q, & \text{if } x + y \text{ even}, \\ -q, & \text{if } x + y \text{ odd}, \end{cases} \tag{17}$$

where q is a small real or integer value. With the DSC measure, the sign changes in the subtraction image are not caused by the stochastic properties of the original images, but rather by the deterministic properties of the pattern $\mathcal{P}(\mathbf{x})$ introduced in one of the images. Note that $\mathcal{M}_{\text{DSC}}$ assumes values in the range $[0, (K - 1)L] \subset \mathbb{Z}$, and is to be maximized.

Apart from Venot *et al.* [154, 157, 158] this measure has been used by Zuiderveld *et al.* [170, 171]. It has also been used by Roos & Viergever [133–135] for the purpose of

[27] The definition presented here deviates from the original definition by Cox & De Jager [32] in the sense that the latter was constructed so as to yield values in the range $(0, 1]$. This was accomplished by subjecting the values $\mathcal{M}_{\text{VOD}}$ as computed using (14) to a non-linear transformation. However, since this transformation is a bijection for the possible range of $\mathcal{M}_{\text{VOD}}$ values, the measure presented here will yield equivalent results.

[28] Note that in the early 1980s, digital angiographic images were usually acquired with a grey-level resolution of 8 bits. As pointed out earlier, the quantization precision of current DSA devices is 10 bits.

reversible interframe compression of medical images, in particular coronary and ventricular X-ray angiograms. Hua & Fram [67] applied the DSC measure to first derivative versions of the mask and contrast images.

IV.B.6 Coincident Bit Counting

Another measure that was designed to be independent of actual grey-values is *coincident bit counting* (CBC). With this measure, the degree of similarity of successive windows is determined by counting the total number of coincident bits in the binary representations of the grey-values of corresponding pixels. This measure was proposed by Chiang & Sullivan [27], and can be defined as:

$$\mathcal{M}_{\text{CBC}}(\mathbf{d}) = \sum_{\mathbf{x}\in\mathcal{W}} \sum_{i=0}^{n-1} b_i(I_0(\mathbf{x})) \otimes b_i(I(\mathbf{x}+\mathbf{d})), \tag{18}$$

where $b_i(\cdot)$ is a function that returns the i-th bit of the binary representation of its argument, $\otimes$ denotes the Exclusive-NOR operator and n is the number of bits in which the grey-values are represented.[29] $\mathcal{M}_{\text{CBC}}$, as defined in (18), assumes values in the range $[0, nKL] \subset \mathbb{Z}$, and is to be maximized.

IV.B.7 Histogram-of-Differences Based Measures

Fundamentally different measures are those based on the normalized histogram of differences, $\mathcal{H}(g)$, defined as:

$$\mathcal{H}(g) = \frac{1}{KL} \sum_{\mathbf{x}\in\mathcal{W}} \delta(I_{\mathbf{d}}(\mathbf{x}), g), \tag{19}$$

where $g \in [-G, G] \subset \mathbb{Z}$ is any grey-value difference and $\delta(x, y)$ the Kronecker delta function defined as

$$\delta(x,y) \triangleq \begin{cases} 1, & \text{if } x = y, \\ 0, & \text{if } x \neq y. \end{cases} \tag{20}$$

With histogram-based measures, the degree of similarity of windows in successive images is not determined by the actual grey-value differences but rather by their relative frequency. An example of such a measure is the *entropy of the histogram of differences* (ENT):

$$\mathcal{M}_{\text{ENT}}(\mathbf{d}) = -\sum_{g=-G}^{G} \mathcal{H}(g) \log \mathcal{H}(g), \tag{21}$$

which assumes values in the range $[0, \log(2G+1)] \subset \mathbb{R}$, and is to be minimized.

This measure was used by Lehmann *et al.* [90] as a quality measure for the alignment of X-ray images in dental DSR. Independently of Lehmann *et al.*, it was soon after proposed by Buzug *et al.* [17, 21] and used for registration of angiographic X-ray images. Later, Buzug *et al.* generalized the concept of histogram-based similarity measures and proved that any measure

$$\mathcal{M}(\mathbf{d}) = \sum_{g=-G}^{G} f(\mathcal{H}(g)) \tag{22}$$

[29] In accordance with the earlier remark (footnote 23), this definition of the CBC measure does not provide a means to deal with border problems, which is the reason why it deviates somewhat, though not fundamentally, from the original definition by Chiang & Sullivan [27].

is a suitable similarity measure for registration purposes, provided that f is a strictly convex, or strictly concave, differentiable function [23–25], the function $f(x) = -x \log x$ being just an example. They proposed several other histogram weighting functions and argued that the function $f(x) = x^2$, leading to the *energy of the histogram of differences* (EHD) measure:

$$\mathcal{M}_{\text{EHD}}(\mathbf{d}) = \sum_{g=-G}^{G} \mathcal{H}^2(g) \tag{23}$$

is computationally cheap and yields accurate results [16,19,20,22–25]. It has recently also been used by the authors of the present paper [104,106]. In contrast with $\mathcal{M}_{\text{ENT}}$, the energy measure $\mathcal{M}_{\text{EHD}}$ is to be maximized, and assumes values in the range $[1/(2G+1), 1] \subset \mathbb{R}$. Both measures take on their respective extreme value when $I_0(\mathbf{x}) = \kappa_1 I(\mathbf{x}+\mathbf{d}) + \kappa_2$, where κ_1 and κ_2 are constants.

IV.B.8 Various Alternative Measures

Hitherto, we have presented only the similarity measures that are most frequently encountered in the literature. Some measures that have been suggested in the context of DSA have remained largely unnoticed, yet are worth mentioning. For example, Potel & Gustafson [120] proposed a variant of the SAVD measure, *viz.*, the *sum of the absolute values of differences above a threshold* (SDT), in which only the absolute difference values that exceed a specified threshold, $\mathcal{T}$, are incorporated, thereby reducing the influence of noise in rather homogeneous regions:[30]

$$\mathcal{M}_{\text{SDT}}(\mathbf{d}) = \sum_{\mathbf{x} \in \mathcal{W}} \max(\mathcal{T}, |I_{\mathbf{d}}(\mathbf{x})|), \tag{24}$$

where $\mathcal{M}_{\text{SDT}} \in [\mathcal{T}KL, GKL] \subset \mathbb{Z}$ is to be minimized.

In contrast to this, Tianxu *et al.* [147] argued that if the noise is not Gaussian, relatively large noise peaks may frequently occur, which significantly spoil the performance of measures such as SAVD and SSD. They proposed to reduce the influence of difference values with a large magnitude, by using a measure that they called the *minimal artifacts criterion* (MAC):[31]

$$\mathcal{M}_{\text{MAC}}(\mathbf{d}) = \sum_{\mathbf{x} \in \mathcal{W}} \frac{A_1}{A_0 + |I_{\mathbf{d}}(\mathbf{x})|}, \tag{25}$$

which assumes values in the range $[A_1 KL/(A_0 + G), A_1 KL/A_0] \subset \mathbb{R}$, and is to be maximized, assuming that A_1 and A_0 are positive constants.

Another variant of the SAVD measure is obtained if only positive pixel differences are taken into account, thereby attempting to reduce the influence of pixels whose difference values are due to the injected contrast medium. This *sum of positive differences* (SPD)

[30] The name and definition of this measure were adopted literally from Potel & Gustafson [120]. Note, however, that they are not consistent. When using the definition of (24), also absolute differences below the threshold $\mathcal{T}$ contribute to the value of $\mathcal{M}_{\text{SDT}}$.

[31] Although one may question the validity of the claim that application of this measure will result in minimal artifacts, we have adopted the original appellation. It must be added that the original definition by Tianxu *et al.* [147] also incorporated a mechanism to correct for local grey-level variations, thereby probably making it a more powerful measure than the one presented here.

measure is defined as:[32]

$$\mathcal{M}_{\text{SPD}}(\mathbf{d}) = \sum_{\mathbf{x}\in\mathcal{W}} \max(0, I_{\mathbf{d}}(\mathbf{x})). \tag{26}$$

As with the SAVD measure, this measure assumes values in the range $[0, GKL] \subset \mathbb{Z}$, and is to be minimized.

A related approach to reduce the negative influence of contrasted vessels is the use of so called *exclusion templates*, which has been put forward by several authors.[33] This involves a presegmentation of the image or windows so as to identify regions that may contain contrasted vessels. In computing the measure of match, only those pixels are included in the summation that do not belong to these regions. Since the number of excluded pixels may vary, this requires normalization of the similarity measure, which can be done simply by dividing by the number of incorporated pixels.

An exclusion template may be obtained in several ways. Ko *et al.* [76] simply applied a threshold to the original subtraction image, where the threshold was taken to be the sum of the mean and one times the standard deviation of the difference values. Earlier, Van Tran & Sklansky [152, 153] had used a similar technique, with the addition that isolated pixels in the resulting binary exclusion template were merged with their surroundings. Finally, Cox & De Jager [32] proposed to subdivide the windows into smaller subwindows and to compute the similarity measure for every individual subwindow. Only the k best matching subwindows are then used to compute the measure of match of the entire window.

IV.C Subpixel Precision

As indicated by Brody *et al.* [12], even subpixel misalignments may produce significant artifacts in the subtraction images. Therefore, it is necessary to provide means to obtain subpixel precision in the displacement computations. Since the image pixels constitute the only available information about the represented scene, this inevitably requires some form of interpolation.

An obvious approach to obtain subpixel precision is to compute the measure of match not only for integer but also for non-integer displacements of the images or windows. This requires resampling of the original pixel data, *e.g.* by means of bilinear interpolation, as has been done by several authors, *viz.*, Potel & Gustafson [120], Yanagisawa *et al.* [167], Pickens *et al.* [118], Fitzpatrick *et al.* [44,46–49], Mandava *et al.* [99], Van Tran & Sklansky [152, 153], Ko *et al.* [76] and Hayashi *et al.* [61]. With this approach, the final precision of the displacement vectors is either determined implicitly by the optimization procedure, or has to be specified explicitly by the user, in terms of an incremental step size.

A frequently applied alternative approach is to use the match values at integer displacements, $\mathcal{M}(\mathbf{d}),\ \mathbf{d} \in \mathbb{Z}^2$, in an interpolation scheme in order to construct a continuous bivariate function, the *match surface*, $\check{\mathcal{M}}(\mathbf{d}),\ \mathbf{d} \in \mathbb{R}^2$ and $\check{\mathcal{M}}(\mathbf{d}) = \mathcal{M}(\mathbf{d}),\ \forall \mathbf{d} \in \mathbb{Z}^2$, and to calculate the extremum of this function analytically by solving $\nabla\check{\mathcal{M}}(\mathbf{d}) = \mathbf{0}$. Obviously, bilinear interpolation cannot be used for this purpose since a bilinearly interpolated surface still has its extremum at the integer extremum position. Buzug *et al.* [22, 25] proposed

[32] This measure is the complementary version of the *sum of negative pixel differences* measure (obtained by replacing "max" by "min" in (26)) mentioned by Potel & Gustafson [120]. The definition of such a measure is directly related to the definition of the difference image $I_{\mathbf{d}}$ and to the normalization of the mask and contrast images.

[33] Not to be confused with the *template-exclusion* technique as proposed by Buzug *et al.* [16, 17, 19, 21, 22, 24, 25] and described in this paper in Section IV.A.

to fit a 6-parameter quadratic function to the match values of the 3×3 neighborhood surrounding the optimum match value of integer displacements,[34] from which the subpixel displacement component can be computed directly. For higher-order bivariate interpolation it can easily be deduced that this will lead to the problem of solving an algebraic equation of degree $n \geqslant 5$ (in either x or y and with coefficients that are functions of the match values at integer displacements), which can only be done numerically.

In order to cope with this problem, several authors have proposed to simplify the problem by constructing two separate monovariate functions $\check{\mathcal{M}}(d_i),\ i \in \{x, y\}$ and to solve $\partial_i \check{\mathcal{M}}(d_i) = 0$ independently for $i \in \{x, y\}$ in order to obtain an estimate for the x and y coordinates of the extremum. Zuiderveld *et al.* [170,171], Cox & De Jager [32] and Hua & Fram [67] used quadratic polynomials for this purpose, and Venot & Leclerc [158] reported the use of cubic splines.[35] Wilson *et al.* [163] applied Brent's algorithm for function optimization [8], in which parabolic fitting is used in an iterative fashion.

IV.D Optimization and Acceleration

Given the similarity measure, $\mathcal{M}$, the optimal displacement vector according to this measure is the vector $\mathbf{d}$ for which $\mathcal{M}$ assumes a global optimum value.[36] Finding this optimum boils down to the problem of function optimization, for which a large number of algorithms exist. In this section we will consider only the approaches that have actually been applied to registration of digital angiographic images. Most of these are well-known optimization techniques, for which numerical recipes have been described by Press *et al.* [124]. We will also describe several acceleration techniques that have been proposed in order to reduce the time required for optimization and computation of the measure of match.

From an implementational point of view, the simplest yet computationally most expensive approach would be to impose constraints on the maximum admissible displacements in both x and y direction and to perform an exhaustive search, *i.e.*, to evaluate the similarity measure for every possible displacement, subject to the constraints $|d_x| \leqslant d_{x_{\max}}$ and $|d_y| \leqslant d_{y_{\max}}$, and to the required (subpixel) accuracy. In this case, the computation time can be reduced considerably by applying a multiresolution approach,[37] in which a full search is iteratively carried out on subsampled and, eventually, supersampled versions of the original images. There are a number of variants to this approach, as have been described by Potel & Gustafson [120], Wilson *et al.* [163], Van Tran & Sklansky [152,153], Tianxu *et al.* [147], Ko *et al.* [76] and Hayashi *et al.* [61]. Cox & De Jager [32] described a different multiresolution approach, in which exhaustive searching was replaced by a three-step optimization procedure. A related technique, called logarithmic search [69], was mentioned by Roos & Viergever [133–135].

Another well-known technique for function optimization is Powell's direction set method [121], in which multidimensional optimization is achieved by successive 1D optimizations, in conjugate directions. Although the original algorithm prescribes a mechanism for optimally updating the search direction after each iteration, frequently the directions are kept fixed to the x and y direction, a simplification often referred to as *hill climbing.* This has been used by Venot *et al.* [157,158], Zuiderveld *et al.* [170,171], Buzug *et al.* [16,18,23,25] and was also used in our recently published algorithm [104, 106]. As an acceleration technique, Zuiderveld *et al.* [170,171] proposed to use the already computed displacement

[34] Since this is an over-constrained problem, they used singular value decomposition.
[35] Although it is not clear from their explanation whether they computed d_x and d_y separately.
[36] Either a minimum or a maximum value, depending on the chosen similarity measure.
[37] Also referred to as a hierarchical or pyramidal approach.

vectors of neighboring control points as initial estimates for the displacements of points yet to be considered. When registering complete image sequences, the displacement vectors of previously registered frames can also be used as estimates [106].

There are a number of algorithms that made use of real multidimensional optimization strategies.[38] For example, Yanagisawa *et al.* [167] used the downhill simplex method of Nelder & Mead [111], with which the optimal 2D displacement vector is found by defining three candidate vectors, the end-points of which constitute a triangle, and by proceeding downhill by means of successive reflections and contractions of this triangle. Venot *et al.* [154] proposed to use a stochastic search approach in which, for each iteration, the displacement vector to be evaluated is computed from the vector of the previous iteration by adding a random vector according to some suitably chosen probability density function. Other algorithms for the simultaneous optimization of a larger number of parameters are genetic search [35], derived from principles of natural population genetics, and simulated annealing [75], an analogue of the physical process of annealing. These types of strategies were used, respectively, by Fitzpatrick *et al.* [43, 44, 46–49, 118] and Mandava *et al.* [99], who also proposed an approach for increasing the accuracy and reducing the computational cost of such algorithms.[39]

Apart from using an adequate optimization technique, acceleration may in some cases also be achieved by reducing the computational cost of the similarity measure. Potel & Gustafson [120] proposed to use the acceleration technique described by Barnea & Silverman [4], in which summation is terminated as soon as the accumulated measure of match exceeds a certain threshold. A similar technique was used by Ko *et al.* [76]. An alternative approach to reduce the computational cost is to use only a limited number of randomly selected pixels when evaluating the similarity measure, as was done by Pickens *et al.* [118], Fitzpatrick *et al.* [44, 47–49] and Mandava *et al.* [99]. The accuracy of the resulting estimated measures of match was increased by employing a stratified sampling procedure [70].

IV.E Grey-Level Distortion Correction

Even if the correct correspondence between the grey-level structures in successive images in a sequence has been recovered (in terms of a displacement vector field), and the mask image has been geometrically deformed accordingly, the background in the resulting subtraction images will not necessarily be entirely homogeneous and their mean intensity may be different for different contrast images. Apart from noise, to which all the components in the imaging chain contribute [10, 30, 59, 71, 84, 93, 114, 160], these artifacts are primarily caused by changes in local densities as a result of contractions and expansions of tissues. Other causes of grey-level distortion artifacts include fluctuations in the intensity of X-rays and, as time elapses, the non-uniform diffusion of the contrast medium into the capillaries. Therefore, a final aspect of any motion correction algorithm is the retrospective correction of remaining grey-level distortion artifacts.

As shown by Fitzpatrick [42], and recalled in this paper in Section III.A, it is possible to construct a 2D geometrical transformation that completely accounts for the projective

[38] That is, entirely self-contained strategies in which 1D optimizations do not figure [124], as opposed to *e.g.* Powell's method.

[39] Recall from Section IV.A that they applied one-to-one polynomial mappings, from the class proposed by Fitzpatrick & Leuze [45], to user-defined regions of interest. In that case, the objective is to simultaneously find the optimal displacement vectors of the four corner points that constitute a region of interest, which boils down to an eight-dimensional optimization problem.

effects of 3D patient motion. Local contractions and expansions of tissues are manifest in the contrast images as negative or positive changes in local grey-levels.[40] As expressed in (5), these changes may be compensated for by incorporating the Jacobian of the geometrical transformation when applying this transformation to the mask image, prior to subtraction. This was done by Pickens *et al.* [117, 118], Fitzpatrick *et al.* [44, 46–49] and Mandava *et al.* [99].

A frequently encountered alternative approach to grey-level distortion correction is to make a distinction between multiplicative and additive changes and to correct for them separately, prior to subtraction. Venot *et al.* [154, 158] proposed to incorporate multiplicative and additive grey-value correction parameters into the optimization strategy. Van Tran & Sklansky [152, 153] proposed to correct for additive variations by adding a correction image $I_{\mathcal{D}}$ to the transformed mask image. The grey-values in $I_{\mathcal{D}}$ were computed by bilinear interpolation of the grey-values at a number of reference points on a regular grid. The grey-values at these reference points were determined by defining a window around corresponding points in the contrast and transformed mask image and by averaging the grey-value differences. Multiplicative variations were corrected by computing the ratio of the averages of grey-values in the contrast and transformed mask image, $r = \langle I \rangle / \langle I_0 \rangle$, and by multiplying the grey-values in the mask image with this factor.[41] The exact same approach was later used by Ko *et al.* [76]. Similar approaches for multiplicative and additive distortion correction were reported by Wu *et al.* [166] and Cox & De Jager [32].

V Discussion

In the previous section we have described the different aspects of retrospective patient motion correction in DSA and we have presented an overview of the techniques that have been proposed in order to solve the various parts of the correction problem. In this section we will further discuss the benefits and limitations of these techniques. Conclusions will be drawn in Section VI.

V.A Control-Point Selection and Displacement Interpolation

In Section IV.A we have pointed out that because of the high computational cost it is usually not admissible to determine the displacement explicitly for every pixel. This has been recognized by many researchers and has led to the concept of control-point based registration. However, this introduces two new problems: the selection of a suitable set of control points, and the construction of the complete displacement vector field from the displacements of these points. In this subsection we will address these problems.

Most control-point based registration algorithms published so far employ regular grids. That is, given the Cartesian coordinate system in which the image is defined, a set of equidistant lines are taken parallel to the x and y axes, and the line-crossings are selected as control points. In the papers mentioned in Section IV.A, either the inter-line distance was chosen arbitrarily, or an "optimal" distance was established empirically, where optimality was defined in terms of image quality and/or computational cost. Since this is a highly subjective procedure, inter-line distances have been reported in the range from five pixels

[40] See footnote 13.

[41] In order to prevent pixels corresponding to contrasted blood vessels to spoil these processes, they were left out of the computations of average values. This was accomplished by using an exclusion template, as described at the end of Section IV.B.

[32] to over 100 pixels [146].[42] Even when the image content is taken into account, by applying some or other exclusion mechanism, it remains a rather arbitrary approach.

In recent publications [104, 106] we have argued that control-point selection should be image-feature based, the reason for this being threefold:

(i) The control points can be selected at those positions where the artifacts can be expected to be largest.

(ii) Since the neighborhoods of those points are known to be structured, the reliability of the displacement estimates will be high.

(iii) With this approach, usually a smaller number of control points suffices, resulting in a reduction of computation time.

We have demonstrated the advantage of algorithms with edge-based control-point selection over algorithms based on regular grids. Although it has not yet been confirmed experimentally, the use of other (additional) features, such as corners and ridges, may be beneficial in some cases.

As mentioned earlier, in Section IV.A, feature-based control-point selection will in general result in an irregular grid. In order to obtain a complete displacement vector field, the computationally cheapest solution is to use linear interpolation, which requires triangulation of the set of control points. The resulting transformation may be considered a "finite-element" approximation of the original transformation. However, it can be expected that in some cases, more complex interpolation schemes, such as thin-plate splines, will yield more accurate approximations, albeit at higher computational cost.

V.B Comparisons of Similarity Measures

In Section IV.B we have stressed the importance of the similarity measure employed to determine the degree of resemblance of windows in successive frames. We have summarized the different measures that can be found in the literature on registration in DSA. Although all of these measures have never been compared in a single evaluation, the partial evaluations reported by several authors enable us to draw some important conclusions.[43]

First, it should be noted that ordinary correlation, *i.e.*, the numerator of the right-hand side of (6), is dependent on actual grey-values. This may lead to serious problems, which can be appreciated from the observation that, given two windows in the contrast image, the first being almost identical to the window in the mask image and the second being more or less homogeneous and showing relatively large grey-values, ordinary correlation will designate the latter window as being most similar to the window in the mask image. This runs counter to intuition, and explains why normalization is mandatory.[44] Similar remarks can be made for frequency-based correlation: the numerator of (10) is the Fourier transform of the ordinary correlation function. Here, normalization with respect to both images is accomplished by eliminating the magnitudes of both spectra, leaving only the phase term.

[42] Note that the inter-line distance parameter is, in principle, independent of the window size parameters K and L (see introduction of Section IV).

[43] In this section we will frequently use the abbreviations introduced in Section IV.B. An overview of them can be found on the frontpage of this paper.

[44] It must be remarked that normalization with respect to I_0 is not strictly necessary for the NCC and CC measures, since the corresponding normalization factor is a constant, *i.e.*, independent of $\mathbf{d}$. See also the explanation in footnote 23.

There are some specific problems connected to Fourier-based correlation. Apart from noise, which also influences spatial correlation measures, the effects of both spectral and spatial leakage further deteriorate the performance of the PC measure. Spectral leakage in the Fourier transforms of the windows in the mask and contrast images results from the non-periodicity of the spatial information in these windows. Spatial leakage in the inverse Fourier transform (11) is caused by the non-periodicity of the cross-power spectrum (10). These effects can be reduced by applying windowing techniques [60]. By using these techniques, Wu *et al.* [166] found that the PC measure yields a more sharply peaked match-function than spatial cross-correlation measures.

Compared to correlation measures, the SAVD measure is more consistent with the ultimate goal of registration in DSA: minimizing the absolute difference values in subtraction images. However, as pointed out by Fitzpatrick *et al.* [44], algorithms based on this measure cannot be expected to proceed consistently beyond the point where the differences due to motion artifacts are reduced to the level of the inherent differences due to the contrast medium. This implies that there may remain artifacts that are as pronounced as the contrasted vessels. The extent to which the presence of contrasted vessels has a negative influence on the performance of this measure is dependent on the relative area of the vessels. It is clear that in order to get rid of this dependency, the similarity measure should be made insensitive to local dissimilarities between the images.

As pointed out by several authors [13,123,136], the SSD measure is directly related to ordinary correlation. By expanding the right-hand side of (13) we obtain:

$$\mathcal{M}_{\text{SSD}}(\mathbf{d}) = \sum_{\mathbf{x}\in\mathcal{W}} I_0^2(\mathbf{x}) + \sum_{\mathbf{x}\in\mathcal{W}} I^2(\mathbf{x}+\mathbf{d}) - 2\sum_{\mathbf{x}\in\mathcal{W}} I_0(\mathbf{x}) I(\mathbf{x}+\mathbf{d}). \tag{27}$$

The first term on the right-hand side of this equation is a constant. If the second term varies only gradually as a function of $\mathbf{d}$, the optimal displacement found using this measure is mainly determined by the third term, which is equivalent to ordinary correlation. Note that in this case the NCC measure also approaches ordinary correlation, which implies that the SSD and NCC measure should yield equivalent results. In other cases, the second term will cause the SSD measure to perform better than ordinary correlation.

Potel & Gustafson [120] carried out a comparison between the CC measure and the SSD, SAVD, SDT and SPD measures, and concluded that the discrepancies between the displacement vectors obtained using the latter measures and the vectors obtained by CC were always less than 0.1 pixel. This can be explained from the fact that they used relatively large windows of 128×128 pixels in images of size 256×256 pixels, thereby diminishing the negative effects of local dissimilarities caused by noise and contrasted vessels. Van Tran & Sklansky [152, 153] also compared the SAVD and SSD measures, using windows of 31×31 pixels in images of size 512×512 pixels, and concluded that the SAVD measure produced the best results.

In contrast with the aforementioned measures, the VOD measure is independent of additive mean grey-level offsets. This may be profitable in cases where the images contain a grey-level gradient, as in the examples shown by Cox & De Jager [32]. They compared the SAVD and VOD measures and found that in those cases the latter performs better indeed. However, they also found that in the absence of any grey-level gradient, the SAVD measure yields more accurate results. This can be explained from the expansion of (14):

$$\mathcal{M}_{\text{VOD}}(\mathbf{d}) = \left[\frac{1}{KL}\sum_{\mathbf{x}\in\mathcal{W}}[I_{\mathbf{d}}(\mathbf{x})]^2\right] - \langle I_{\mathbf{d}}\rangle_{\mathcal{W}}^2. \tag{28}$$

In those cases where the variation, as a function of **d**, of the second term on the right-hand side of (28) is negligible, the VOD measure becomes equivalent to the SSD measure and, in accordance with the results of Van Tran & Sklansky [152, 153], should perform worse than the SAVD measure.

The first measure that was explicitly designed to be relatively insensitive to local dissimilarities, as caused by *e.g.* contrasted vessels, is the DSC measure. As pointed out by Fitzpatrick *et al.* [44], the value of $\mathcal{M}_{\text{DSC}}$, as computed by using (15), may be considered an estimate of the area (in pixels) within which the absolute differences are less than q:[45]

$$\mathcal{M}_{\text{DSC}}(\mathbf{d}) \approxeq \sum_{\mathbf{x}\in\mathcal{W}} \eta(q - |I_{\mathbf{d}}(\mathbf{x})|), \tag{29}$$

where $\eta(x)$ is the step-function defined as:

$$\eta(x) \triangleq \begin{cases} 1, & \text{if } x > 0, \\ 0, & \text{if } x \leqslant 0. \end{cases} \tag{30}$$

The robustness of the DSC measure against the inflow of contrast may then be explained from the fact that the decrease of the sum on the right-hand side of (29), caused by a total of n affected pixels, is only n, regardless of the magnitude of the actual difference values.[46] Venot *et al.* carried out a comparison of the CC, SAVD and DSC measures and confirmed the superiority of the latter [157].

A disadvantage of the DSC measure is the associated parameter, q, which needs to be tuned. Venot *et al.* [157] demonstrated that if the variance, σ^2, of the noise in the subtraction images is known, there is no advantage selecting values of q larger than 2σ. This upper bound, however, is dependent on image content. In their evaluations they used $q = 1$ [154, 157] and $q = 2$ [158]. Zuiderveld *et al.* [170, 171] used values for q of about 10. A value of 8 was reported by Hua & Fram [67], who also claimed that even more accurate registration results are obtained by applying the DSC measure to the first derivative versions of the original images. In the presence of a grey-level gradient, this may indeed be true, since the low frequency variations are reduced by first derivative filtering, *i.e.*, edge enhancement.

The competence of CBC as a measure of similarity is highly questionable. Analogous to sign change measures, the CBC measure was designed so as to ascribe equal weight to every pixel within the windows to be compared, irrespective of their grey-values [27]. As explained by Chiang & Sullivan [27], the optimal displacement according to this measure is the displacement for which the number of matching bits is maximal. However, the idea behind this stems directly from correlation. In fact, upon taking a closer look at (18) it must be concluded that CBC is nothing but a rather unfortunate implementation of ordinary correlation. Although it is true that this measure assigns equal weight to all

[45] Similarly, the expected value of the SSC measure is approximately equal to the area within which the absolute differences are insignificant in comparison to the noise in the images [44].

[46] For the DSC measure itself, the decrease caused by a run of m contiguous affected pixels is either $m-1$, m, or $m+1$ (depending on whether the run contains an even or an odd number of pixels, whether or not the run starts or ends at the border of the window $\mathcal{W}$, and the position of the run relative to the pattern $\mathcal{P}$ defined in (17)). For a total of n affected pixels (partitioned into one or more runs), the total decrease will be approximately n.

pixels, it suffers from peculiar inconsistencies. For example, consider a 10 bit pixel with value 511, binarily represented as 01|1111|1111. A small amount of noise may turn this pixel value into 510 or 512, represented as 01|1111|1110 and 10|0000|0000, respectively. According to the CBC measure, 511 matches very well with 510, but extremely bad with 512, which runs counter to intuition.[47] This also shows that it is not true that lower order bits tend to be more contaminated with noise, while higher order bits are more locally uniform among neighboring pixels, as was asserted by Chiang & Sullivan [27]. In fact, it can quite easily be shown that for *any* grey-value, the effect of noise on the CBC measure is asymmetric with respect to the sign of the change. Therefore, contrary to what was claimed, the distribution of the noise *does* affect the performance of CBC. In their paper, Chiang & Sullivan [27] evaluated the performance of the CBC measure by comparison with only the SSC measure, and concluded that CBC was superior. However, as pointed out several times by Venot *et al.* [154, 157, 158], the SSC is not an adequate measure for DSA because of the relatively low noise level. Therefore, we cannot assign much value to this evaluation, and we are quite confident that the DSC measure, or even CC or NCC, would have outperformed the CBC measure.

Similarity measures based on the histogram of differences take advantage of the fact that in the case of optimal alignment, only a small number of difference values have a high relative frequency, while the majority of difference values will have a low relative frequency. This results in a sharply peaked histogram, whether a window $\mathcal{W}$ contains opacified vessels or not, the former case resulting in two peaks and the latter in only one peak. In the case of misalignment, the histogram will have a larger dispersion in both cases. This dispersion could be measured on the abscissa by computing, *e.g.* the standard deviation of the histogram, as was done by Wenzel [161] in dental DSR. However, the dispersion is more adequately computed on the ordinate axis, by means of convex or concave weighting functions, as proposed by Buzug *et al.*, since these functions are more sensitive to small changes in the histogram. Buzug *et al.* published several comparisons between ordinary correlation and the SSD, DSC and ENT measures [18, 20, 21, 25], and demonstrated the superiority of the latter.[48] Later, they showed that the EHD measure performs comparably, at a reduced computational cost [20, 23, 25].

In summary, in contrast with all other similarity measures used in DSA, histogram-based measures consider *relative frequencies* of difference values. As a consequence, these measures are neither sensitive to mean grey-level offsets, nor local dissimilarities caused by contrasted vessels (regardless of their relative areas), and therefore do not require exclusion templates. Furthermore, they are computationally cheap [91], do not require the tuning of parameters and yet lead to very smooth match surfaces [18–21, 23, 25], which allows for efficient optimization. In conclusion, of all similarity measures developed so far, the EHD measure has been shown to be most adequate for registration in DSA.

V.C Interpolation Techniques for Subpixel Precision

In Section IV.C we have argued that, since even subpixel misalignments may produce significant artifacts, the displacement computations should be carried out with subpixel precision, which requires interpolation. As can be observed from the overview in Section

[47] Similar remarks were made by Venot *et al.* [159].

[48] It is worth noting that, in the context of dental radiography, Lehmann *et al.* [91] carried out a comparative evaluation of CC, SAVD, VOD, ENT, and some additional measures that have hitherto not been used in DSA. They concluded that ENT was the most adequate similarity measure, although it must be pointed out that, inherently, their evaluation included only regions lacking contrasted vessels.

IV.C, the techniques that have been proposed for this purpose may be divided into two categories. With the first type of techniques, the mask or contrast image is interpolated and resampled so as to allow for an explicit evaluation of the chosen similarity measure at non-integer displacements. With techniques from the second category, the match values of integer displacements are interpolated so as to obtain a continuous bivariate match surface, from which an optimum displacement vector may be determined analytically.

It must be pointed out that there is no theoretical basis to support the use of match-interpolation techniques. In the papers referred to in Section IV.C, choices for a particular interpolation scheme were rather arbitrary, and were based on demands regarding computational cost, rather than on theoretical foundations. In contrast, for interpolation of the original images one can appeal to Shannon's sampling theorem [142]. Image reconstruction and resampling can be performed accurately by applying either polynomial kernels [105] or windowed sinc-functions [165]. In this case, the final precision of the displacement vector must be specified explicitly by the user. Several authors have reported that an accuracy of 1/10th of a pixel is sufficient for DSA [152, 153, 163, 167].[49]

In summary, it can be expected that image-interpolation techniques will, in general, yield better results than match-interpolation techniques. Although, to our knowledge, no thorough quantitative analyses have been carried out, our initial experiments support this hypothesis [106]. It must be remarked that image interpolation is computationally more expensive than match interpolation. However, we have recently demonstrated that the computational cost can be reduced considerably by efficient implementation [104, 106].

V.D Optimization Strategies and Related Issues

Despite its robustness, the use of an exhaustive search procedure for optimization of the chosen similarity measure is usually not a feasible approach. Although computer hardware is rapidly becoming faster, our recent experiments have indicated that this approach is still computationally too expensive. Therefore, a more efficient strategy is demanded.

The use of sophisticated multidimensional optimization techniques such as the downhill simplex method, stochastic or genetic search, and simulated annealing are adequate for the simultaneous optimization of a large number of parameters. When using a control-point based registration approach, as we have recommended in Section V.A, one may choose to compute the local displacement vectors of all control points simultaneously, in analogy with the approach by Fitzpatrick *et al.* [43, 44, 46–49, 99, 118]. However, it is computationally cheaper to compute the displacements of the individual control points separately, in a successive fashion.

The applicability of simple optimization techniques for the computation of individual displacement vectors is determined by the behavior of the employed similarity measure. For example, if the resulting match surface has a pronounced global optimum, but in addition shows many local optima, hill climbing is very likely to fail in finding the global optimum. The same argument holds for some of the multiresolution techniques, and probably explains why the three-step search procedure of Cox & De Jager, in combination with the VOD measure, did not perform adequately [32].

As hinted at in Section IV.A, the behavior of a similarity measure is strongly related to the size of the windows. For example, while Venot *et al.* [158] recorded successful use of hill climbing for the optimization of the DSC measure for windows of size 70×70 pixels, Roos [133, 135] reported that in at least 30 percent of all cases this technique, as well as

[49]Note that on modern DSA devices the manual pixel-shifting technique has an accuracy of 1/8 pixel.

logarithmic search, did not properly optimize the DSC measure for windows of 31×31 pixels. In Section V.B we have recalled the experiments of Buzug *et al.* [18, 20, 21, 23, 25] and Lehmann *et al.* [91], from which it was concluded that the EHD measure is the most adequate for registration in DSA. Buzug *et al.* [19] reported that with this measure, as opposed to others, a window size of 50×50 pixels already leads to very smooth match surfaces, which allows for optimization by hill climbing [16, 18, 23].

V.E Multiplicative versus Additive Grey-Level Distortions

As can be concluded from Section IV.E, techniques for retrospective correction of remnant grey-level distortion artifacts in subtraction images, *i.e.*, after application of the obtained geometrical transformation to the mask image, can be divided into multiplicative and additive approaches. Before being able to judge the validity of these approaches, we must go into more detail about the physics and signal processing behind the acquisition of digital angiographic images.

According to the Lambert-Beer attenuation paradigm (3), X-rays incident on the detector matrix (image intensifier) have been attenuated exponentially by the encountered matter. In the subsequent signal processing chain, the detected signal is further amplified and processed. It has been argued by Kruger *et al.* [82] that, prior to subtraction, images should be processed logarithmically. There are several reasons for this:

(i) Uniformity of contrasted vessels in the resulting subtraction images. It can easily be derived that, with linear processing, the grey-values in contrasted vessels are modulated by the background structures in the mask image. This type of distortion is removed by logarithmic processing.

(ii) With logarithmic processing, the grey-values in contrasted regions of the subtraction images are directly proportional to the thickness of the underlying vasculature. This is an important property for possible subsequent quantitative analyses.

(iii) Logarithmic subtraction imaging reduces the bias introduced by the possible spatially non-uniform detection properties of the image intensifier.

Therefore, logarithmic post-processing is the standard in modern DSA imaging devices. It can be derived from (3) that in this case the grey-value I at position $\mathbf{x}$ in the resulting images becomes:

$$I(\mathbf{x}) = \ln[\Phi_{\varnothing}(\mathbf{x})] - \mathcal{L}(\mathbf{x}). \tag{31}$$

From the analysis by Fitzpatrick (see Section III.A), it can be concluded that contractions and expansions of tissues will result in spatially varying multiplicative grey-level distortion artifacts. These artifacts may be corrected for by incorporating the Jacobian of the obtained geometrical transformation. However, as mentioned by Fitzpatrick [42], such an approach is valid only when subject to the proportionality restriction expressed in (4). From (31) it can be appreciated that (4) holds only when the acquisition system is properly calibrated so as to correct for $\ln[\Phi_{\varnothing}(\mathbf{x})]$. This must be accounted for when applying this technique [44, 46–49, 118].

Also notice that the complexity of the obtained transformation directly determines the complexity of the Jacobian factor to be computed. For instance, if the displacement vector field is constructed by interpolation from the displacements of the control points by using thin-plate splines, the Jacobian will be a non-linear function of x and y. The use of piecewise bilinear interpolation will cause the Jacobian factor to be piecewise linearly dependent on x and y. When using linear interpolation between control points, the Jacobian can easily be shown to become piecewise constant [106]. Furthermore, it must be pointed out that because of the reasons mentioned in Section III.B, the displacement vector field $\mathbf{d} : \mathbf{D} \rightarrow \mathbb{R}^2$ as found by whatever registration approach is very likely not to be an element of the class of possible mappings $\Psi : \mathbf{D} \rightarrow \mathbb{R}^2$ (see Section III.A). This implies that, regardless of the complexity of $\mathbf{d}$, the accuracy of the correction factor $J_{\mathbf{d}}^{-1}$ will be limited.

The effects of X-ray intensity fluctuations, *i.e.*, temporal changes in $\Phi_{\varnothing}$, and non-uniform diffusion of contrast material into the capillaries, may be assessed as follows. Assume that a mask image I_m and a contrast image I_c are produced by X-rays with intensities Φ_m and Φ_c, respectively:

$$I_m(\mathbf{x}) = \ln[\Phi_m(\mathbf{x})] - \mathcal{L}_m(\mathbf{x}), \tag{32}$$

$$I_c(\mathbf{x}) = \ln[\Phi_c(\mathbf{x})] - \mathcal{L}_c(\mathbf{x}) - \mathcal{L}_{\mathcal{I}}(\mathbf{x}), \tag{33}$$

where $\mathcal{L}_{\mathcal{I}}$ denotes the contribution of the contrast medium. Only in the case of complete absence of motion artifacts, or complete motion correction, we have $\mathcal{L}_c(\mathbf{x}) = \mathcal{L}_m(\mathbf{x})$, $\forall \mathbf{x} \in \mathbf{D}$, in which case the subtraction image becomes:[50]

$$I_c(\mathbf{x}) - I_m(\mathbf{x}) = \ln[\Phi_c(\mathbf{x})] - \ln[\Phi_m(\mathbf{x})] - \mathcal{L}_{\mathcal{I}}(\mathbf{x}). \tag{34}$$

From this it can be concluded that in the case of logarithmic processing, fluctuations in X-ray intensity and the non-uniform diffusion of contrast medium both result in additive grey-level distortions in the subtraction images, as was correctly mentioned by Fitzpatrick *et al.* [44] and Cox & De Jager [32]. In the case of linear post-processing of the acquired images, it can be shown that, subject to some restrictions [82], both phenomena result in multiplicative distortions. The situation where X-ray intensity fluctuation has a multiplicative effect, while at the same time the diffusion of contrast medium has an additive effect (or *vice versa*), as mentioned by Van Tran & Sklansky [152, 153], does not occur. Nor does the contrast medium yield both multiplicative and additive distortions, as was asserted by Ko *et al.* [76]. The idea of multiplicative correction to eliminate the effects of changes in X-ray intensity, as originally proposed by Venot *et al.* [154, 158] and also used by Wu *et al.* [166], was based on the assumption of linear post processing.

V.F Suggestions for Future Research

Although there exist 2D geometrical transformations that account for the projective effects of a 3D transformation, we have argued that successful application of image registration techniques to recover any such transformation is limited. To some extent, the problem of independently moving superimposed structures may be solved by using additional information, either from models or from the combination of several projections, possibly at different angles. Ro *et al.* [132] described an approach for the simultaneous correction of artifacts caused by both cardiac and respiratory motion, by a specific combination of mask images taken at different cardiac and respiratory phases. Although preliminary evaluations failed to prove the significance of the improvements resulting from their algorithm [132], such approaches are potentially useful and deserve further investigation.

[50] The minus sign in front of $\mathcal{L}_{\mathcal{I}}(\mathbf{x})$ indicates that contrasted vessels appear dark on a bright background. This is the standard setting in modern DSA imaging. Obviously, reverse subtraction, as was done in the early 1980s, will yield the opposite effect.

However, it must be emphasized that the combined subtraction of several mask images reduces the signal-to-noise ratio.

At several points in this paper we have broached the subject of computational cost. We note that several concepts, such as control-point selection, match interpolation for subpixel precision, or multiresolution optimization, were developed from the sheer necessity to prevent excessive computation times. Although the available time for image post-processing may differ from case to case, minimization of the computational cost of the individual steps of a motion correction algorithm is important from another point of view: the trade off with complexity. For example, a speed up of similarity evaluations allows for the selection of a larger number of control points, or a higher order displacement interpolation scheme, which will improve the accuracy of the registration. Therefore, an interesting topic for future research is efficient *implementation*. Most algorithms published so far were implemented entirely in software. It is obvious that hardware implementations will considerably reduce computational cost. We have already been able to virtually diminish the computation time required for the deformation of images, by using a hardware-accelerated OpenGL graphics architecture. Since the bulk of the computation time is taken up by similarity evaluations, the use of dedicated hardware rather than general purpose processors for this purpose is an interesting option.

V.G Final Remarks

We note that the discussion in this review paper was primarily focused on retrospective motion estimation for the purpose of image enhancement, *i.e.*, the reduction of artifacts by motion *correction*. There also exist several papers on motion estimation for the purpose of motion *analysis* [29, 148]. However, since these algorithms were specifically developed for the analysis of cardiac or vascular motion ("vessel tracking"), they were considered outside the scope of this paper.

Finally, it must be emphasized that the purpose of this paper was not to promote techniques for retrospective motion correction, at the detriment of techniques for prospective avoidance of artifacts. Of course, prevention is better than cure: if the latter techniques yield satisfactory results, they are greatly preferred. In general, however, artifacts cannot be entirely avoided and in such cases retrospective motion correction will prove useful.

VI Conclusions

In this paper we have reviewed the techniques described in the literature for reduction of motion artifacts in DSA. We have summarized the different types of artifacts that have been reported, as well as the techniques that have been proposed to prevent them.

The main purpose of this paper was to present a detailed overview of techniques for retrospective motion correction by image registration and grey-level distortion correction. To this end, we have described the different problems connected with patient motion in angiographic X-ray projection images, as well as the techniques that have been developed to solve these problems. From the evaluations and experiences reported by many authors, we draw the following conclusions:

- In ordinary X-ray projection imaging, it is possible to construct a 2D geometrical transformation that completely accounts for the effects of a 3D transformation of the original objects. However, it is practically impossible to exactly retrieve such a transformation from the projection images, mainly due to the aperture problem and the use of neighborhood operations. In angiography, the presence of additional local contrast in the live images may further limit registration accuracy.

- The computation of local motion or displacements of structures in images can be carried out either by optic-flow or by template-matching based techniques. In practice, the basic assumptions of optic-flow techniques do not apply to digital X-ray projection images. Also, these techniques are sensitive to the inflow of contrast. Template-matching techniques, however, can be made relatively robust against this phenomenon, by applying an adequate similarity measure (see further). Template-matching techniques also use more information to assess local displacements. Therefore, template matching is preferred over optic flow.

- Because of the high computational cost (even with the current status quo of computer technology), it is usually inadmissible to determine the correspondence between images explicitly for every pixel. To reduce computation times to a clinically acceptable level, only a limited number of control points should be considered. Since the computation of displacement vectors will be accurate only in regions containing sufficient image structure, the selection of control points should be based on image content, rather than on regular grids. Appropriate features to extract structured regions are edges, corners, ridges, *etc.*

- Feature-based control-point selection will usually result in irregular grids. In order to obtain a complete displacement vector field, the computationally cheapest approach is to use linear interpolation, which requires triangulation of the set of control points and can be carried out very fast using graphics hardware. More complex interpolation schemes, such as thin-plate splines, are likely to yield better results. However, this will drastically increase computational cost.

- The use of template matching for the computation of local displacements of grey-level structures requires a measure defining “similarity”. Of all similarity measures developed so far, the energy of the histogram of differences (EHD) measure has been shown to be the most adequate measure for registration in DSA. It is insensitive to mean grey-level offsets and local dissimilarities caused by contrasted vessels. Furthermore, it is computationally cheap, it does not require exclusion templates, nor tuning of parameters and yet leads to very smooth match surfaces.

- Since even subpixel misalignments may produce significant artifacts in subtraction images, displacement computations should be carried out with subpixel accuracy. This may be achieved either by interpolation of the image data, and evaluations of the chosen similarity measure at non-integer displacements, or interpolation of the match values at integer displacements, and analysis of the resulting continuous match surface. In general, the former technique can be expected to yield better results. An accuracy of 1/10 pixel is usually sufficient.

- To further reduce computation time, the number of similarity evaluations should be as small as possible. This requires the use of an efficient optimization strategy. The applicability of simple optimization techniques for the computation of individual displacement vectors is determined by the behavior of the employed similarity measure. As pointed out before, the EHD measure has been shown to yield very smooth match surfaces, which allows for a computationally cheap hill-climbing procedure.

- After application of the transformation, as obtained by the registration procedure, to the mask image, there may be remaining grey-level distortion artifacts. These artifacts may be the result of contractions and expansions of tissues, fluctuations in the intensity of X-rays, or the non-uniform diffusion of the contrast medium. In the case of logarithmic amplification of the acquired images, artifacts caused by tissue deformations lead to spatially varying multiplicative grey-level distortions. In theory this distortion is described by the Jacobian of the transformation, subject to the restriction of proper calibration of the acquisition system. In practice, the effectiveness of the Jacobian correction factor is limited by the accuracy and complexity of the obtained transformation. Artifacts caused by X-ray intensity fluctuations or contrast diffusion both result in spatially varying additive grey-level distortions.

To further improve the performance of registration algorithms, future research should focus on the use of additional knowledge, either from models or from the combined information of multiple projections, possibly from different angles. Another interesting topic is efficient implementation. Hardware implementations will considerably reduce the computational cost of the algorithms, which may also be exploited to increase their complexity. Since, at his point, the bulk of the computation time is taken up by similarity evaluations, the use of dedicated hardware for this purpose is an interesting option.

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