In vivo strain assessment of the abdominal aortic aneurysm

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The only criteria currently used to inform surgical decision for abdominal aortic aneurysms are maximum diameter (>5.5 cm) and rate of growth, even though several studies have identified the need for more specific indicators of risk. Patient-specific biomechanical variables likely to affect rupture risk would be a valuable addition to the science of understanding rupture risk and prove to be a life saving benefit for patients. Local deformability of the aorta is related to the local mechanical properties of the wall and may provide indication on the state of weakening of the wall tissue. We propose a 3D image-based approach to compute aortic wall strain maps in vivo. The method is applicable to a variety of imaging modalities that provide sequential images at different phases in the cardiac cycle. We applied the method to a series of abdominal aneurysms imaged using cine-MRI obtaining strain maps at different phases in the cardiac cycle. These maps could be used to evaluate the distensibility of an aneurysm at baseline and at different follow-up times and provide an additional index to clinicians to facilitate decisions on the best course of action for a specific patient.

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1. Introduction

In clinical practice, surgery is advised to patients presenting with abdominal aortic aneurysms (AAAs) exceeding 5.5 cm in maximum diameter (Brown et al., 1999). However, there is evidence that aneurysms smaller than this threshold can and do rupture (Scott, 2002; Lederle et al., 2002; Powell and Brady, 2004). Conversely, some larger aneurysms do not rupture during the lifespan of the patient. An aneurysm ruptures because the local strength of the wall is insufficient to sustain the instantaneous load due to blood pressure. Local wall weakening has been reported and can be the result of an imbalance between production of new constituents and degradation of extracellular matrix (Helltenthal et al., 2009) in response to a stress-mediated mechanism that attempts to maintain homeostasis, or the optimal wall thickness and composition (Choke et al., 2005). Therefore, a general indication based on diameter measurements alone may not be sufficient to discriminate whether AAAs are close to rupture. Instead, individually tailored rupture indices are needed that take into account the local properties of the wall, their evolution in time as well as the regional stress level.

Wilson et al. (2003) measured the distensibility of the aorta in a population of AAAs not considered for repair due to small aneurysm size, comorbidities or patient unwillingness. Distensibility was measured at different follow-ups as the increment in diameter in response to the pulse pressure (diastolic minus systolic pressure). Aneurysms that ruptured during follow-up were characterized by higher diastolic pressure and larger diameter, and their distensibility at baseline was higher; in addition, changes in distensibility were correlated with the risk of rupture. Di Martino et al. (2006) performed tensile tests on samples of aortic wall excised from electively repaired and ruptured AAAs, and showed that maximum tissue stiffness was inversely correlated with wall strength, suggesting lower stiffness as a possible predictor of AAA rupture. In addition, the study showed that arterial wall stiffness is not homogeneous in the presence of an aneurysm, supporting the hypothesis that the wall remodels locally.

These results by Wilson et al. (2003) and Di Martino et al. (2006) suggest that a new predictor of AAA rupture could be maximum diameter and growth rate with measures of local tissue distensibility in vivo.
Algorithms to measure wall strains for biological structures have been previously proposed. Namely, the speckle tracking technique takes advantage of the ability of echography to detect the velocity field in the scanned volume, and has been used to assess ventricular function (Helle-Valle et al., 2005; Edwardsen et al., 2006; Kim et al., 2007), as well as arterial strains (Estensen et al., 2013; Yang et al., 2011). Limitations related to this approach are the exclusiveness of the imaging technique from which data can be obtained, and the strong influence of the orientation of the hand-held scanning probe on the results. Veress et al. proposed hyperelastic warping to quantify kinematics using local image intensity changes to compute forces to be applied to the reconstructed geometry to register the images at different timesteps and compute displacements (Veress et al., 2005a,b; Phatak et al., 2009). This approach is advantageous when the elastic behavior of the vessel wall is the only contribution to the deformation. Conversely, in an AAA, the presence of intraluminal thrombus (ILT) and surrounding structures creates a complex non-linear system. Furthermore, the hyperelastic warping method requires the definition of a constitutive model, which may influence the outcome. MRA imaging has been adopted to measure strains on thick tissues. However, the method has not been validated on tissues thinner than the cardiac ventricular chambers and the technique provides strains only on cross-sections of the structure.

Drawing inspiration from motion analysis methods used in computer vision, we propose a 3-D image-based approach to measure deformations in vivo that is applicable to a variety of biological structures and across multiple tomographic imaging techniques. Optical flow has been used for several years to compute motion fields from sequential images. The basic tenet of the method is that the brightness intensity of a moving object remains constant between two images separated by a small interval of time. This is used to approximate the velocity at each pixel and to compute a displacement field. The method was first introduced for 2D images by Horn and Schunck (1981). They proposed a global method to compute displacements that minimize the differences between the image at time 0 and the image at time t. The algorithm uses regularity constraints to yield smooth velocity fields and make the problem tractable. Several variations of the original method have been proposed, including methods that work on individual sub-regions of the image (Lucas et al., 1981) and methods that use multi-scale strategies to improve tracking for larger displacement fields (Brox et al., 2009).

As a first step, we extended the original Horn and Schunck method to 3D image data and tested its validity in the case of AAA wall strain. We computed deformation directly from the optical flow of time-wise consecutive images, without performing a finite element simulation so that no constitutive model for the wall or ILT is required. Instead, the deformation comes directly from the wall motion and is due to the combined effect of the pulsatile blood pressure, the properties and local thickness of the wall and ILT, and the surrounding structures.

We validated our approach comparing the first principal Green–Lagrange strains obtained from a finite element simulation of a AAA geometry under cyclic pressure and the corresponding strains obtained from synthetic DICOM stacks generated from the meshes corresponding to 20 phases of the simulation.

Finally, as a demonstrative application, we applied the technique to nine cases of AAA dynamically imaged over the cardiac cycle through cine-MRI. We obtained maps of local deformation undergone by each AAA throughout the cardiac cycle. These maps may be used to evaluate the distensibility of an aneurysm at baseline when the aneurysm is diagnosed and at different follow-up times and could be used, in combination with clinically adopted indices, to inform the clinician on the best course of action for a specific aneurysm.

2. Materials and methods

Cine-MRI scanning: Cine-MRI scans of nine human AAA patients were obtained from the Division of Vascular Surgery at the Allegheny General Hospital, Pittsburgh, PA, following a protocol approved by the ethical commission. All images were obtained on a General Electric 1.5 T imager (Signa Excite, GE Medical Systems). Repetition time/echo time/flip angle of 3.4 ms/1.5 ms/45° were adopted, with a 75% k-space acquisition, 256 × 256 matrix, 6-mm slice thickness, no gap. The images consist of 20-phase ECG gated DICOM series taken at n levels across the AAA, each describing the in-plane evolution of a cross-section of the imaged aorta at 20 time points throughout the cardiac cycle. For the images under study, n varies from patient to patient, ranging from 24 to 31. The spatial resolution achieved, with 1.4 mm in the plane and 6.0 mm between planes, is highly anisotropic.

Initial aortic mesh: In order to identify and segment the AAA geometry across all slices for the same phase, we adopted an active-contour based segmentation approach, taking advantage of the Interactive Toolkit (ITK) pipeline (Yushkevich et al., 2006; Golbi et al., 2008). At first, we selected a region of interest (ROI) containing the AAA within the DICOM stack corresponding to Phase 0, in order to reduce the size of the 3-dimensional data set, and we resampled the ROI to a 2 mm isotropic resolution, by means of cubic interpolation. The initial active contour was defined by means of a spherical balloon inside the AAA that could expand in a volume identified by a lower and an upper grayscale threshold. The balloon contour evolution was dictated by weighting parameters according to the approach by Caselles et al. (1993).

The isosurface comprising the segmented region was exported as an stl triangular mesh. This initial segmentation was smoothed using a Taubin filter (Taubin, 1995) to obtain the desired smoothing and minimize the shrinkage of the structure. Finally, the mesh was simplified using a Quadric Edge Collapse Decimation (Garland and Hecktber, 1997) to reduce the number of shells to approximately 3000.

In vivo velocity field detection: The displacement of each node of the initial mesh from phase n to phase n + 1 was computed approximating nodal velocities using a 3D extension of the optical flow method (Horn and Schunck, 1981; Fleet and Weiss, 2006). This method follows the displacement of an object between images taken at subsequent time steps by detecting the grayscale feature corresponding to the object and computing its velocity. The basic assumption of the method is that the brightness intensity of an object remains unaltered across two successive images if the displacement is relatively small. The second assumption is that there is a smooth change of the intensity values between two consecutive phases. The algorithm, described in detail in Appendix A, computes the velocity field for each voxel in the DICOM stack using a minimization function. The velocities obtained between stack n and n + 1 were added to the nth nodal position of the aortic surface mesh and multiplied by dt = 1 in order to obtain the (n + 1)th nodal position, describing the geometrical configuration of the aorta at timestep n + 1.

Computation of deformation: Given the deformation gradient F at point x in the reference configuration, the push-forward of a material vector v attached at X is the spatial vector v' attached at point x (the current placement of X) in the current configuration and defined as

\[ v' = Fv. \]

After defining point X as node 1 of each triangular shell element, we defined a vector \( A_1 \) leading from node 1 to 2, a vector \( A_2 \) leading from node 1 to 3, and a vector \( A_3 \) defined by the normal to the element in its reference configuration. The corresponding vectors \( a_i \) in the current configuration are obtained as

\[ a_i = \hat{a}_i^T F_i. \]

where \( \hat{a}_i \) is the ith component of \( A_i \), \( a_i \) the ith component of \( A_i \), and \( F_i \) the ith component of \( F \). While \( A_i \) was imposed to have magnitude 1, \( a_i \) was imposed to have a magnitude such to ensure incompressibility of the wall tissue. As all three material \( A_i \) and spatial \( a_i \) vectors are known, a system of equations can be solved to find all components of \( F \).

From F, the right Cauchy–Green deformation tensor C is computed as \( C = F \cdot F^T \), where \( F^T \) is the transposed matrix of F. The Green–Lagrange strain E can therefore be computed as \( E = (C - I)/2 \), with principal strains computed as its eigenvalues.

Validation: To validate our approach, we used a Computed Tomography scan of a patient’s aneurysm obtained following a protocol approved by the ethics board at the University of Calgary. A mesh of the abdominal aeurysm wall was obtained using VASCOPS (VASCOPS GmbH, Graz, Austria). A finite element simulation was performed on the aneurysm model using Abaqus (vs. 6.13, Dassault Systemes, Waltham, MA). The simulation consisted of a loading cycle to 300 mmHg and symmetric unloading cycle. The upper and lower ends of the aneurysm were constrained in all three directions. Non-linear material properties were used, following the strain energy function proposed by Ragavhan and Vorp (2000) of the form

\[ W = a|\varepsilon| - b|\varepsilon|^2 \]

where \( a \) and \( b \) are the material parameters, \( |\varepsilon| \) is the first invariant of the right Cauchy–Green tensor. The parameters used, i.e. \( a = 113.4 \) kPa and \( b = 9.2 \) kPa, were obtained from non-linear regression using uniaxial tensile tests on a polymeric material that exhibited a stiffness similar to that of a human aorta. The maximum
pressure of 80 mmHg was chosen to obtain a wide range of deformation, from no deformation to values close to the deformation in a healthy aorta. The first principal Green–Lagrange strains computed at the different phases with respect to phase 1 were recorded and used as ground truth in the subsequent comparison. The mesh at different phases from the simulation was exported in .stl format, imported in Simpleware’s +CAD Module (Simpleware Ltd., Exeter, United Kingdom) and used to generate synthetic DICOM image stacks at different resolutions: 0.5 mm, 1.0 mm, 1.5 mm isotropic resolutions, and 1.5 mm in-plane, 6.00 mm longitudinal resolution, in analogy to the resolution available from the MRI scans. Fig. 1 shows one section across a synthetic DICOM stack. The strain maps obtained from the synthetic DICOM images were compared with the corresponding ground truth using a Spearman correlation coefficient $\rho$. To assess the effect of noise, different levels of Rician noise were added to the 1.5 mm synthetic isotropic-resolution DICOM stack corresponding to signal-to-noise ratio (SNR) levels ranging from around 40 to 14 dB. The effect of noise was assessed using a Spearman correlation coefficient.

3. Results

Validation: Fig. 2 plots cross-sections of the synthetic aneurysm showing the nodes of the mesh being tracked by the algorithm at different phases (using 1.5 resolution and SNR of 42.3 dB). Table 1 reports Spearman’s $\rho$ correlation coefficients calculated between ground truth and the results obtained from the synthetic DICOMs for each of the resolutions studied.

Table 1

<table>
<thead>
<tr>
<th>Resolution</th>
<th>Correlation to ground truth</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mm isotropic</td>
<td>0.81</td>
<td>$p &lt; 0.01$</td>
</tr>
<tr>
<td>1.0 mm isotropic</td>
<td>0.82</td>
<td>$p &lt; 0.01$</td>
</tr>
<tr>
<td>1.5 mm isotropic</td>
<td>0.84</td>
<td>$p &lt; 0.01$</td>
</tr>
<tr>
<td>1.5 mm orthotropic</td>
<td>0.76</td>
<td>$p &lt; 0.01$</td>
</tr>
</tbody>
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Fig. 3 shows maps of the computed vs. ground truth displacements and the computed vs. ground truth strain for Phase 8 for the DICOM stack with 1.5 mm/pixel resolution. For the same resolution (1.5 mm/pixel), Fig. 4 shows medians and spread of the first principal Green–Lagrange strain for the ground truth (upper panel) and the synthetic DICOM stacks for all the 20 phases studied.

Patient-specific AAAs: Fig. 5 plots the first principal Green–Lagrange strain distribution computed at the systolic peak of pressure for each aneurysm analyzed. In addition to regions corresponding to healthier walls (neck, iliac arteries), higher values of strain were found at the junction between the neck and the bulge of the aneurysm. Median strains were computed for each patient and are shown in Fig. 6 for each instant in the cardiac cycle. The box plots in Fig. 7 compare the median and the spread for each aneurysm.

The average maximum principal Green–Lagrange strain computed was 0.07, with a standard deviation of 0.02. Table 3 reports...
maximum principal strain, maximum diameter of the aneurysm, age and gender for each patient studied.

4. Discussion

We developed a software technique that allows the user to perform the following steps: (1) reconstruct and mesh a 3D model of the aneurysm at phase 0; (2) compute nodal displacements at each subsequent phase using an optical flow technique; (3) create three-dimensional maps of local in vivo strains for the aneurysm wall under study.

From the validation step, we concluded that the algorithm computes strains on a AAA geometry with strong correlation between measured and theoretical (ground truth) values. The displacements were computed with high accuracy (errors lower than 2% of the
The strains computed from the algorithm appear to underestimate ground truth at the phases corresponding to higher deformation, however the strain patterns were captured correctly for all phases at all the resolutions considered. In assessing these results it must be considered that the validation was obtained on artificial images that presented very little variability in brightness (see Fig. 1). Real tomographic images have a much greater variability due to heterogeneous tissue properties, providing more contrasted features that can be tracked by the algorithm. We are currently assessing other validation approaches that could allow the use of real images, such as the use of in vivo sonomicrometry markers.

Comparing the results from noise-free stacks with those obtained applying varying levels of Rician noise (Gudbjartsson and Patz, 1995), we conclude that the technique is robust to noise for a wide range of SNR levels.

A strong correlation was obtained between measured and true first principal Green–Lagrange strains at all the resolutions considered. However, a decrease in Spearman’s $\rho$ correlation coefficient can be observed in the case of anisotropic voxel resolution, due to the lower spatial resolution in the $z$-direction affecting the tracking of longitudinal motion.

We applied the technique to nine patients undergoing surveillance for AAA at the Allegheny General Hospital in Pittsburgh, PA. Strains are highly heterogeneous within each aneurysm as well as across patients. The average maximum first principal Green–Lagrange strain is consistent with results by Imura et al. (1986) who measured 2D strain from ultrasound. The unique feature of our algorithm is the ability to depict the spatial distribution of deformation in vivo, which depends on the presence of surrounding structures, on the complex fluid dynamics inside the lumen and on the local wall mechanical properties (Raghavan et al., 2006). One of
the advantages is that the displacement of the wall behind thick or thin layers of thrombus can be obtained without requiring the direct simulation of IIT, thus limiting assumptions on IIT properties or its mechanical role (Thubrikar et al., 2003). For all the AAAs investigated we found higher values of strains at the junction between the neck and the bulge of the aneurysm (Fig. 5) where healthier vascular wall tissue transitions to aneurysm tissue. 

Local weakening of the wall has been recognized to play an important role in the assessment of rupture risk for AAAs (Vande Geest et al., 2006; Auer and Gasser, 2010). Deformability as well as its changes through time are correlated to the degree of weakening of the wall (Wilson et al., 1998; Di Martino et al., 2006). Our method allows for a local in vivo assessment of deformation where one phase of the cardiac cycle is used as a reference. Consequently, a map of maximum strain values could be computed at baseline, and then at each of the patient's follow-ups, making it possible to track global and local changes in distensibility.

There are several limitations to be acknowledged in this preliminary work. The Horn–Schunk (Horn and Schunck, 1981) optical flow approach is a global gradient-based approach. In other words, to solve an underdetermined linear system, the method takes advantage of a global constraint (the spatial coherence parameter) that forces the partial derivatives of neighboring motion vectors to be small (Barron et al., 1994; Senst et al., 2012). We deemed this acceptable due to the relatively small deformation of the AAA wall. Furthermore, we chose not to adopt a local gradient approach, such as the one by Lucas–Kanade (Lucas et al., 1981) that may elicit sharp discontinuities in disagreement with our hypothesis of smooth continuum motion. An interesting category of optical flow methods uses a multi-scale pyramidal approach that improves the results in the case of large deformations (Brox et al., 2009). Given the good temporal resolution achieved with cine-MR and the limited motion of the aortic wall, small displacements occur between any nth to (n+1)th phase. In accordance, we chose a Horn–Schunk non-pyramidal approach. We assumed that objects (or wall features) maintain constant brightness across subsequent images. This is consistent with the sequence used for the image acquisition: contrast and brightness are mainly determined by tissue properties that do not change through the cardiac cycle (Bieri and Scheffler, 2013). The method is resilient to the presence of noise when synthetic Rician noise (Gudbjartsson and Patz, 1995) is introduced. It is entirely possible that multi-scale methods may prove better when the method is applied to high-resolution CT images. The cine-MRI data had lower resolution in the z-direction with respect to the in-plane resolution. This certainly reduced the accuracy of the strain estimations, as demonstrated by the validation experiments; greater spatial resolution would offer improvements in the spatial results. It is important to remark that our approach aims at describing the spatio-temporal maps of deformation with respect to the end-diastolic configuration of the aorta, which we considered as a reference. The current approach does not provide a measure of deformation of the arterial wall with respect to its unloaded, zero-pressure configuration, as this is beyond the scope of this study. Finally, the density of the initial mesh was chosen in relation with the voxel size and to keep memory allocation tractable. The choice of mesh size and mesh smoothing may impact the results and warrants further investigation.

Conflict of interest statement

There is no conflict of interest related to this paper.

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Appendix A. Supplementary data

Supplementary data associated with this paper can be found in the online version at http://dx.doi.org/10.1016/j.jbiomech.2014.11.016.