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Research Paper

On the prospect of patient-specific biomechanics without patient-specific properties of tissues

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ABSTRACT

This paper presents main theses of two keynote lectures delivered at Euromech Colloquium “Advanced experimental approaches and inverse problems in tissue biomechanics” held in Saint Etienne in June 2012. We are witnessing an advent of patient-specific biomechanics that will bring in the future personalized treatments to sufferers all over the world. It is the current task of biomechanists to devise methods for clinically-relevant patient-specific modeling. One of the obstacles standing before the biomechanics community is the difficulty in obtaining patient-specific properties of tissues to be used in biomechanical models. We postulate that focusing on reformulating computational mechanics problems in such a way that the results are weakly sensitive to the variation in mechanical properties of simulated continua is more likely to bear fruit in near future. We consider two types of problems: (i) displacement-zero traction problems whose solutions in displacements are weakly sensitive to mechanical properties of the considered continuum; and (ii) problems that are approximately statically determinate and therefore their solutions in stresses are also weakly sensitive to mechanical properties of constituents. We demonstrate that the kinematically loaded biomechanical models of the first type are applicable in the field of image-guided surgery where the current, intraoperative configuration of a soft organ is of critical importance. We show that sac-like membranes, which are prototypes of many thin-walled biological organs, are approximately statically determinate and therefore useful solutions for wall stress can be obtained without the knowledge of the wall’s properties. We demonstrate the clinical applicability and effectiveness of the proposed methods using examples from modeling neurosurgery and intracranial aneurysms.

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1. Introduction

Computational mechanics has enabled technological developments in almost every area of our lives. One of the greatest challenges for mechanists is to extend the success of

computational mechanics to fields outside traditional engineering, in particular to biology, biomedical sciences, and medicine (Oden et al., 2003). By extending the surgeon’s ability to plan and carry out surgical interventions more accurately and with less trauma, computer-integrated surgery (CIS) systems will

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improve clinical outcomes and the efficiency of health care delivery. CIS systems will have a similar impact on surgery to that long since realized in computer-aided design (CAD) and computer-integrated manufacturing (CIM).

Before this grand vision can be realized, a number of theoretical and technological difficulties associated with accurate and clinically practical simulation of the mechanical responses of human organs must be addressed. One of the most challenging is the problem of identifying patient-specific properties of tissues. The difficulty of obtaining patient-specific mechanical properties of soft tissues has stimulated a lot of research in experimental mechanics, leading in particular to the application of MR and ultrasound elastography initially developed for diagnosis (Muthupillai et al., 1995; Sarvazyan et al., 1998; Xu et al., 2007), as well as renewed interest in inverse problems (Gee et al., 2010; Lu and Zhao, 2009; Sinkus et al., 2010; Zhao et al., 2009).

In this paper, summarizing the content of two keynotes delivered at Euromech Colloquium “Advanced experimental approaches and inverse problems in tissue biomechanics” held in Saint Etienne in June 2012, we postulate that focusing on reformulating computational mechanics problems in such a way that the results are weakly sensitive to the variation in mechanical properties of simulated continua is more likely to bear fruit in near future. In particular we focus on two types of problems:

- (i) pure-displacement (Ciarlet, 1988) and displacement-zero traction problems (Miller and Wittek, 2006; Miller et al., 2010) whose solutions in displacements are weakly sensitive to mechanical properties of the considered continuum; and
- (ii) problems that are approximately statically determinate and therefore their solutions in stresses are weakly sensitive to mechanical properties of constituents (Gere and Timoshenko, 1997; Lu et al., 2008; Timoshenko, 1981).

In the field of patient-specific biomechanics the first type of problems is prevalent in the area of image-guided surgery, where we are interested in the current, intraoperative configuration of an organ of interest and have at our disposal detailed preoperative images as well as some, often very limited, intraoperative information. Therefore it is possible to determine deformations of soft organs during surgery without knowledge of patient specific properties of tissues. The second type of problems has been identified in the field of biomechanics of intracranial aneurysms that can be approximately modeled as thin-walled structures that are known to be statically determinate. If we formulate the equilibrium boundary value problem inversely, as explained in Section 2.2, we are able to determine the aneurysm wall stress distribution without the knowledge of patient-specific mechanical properties of the tissues comprising the wall.

This article is organized as follows. In Section 2 we put forward the arguments why in certain cases we are able to obtain meaningful patient-specific results without the knowledge of particular patient's tissue properties. In Section 3 we give application examples taken from the areas of neurosurgical simulation and aneurysm modeling. Section 4 contains discussion and conclusions.

2. Theoretical arguments for unimportance of mechanical properties of tissues

2.1. Pure displacement and displacement-zero traction problems

As suggested in papers (Miller, 2005a; Miller and Wittek, 2006), in problems where loading is prescribed as forced motion of boundaries, the unknown deformation field within the domain depends very weakly on the mechanical properties of the continuum. To see why, first consider an (over-simplified) quasistatic, linear elastic case. Then the following dimensional reasoning applies: the loading is provided by the enforced motion of boundaries measured in meters [m]; the result of computations are displacements measured in [m]; therefore the result cannot depend on the stress parameter measured in $[Pa=N/m^2]$. We should note here that the result can depend on (dimensionless) Poisson's ratio and on (dimensionless) ratios of stress parameters if the model contains materials with different stiffness. The dependence on the volumetric response (e.g., Poisson's ratio) is of minor consequence for soft organ biomechanics because tissues such as the brain, liver, kidney or prostate are considered almost incompressible (Bilston, 2011; McNearney et al., 2010; Miller, 2000, 2011).

In the general nonlinear case the displacement results will still remain insensitive to the stress parameter appearing in the nonlinear material law, but may depend on the particular form of that law (as the functional form of a constitutive law does not have a dimension). This dependency can, however, be expected to be rather weak, as explicitly demonstrated in Miller (2001, 2005b) where the shapes of compressed and extended cylinders were shown to be essentially independent of the material law used for the cylinder's material, see Fig. 1. These results suggest a move away from mechanics towards kinematics: the main quantities of interest in this approach are displacements, strains and their histories. Insensitivity to material properties is the feature of great importance in biomechanical modeling, where there are always uncertainties in patient-specific properties of tissues.

2.2. Statically determinate structures

As discussed in virtually any elementary solid mechanics text, the stress in a deformable solid depends on the applied load, geometry, boundary conditions and properties of the material comprising the body. There is, however, a family of structures in which the stress field depends on the load, the boundary conditions and the geometry, but not the material property. Structures as such are called statically determinate (Gere and Timoshenko, 1997; Timoshenko, 1981). Truly statically determinate systems are rare in finite deformation regime, but there are problems that are approximately so in the sense that the stress distribution depends weakly on the material properties. Exploiting this feature, we may obtain reasonably accurate stress solutions without invoking accurate material description, which we know is difficult to obtain in biological systems.

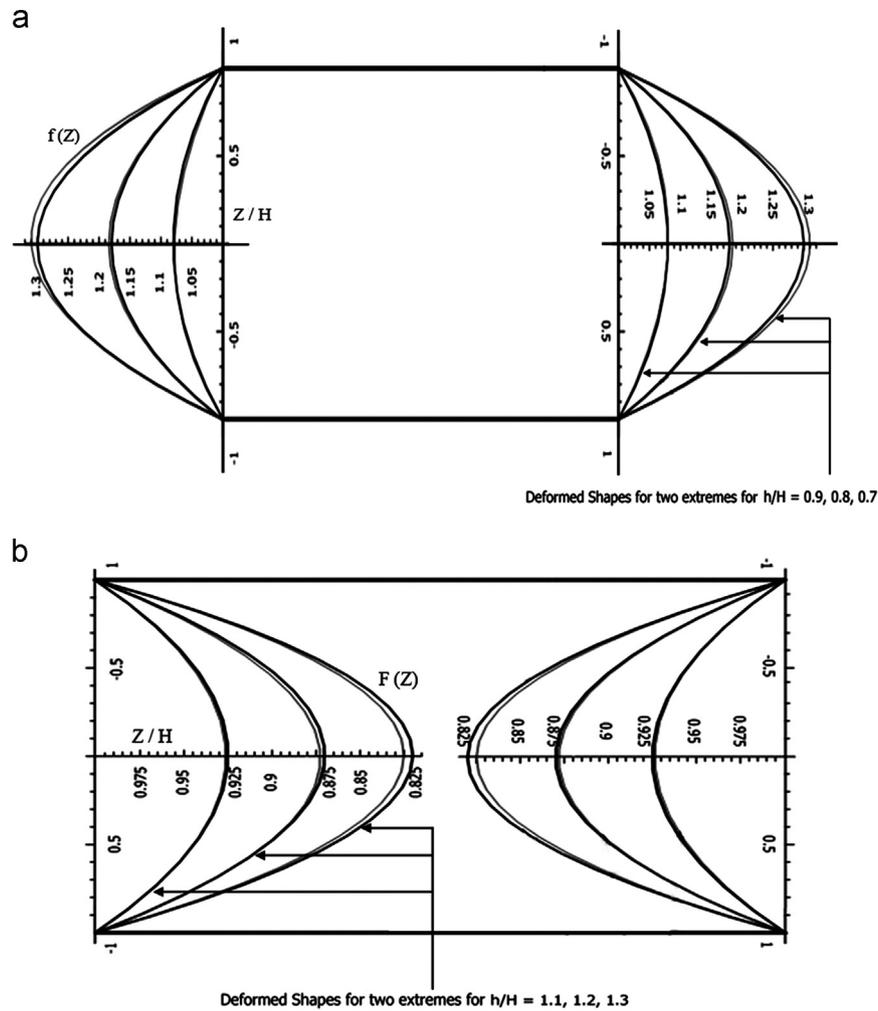


Fig. 1 – Shapes of cylinders modeled as Extreme-Mooney and neo-Hookean materials. (a) compression by 10, 20 and 30%. (b) extension by 10, 20 and 30%. Z/H denotes a dimensionless coordinate along the height of the cylinder. $f(Z)$ stands for the shape of the side of the deformed cylinder. Shape of a cylinder made from a “real” material is expected to fall between the two extremes.

We will focus on a particular type of structures, sac-like membranes, which are prototypes of many thin-walled biological organs. In an idealized membrane structure, the stress in the wall can be viewed as locally in a plane stress state described by three components. If the membrane surface is curved in space, the equilibrium equation breaks into three component equations. Thus, the equilibrium problem is closed (three equations for three components) (Lu et al., 2008). In a pure traction boundary problem, the stress resultant (i.e., tension) should be completely determined without reference to the mechanical properties of the material. If the wall thickness is also known, the wall stress can be readily inferred. A prominent example is a pressurized axisymmetric membrane closed at the pole for which the principal stress resultants (T_1, T_2) follows the Laplace law

$$T_1 = \frac{P}{2\kappa_2}, \quad T_2 = \frac{P}{\kappa_2} \left(1 - \frac{\kappa_1}{2\kappa_2} \right) \quad (1)$$

Notably the solution involves only the transmural pressure P and principal curvatures (κ_1, κ_2) , not material parameters. The Laplace law, albeit for idealized geometry, has

been utilized in early studies of aneurysm mechanics (Humphrey and Kyriacou, 1996; Kyriacou and Humphrey, 1996; Shah et al., 1998).

The equilibrium problem is no longer closed if displacement boundary conditions are involved. However, as indicated in classical papers (Goldberg, 1965; Rossettos, 1966; Wu and Peng, 1972), for membrane structures fixed along a basal edge, the stress solution exhibits a boundary layer phenomenon: the influence of material properties is pronounced only in a thin layer near the fixed edge. Outside the boundary layer the stress approaches asymptotically a static solution. These findings were obtained in axisymmetric membranes where analytical solutions are available, and under the assumption that the structure is sufficiently deep (i.e., the distance from the apex to the basal edge is greater than or comparable to the lateral dimension). Recent numerical simulations conducted by the authors' group (Lu et al., 2008; Zhou et al., 2010) confirmed the boundary layer phenomenon for deep membranes without geometric symmetry.

If a membrane structure has undulated surface features, bending moments and transverse shear forces are needed to

achieve equilibrium and thus static determinacy no longer holds. However, since the most efficient way for a thin-walled sac-like structure to sustain a transmural pressure is by in-plane tension, it is reasonable to expect that biological organs are optimized by nature to adapt this mechanism. Thus, even though the presence of the bending stress and transverse shear force is necessary, the in-plane stress is expected to dominate, at least in regions that are relatively smooth and distanced from boundaries or holes. As such, the wall tension is expected to be approximately statically determinate.

The property of static determinacy can be profitably exploited in biomechanics of intracranial aneurysms, as shown in Section 3.2. In aneurysm analysis, one typically seeks the wall stress, as the stress is thought to be a risk factor. A major challenge in aneurysm analysis is that certain critical information including patient-specific wall tissue properties is often unknown.

3. Examples from computational biomechanics for medicine

3.1. Computation of brain deformations during surgery

Let us consider non-rigid image registration in image-guided procedures where high resolution preoperative scans are warped onto lower quality intraoperative ones (Ferrant et al., 2001; Warfield et al., 2005b). The task of particular clinical interest is registering high-resolution preoperative MRIs with lower quality intraoperative imaging modalities, such as intraoperative ultrasound and multi-planar MRIs.

The brain, whose detailed preoperative image is available, deforms after craniotomy due to a number of physical and physiological reasons (so-called brain shift). We are interested in the intraoperative (i.e., current) position of the brain, of which partial information is provided by low-resolution

intra-operative images. In mathematical terms this problem can be described by equations of solid mechanics.

Consider motion of a deforming body in a stationary coordinate system, Fig. 2.

Boundary conditions may prescribe kinematic variables such as displacements and velocities (essential boundary conditions) or tractions (natural boundary conditions, these also include point forces). It should be noted that “boundary conditions” do not have to be applied at the physical boundary of the deforming object.

Depending on the amount of information about the intraoperative position of the brain available from intraoperative imaging modalities, neuroimage registration can be described in mathematical terms in two ways. If the entire boundary of the brain can be extracted from the intraoperative image then we know the initial position of the domain (i.e., the brain), as determined from preoperative MRI and the current position of the entire boundary of the domain. We are looking for the unknown displacement field within the domain (the brain), in particular the current position of the tumor and critical (from the perspective of a surgical approach) healthy tissues. No information of surface tractions is required for the solution of this problem. Problems of this type are called in theoretical elasticity “pure displacement problems” (Ciarlet, 1988).

If only limited information is available about the boundary (e.g., only the position of the brain surface exposed during craniotomy and perhaps current positions of clearly identifiable anatomical landmarks, e.g., as described in Nowinski (2001)) and no external forces are applied to the boundary, a slightly different mathematical description is needed:

- Known: initial position of the domain (i.e., the brain), as determined from preoperative MRI.
- Known: current position of some parts of the boundary of the domain (the brain); zero pressure and traction forces

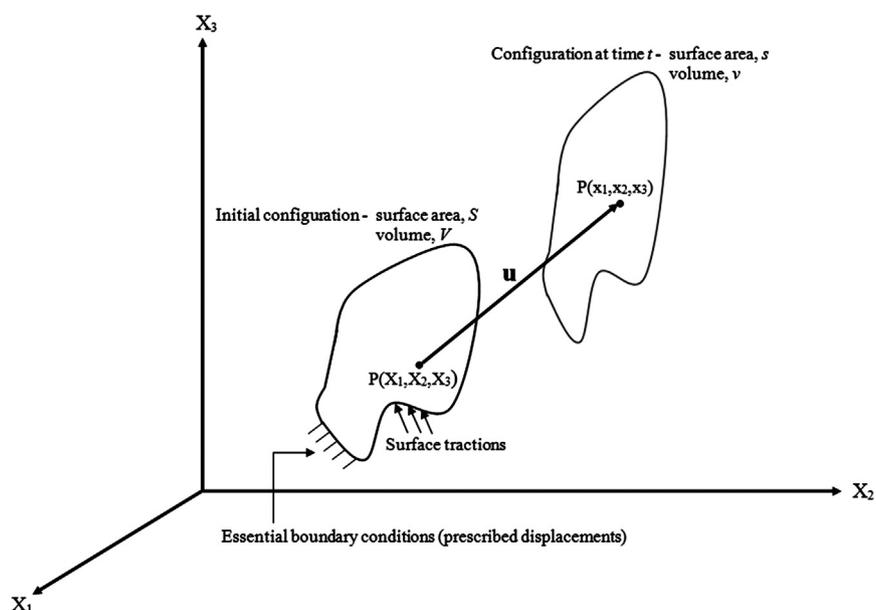


Fig. 2 – Motion of a body in a stationary coordinate system. Initial configuration, described by upper case coordinates, can be considered as a high quality preoperative image. Current, deformed configuration (described by lower-case coordinates) is unknown, however partial information is available from a lower resolution intraoperative image.

everywhere else on the boundary. Consequently contacts need to be modeled kinematically as e.g., in [Joldes et al. \(2009a; 2008\)](#).

- Unknown: displacement field within the domain (the brain), in particular current position of the tumor and critical healthy tissues.

Problems of this type are very special cases of so called “displacement—traction problems” ([Ciarlet, 1988](#)) that have not, to the best of our knowledge, been considered as a separate class and no special methods of solution for these problems exist. In [Miller and Wittek \(2006\)](#) it was suggested to call such problems “displacement—zero traction problems”.

The solutions in displacements – the variable of interest in the context of image-guided surgery – for both pure displacement and displacement-zero traction problems are only very weakly sensitive to mechanical properties of the deforming continuum, and therefore can be obtained without knowledge of patient-specific properties of the brain tissue.

In the case of the full-scale brain deformation computation our experience confirms the expected insensitivity of computed displacement fields to chosen tissue constitutive models ([Wittek et al., 2009](#)). [Table 1](#) contains observed and computed displacements for centers of gravity of ventricles and tumor for a case of tumor removal described in detail in [Wittek et al. \(2007\)](#). In the computations the same general geometrically nonlinear formulation was used together with various constitutive models.

When interpreting the results summarized in [Table 1](#) one should take into account that the accuracy of determining positions of centers of gravity of tumor and ventricles is limited by the voxel size in the intraoperative MRI images used in this study—0.85 mm × 0.85 mm × 2.5 mm. We also need to consider that the accuracy of manual neurosurgery is approximately 1 mm ([Warfield et al., 2005a](#)). Therefore, for practical purposes, values differing by less than 0.80 mm can be considered the same. The slightly different results seen in the last row of [Table 1](#) are due to the fact that linear elastic constitutive model is not compatible with finite deformation solution procedure ([Bathe, 1996](#)). It is apparent that the choice of the constitutive model does not make any practical difference in the solution for displacements and therefore we recommend the use of Neo-Hookean material model.

Of course, as discussed in [Section 2.1](#), theoretically the results should depend on the (dimensionless) ratio between the tumor and healthy tissue stiffness. We simulated tumor to be between three times more compliant to nine times stiffer than the healthy brain. There is no noticeable difference in the results. The reason is that the tumor’s volume is low as compared to the volume of the cranium and therefore the tumor is essentially “carried” in the displacement field of the brain.

The result given in [Table 1](#) above is important because it demonstrates the utility of computational biomechanics even in the most common situation when the patient-specific properties remain unknown. It also shows that reasonably accurate results can be expected while using even the simplest constitutive model for the brain tissue. In [Fig. 3](#) we present displacement fields within the brain for five cases of craniotomy-induced brain shift. The patient-specific meshes used in the computations were similar to the one shown in [Fig. 4](#). We used geometrically nonlinear solution procedure ([Joldes et al., 2009b](#)) and the simplest, almost incompressible neo-Hookean material model with (arbitrarily but reasonably ([Miller and Chinzei, 2002](#)) chosen) Young modulus $E = 3000$ Pa for parenchyma and 9000 Pa for the tumor. Ventricles were modeled as a very soft compressible solid. In [Fig. 5](#) we compare our predicted configurations of the brains with the positions measured using intraoperative MRI facility at Brigham and Women’s Hospital in Boston. We chose anatomical features that can be classified in the image as edges ([Canny, 1986](#)) for qualitative assessment of the accuracy of alignment.

It is clear that despite the lack of information about patient-specific brain properties the predicted shape of the brain agrees very well with that measured using intraoperative MRI. A quantitative evaluation of accuracy is given in [Table 2](#). We used 90% Hausdorff distance ([Zhao et al., 2005](#)). Hausdorff distance is currently considered the most reliable measure of misalignment of neuroimages ([Fedorov et al., 2008](#); [Garlapati et al., 2012](#); [Wittek et al., 2010](#)).

As it is unreasonable to expect the quality of neuroimage registration to be better than two voxels—~1.7 mm in the five cases summarized above, we can conclude that the 90% Hausdorff distance of ~2 mm is a very good result, and better than what can be obtained with a state of the art BSpline image registration algorithm ([Balci et al., 2007](#); [Mostayed et al., 2012](#); [Rohlfing et al., 2003](#); [Rueckert et al., 1999](#)) available within 3DSlicer (www.slicer.org). It is worth noting

Table 1 – Observed and computed center of gravity displacements for ventricles and tumor. The computations were conducted using geometrically non-linear finite element procedures. The patient-specific finite element mesh of the brain used for computations is given in [Fig. 3](#).

Material model	Center of gravity displacements (mm)					
	Ventricles			Tumor		
	ΔX	ΔY	ΔZ	ΔX	ΔY	ΔZ
MRI determined	3.4	0.2	1.7	5.5	-0.2	1.7
Ogden-based hyperviscoelastic material (Miller and Chinzei, 2002)	2.6	-0.1	2.1	5.2	-0.4	2.7
Ogden hyperelastic material	2.6	-0.1	2.1	5.2	-0.4	2.7
Neo-Hookean hyperelastic material (Wittek et al., 2010)	2.6	-0.1	2.1	5.2	-0.4	2.7
Linear elastic material	2.6	-0.1	2.1	5.0	-0.5	2.7

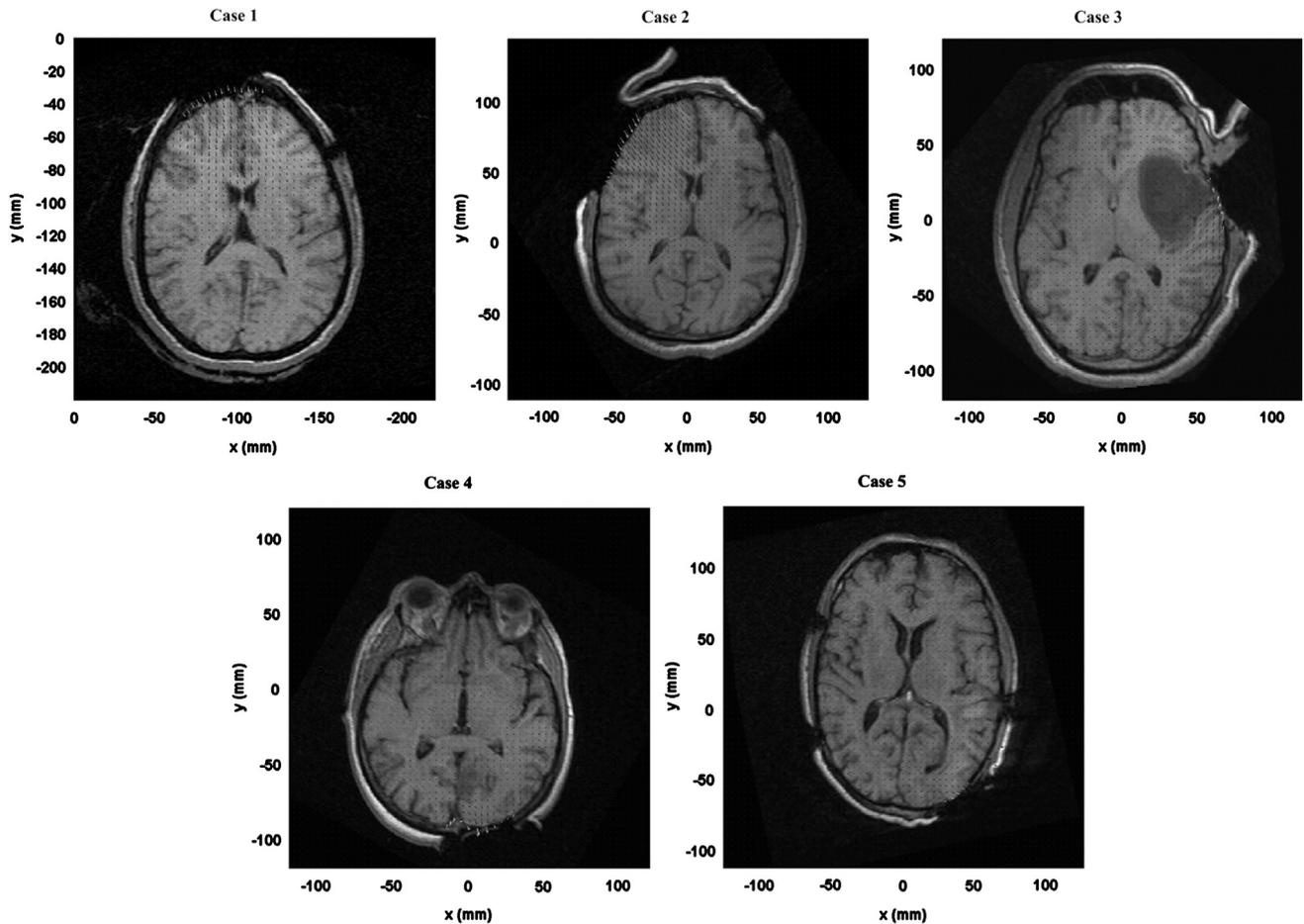


Fig. 3 – Craniotomy-induced deformation fields computed using biomechanical models for five cases of neurosurgery. Green arrows indicate loading via enforced motion of a boundary in the area of craniotomy. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

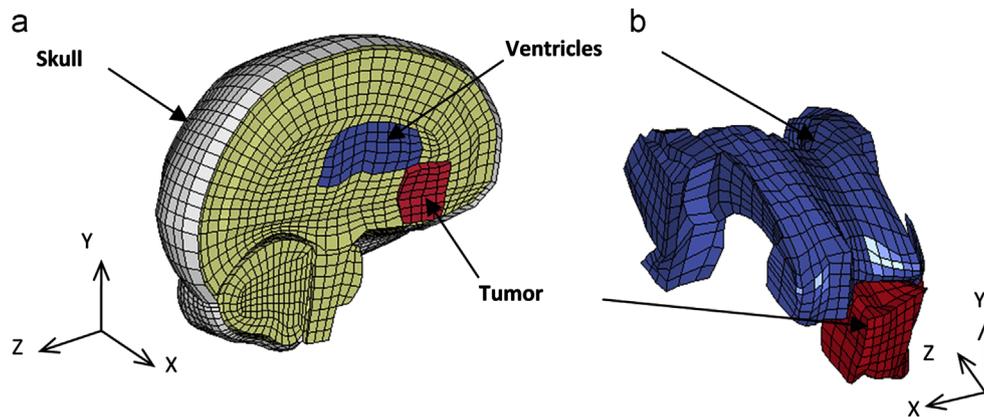


Fig. 4 – Finite element mesh used to compute results given in Table 1.

here that to obtain the deformation field within the brain using a biomechanical model formulated as a displacement-zero traction problem, only positions of a small number of points distributed on the brain surface exposed during craniotomy need to be acquired intraoperatively in order to define model loading (Fig. 3). On the other hand, image-based registration algorithms such as BSpline require ca. 4 million points from the volumetric intraoperative image to work with.

3.2. Computation of wall-stress distribution in intracranial aneurysms

Predicting the wall stress in intracranial aneurysms (ICAs) has long been a point of interest in the biomechanics community. ICAs are localized dilatations in the cerebral arterial wall. They start as a small outpouching, but may enlarge to ~30 mm in diameter. Values of wall thickness

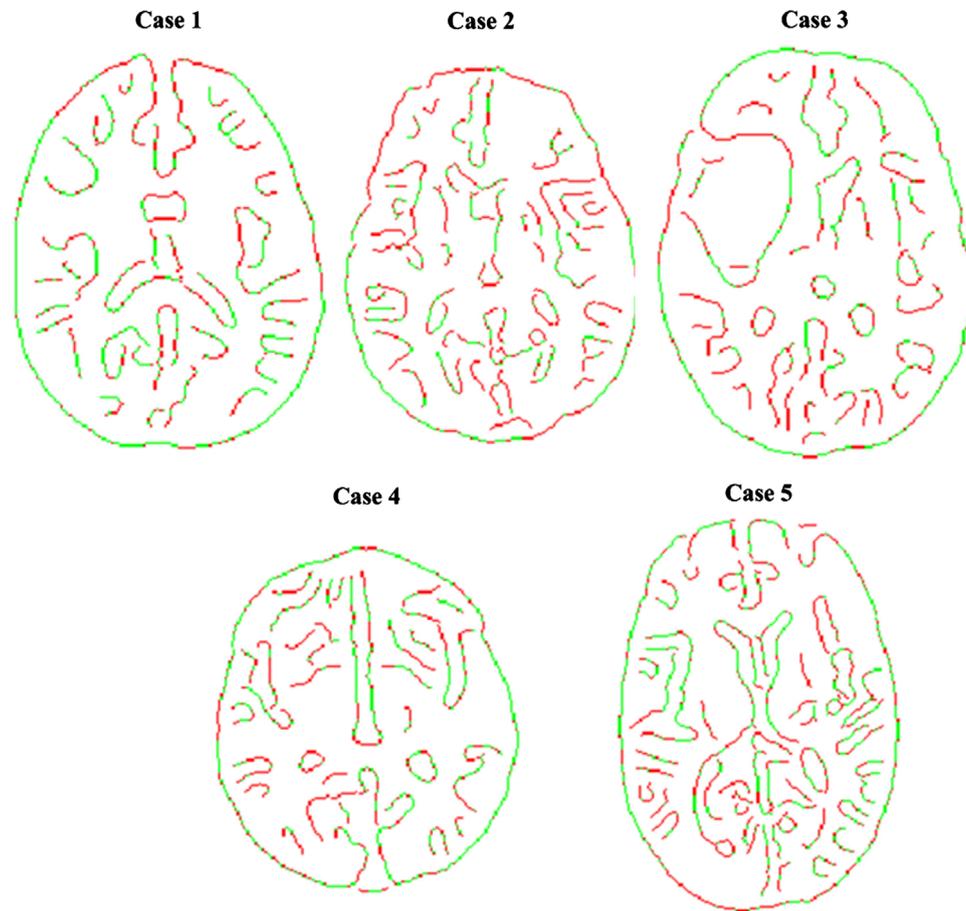


Fig. 5 – Canny edges extracted from intraoperative images and the deformed preoperative images using computed deformation field overlaid on each other. Red color represents the non-overlapping pixels of the intraoperative slice. Green color represents the overlapping pixels. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2 – 90 percentile Hausdorff distance values for five patient-specific cases.

Case	Biomechanics (mm)	BSpline non-rigid image registration algorithm (mm)
1	2.06	2.49
2	2.49	3.19
3	2.49	3.52
4	2.11	2.54
5	2.49	3.03

range from 16 to 300 μm (Canham and Ferguson, 1985) while a slightly higher range of 30–500 μm was also reported (Humphrey and Canham, 2000; Seshaiyer et al., 2001). In their service environment, ICAs are subjected to arterial blood pressure from inside and exposed to the cerebral fluid outside. From the standpoint of mechanical modeling, ICAs can be described as membrane or thin shell structures subjected to transmural pressure. Based on the argument in Section 2.2, ICAs may be regarded as approximately statically determinate structures.

To capitalize on static determinacy, we must formulate the stress equilibrium problem inversely, taking the deformed configuration as given. This is because the argument for

static determinacy holds only when the deformed configuration is given. In the Laplace law, Eq. (1), the geometric parameters are those of the current configuration. If the deformed configuration is yet to be determined, the influence of material model is implicit.

We have developed inverse elastostatic methods for solving membrane or shell equilibrium problems on given deformed configurations (Lu et al., 2008; Zhou et al., 2010). The inverse elastostatic method addresses problems in which the deformed configuration and the applied load are known while the undeformed is not. The inverse analysis takes the deformed configuration as the starting geometry, and solves for the undeformed configuration and thereby determines

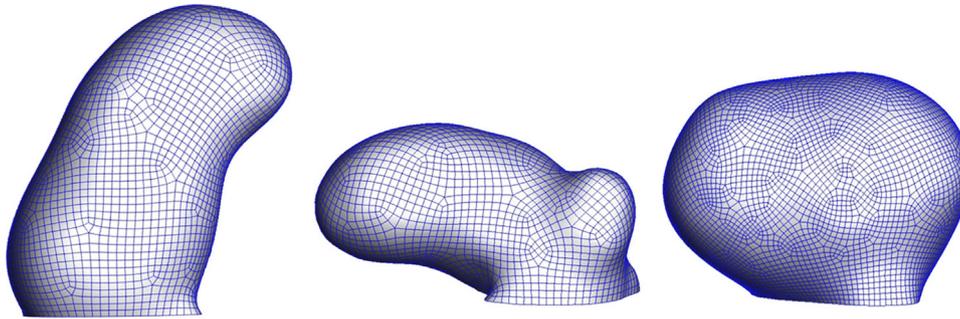


Fig. 6 – Finite element models of three aneurysms. They are numbered 1 through 3 from left to right.

the stress in the given deformed state. This reverted paradigm of analysis is possible for nonlinear elastic material body, because in such material the stress depends on the relative deformation between two configurations. If one of them is known, the other can be solved from equilibrium. There are several ways to formulate inverse elastostatic problems. We followed the approach advocated by Yamada (1995) and Govindjee and Mihalic (1996, 1998), whereby the inverse problem is solved using the standard equilibrium equations with a re-parameterization of the constitutive law, that is expressing the stress as a function of the inverse deformation gradient. The advantage of this approach lies in that it applies to any hyperelastic constitutive equation. Lu's group developed inverse formulations for soft tissue continuum (Lu et al., 2007a,b), nonlinear membranes (Lu et al., 2008), and stress-resultant shells (Zhou and Lu, 2008).

The inverse elastostatic method was originally motivated by the need of determining the unloaded geometry in inverse design. In the context of aneurysm analysis, we use it as a stress solver. The analysis will predict an unpressurized configuration as a by-product; however, this solution is not the concern. If the material description is inaccurate, the unloaded geometry is not expected to be accurate. However, the wall tension should be insensitive to the material model used in the analysis given that the structure is nearly statically determinate. It is worth noting that this inverse paradigm is naturally suited to image-based patient-specific modeling, because in vivo images of an aneurysm correspond to a deformed geometry, the one at least under the diastolic pressure.

In a recent NIH-funded study, we have analyzed 26 ICAs and compared the sensitivity of the stress solution with respect to material model. Fig. 6 shows three representative aneurysms used in the study. The meshes were derived from patient specific images. All three aneurysms have surface undulations and therefore are modeled as shell structures.

As the baseline description we used Fung model (Fung, 1993) to describe the wall tissue. The energy function has the form

$$W = c(e^Q - 1), \quad Q = d_1 E_{11}^2 + d_2 E_{22}^2 + 2d_3 E_{11} E_{22} + d_4 E_{12}^2 \quad (2)$$

Note that this is surface energy function defining the stored energy per unit undeformed surface area. The stiffness parameter c has the dimension of force per unit length. Parameters d_1, d_2, d_3, d_4 describe a planar orthotropic distribution. (E_{11}, E_{22}, E_{12}) are components of the in-plane

Green-Lagrange strain tensor in the local material axes. In our analyses the principal material axis is assumed to be parallel to the basal plane. The material parameters are set to be $c=0.056 \text{ N/mm}$, $d_1=17.58$, $d_2=12.18$, $d_3=7.57$, $d_4=4.96$. These values are based on the parameters reported in Seshaiyer et al. (2001), and adjusted to ensure that the maximum stretches in all three aneurysms are below 1.05 when under 100 mm Hg lumen pressure. The stress resultant shell element (Simo and Fox, 1989a, 1989b; Simo et al., 1990), and the corresponding inverse formulation (Zhou and Lu, 2008), employed in this study, require constitutive equations for the in-plane, bending, and transverse shear responses. We have proposed a strategy for deriving approximate bending and transverse shear functions from the in-plane constitutive equation, see (Zhou and Lu, 2008) for details. This strategy was adapted in the current study. The bending and transverse shear functions are not accurate, but since the structures are thin (the thickness to diameter ratio is <0.04 in all three models), the bending stress is orders of magnitude smaller than the in-plane stress. For this reason, we do not expect that improved bending descriptions will change the stress results in any significant manner.

A uniform transmural pressure of 100 mm Hg is applied. The pressure follows the surface normal as the aneurysms deform. Displacement degree-of-freedom on boundary edges are fixed. The wall thickness for all models is set uniformly at 0.2 mm. In forward analyses, the image-derived geometry is taken as the undeformed geometry that is to deform further under the lumen pressure (100 mm Hg). In the inverse analyses, the imaged geometry is taken as the deformed geometry over which the equilibrium problem is solved.

To examine the influence of material description, we introduced three comparative models, labeled as Material B–D hereafter, and computed the corresponding stress solutions using both inverse and forward methods. Materials B and C still admit the Fung function; in Material B the stiffness parameter c is enlarged 100 times while in Material C the values of d_1 and d_2 are interchanged. Material D assumes a different stress–strain function, a neo-Hookean model of the form $W = \mu_1/2(I_1 + I_2^{-1} - 3) + \mu_2/4(I_1 - 2)^2$. Here $I_1 = \text{tr}C$ and $I_2 = \det C$ are the principal invariants of the in-plane deformation tensor $C = F^T F$. Material parameters were set to be $\mu_1 = 1.7 \text{ N/mm}$, $\mu_2 = 2.8 \text{ N/mm}$. The baseline Fung model is referred to as Material A.

Inverse stress solutions from all material models are depicted in Fig. 7. As shown in the figure, the distributions

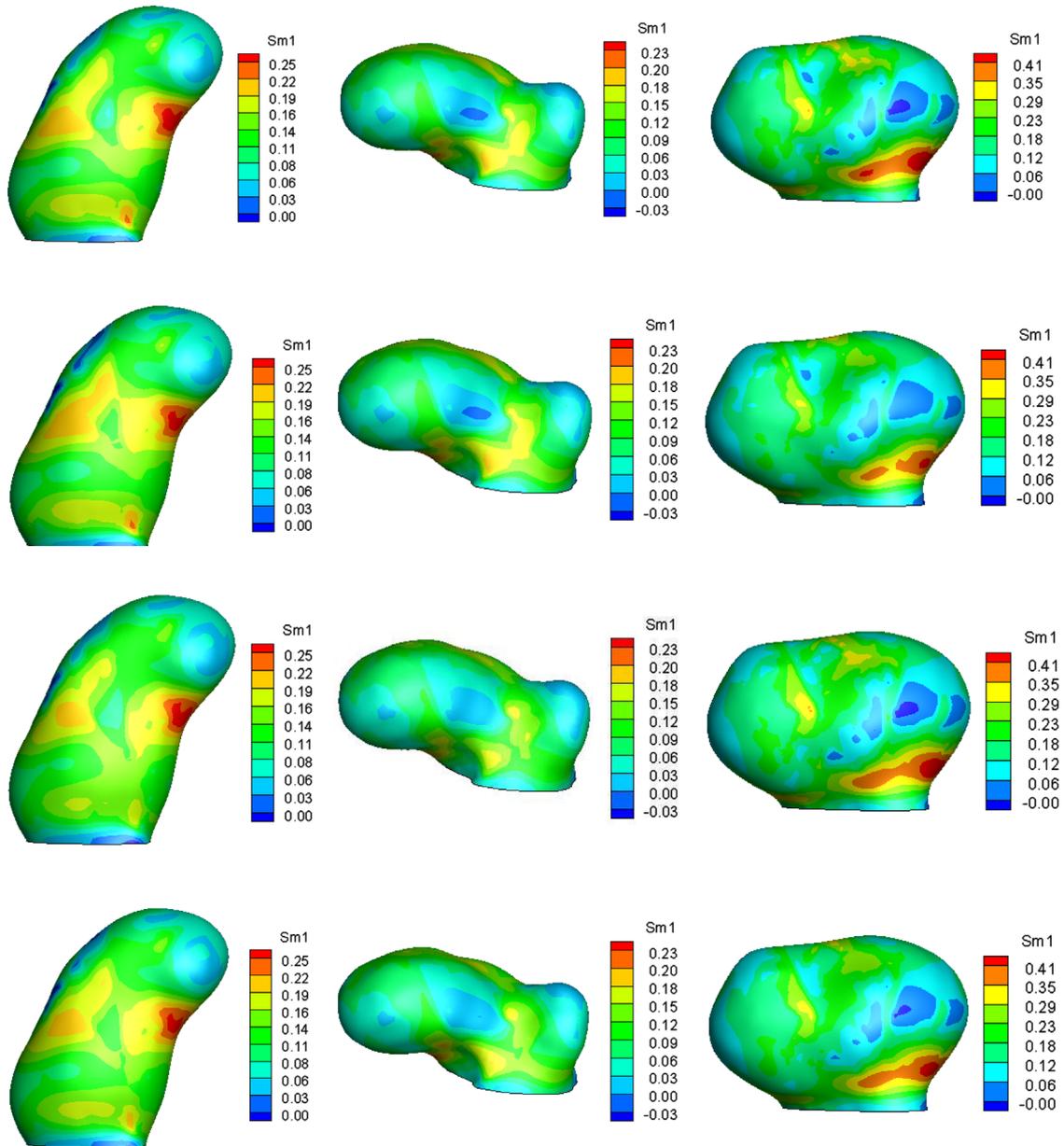


Fig. 7 – Distributions of the 1st principal stress, inverse solution. From top to bottom: Materials A, B, C, D.

Table 3 – Maximum principal stress under different material models (units: N/mm^2).

Aneurysm	Inverse solution				Forward solution			
	Mat A	Mat B	Mat C	Mat D	Mat A	Mat B	Mat C	Mat D
1	0.2744	0.2672	0.2807	0.2680	0.2479	0.4319	0.2551	0.3941
2	0.2573	0.2557	0.2696	0.2668	0.2488	0.4017	0.2578	0.3981
3	0.4861	0.4740	0.4517	0.4641	0.3786	0.7634	0.3875	0.7676

appear similar. The forward solutions differ significantly between models; they are not plotted but the maximum values of the principal stresses are tabulated in Table 3.

Evidently, the inverse stress solutions are far less sensitive to material description. For example, under the 100 times

increase in the stiffness parameter c , the changes in the maximum principal stress (compared to the baseline model) are below 2.9% in all three aneurysms. In contrast, the forward analysis predicted differences greater than 60% in all aneurysms (the difference in the third aneurysm exceeds 100%). The neo-Hookean model has completely different

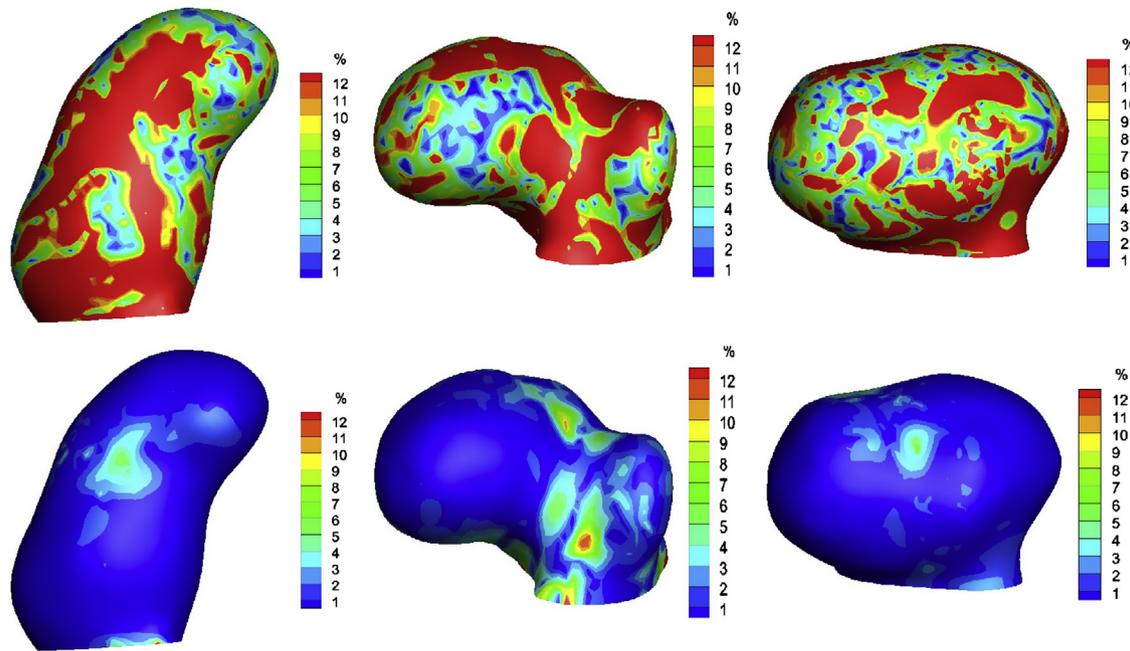


Fig. 8 – Percentage differences in principal stresses when the stiffness parameter c is enlarged 100 times. Upper row: forward analysis; lower: inverse analysis.

symmetry characteristics, and yet the inverse stress solutions differ minimally from other models.

To further elucidate the stress sensitivity, the pointwise percentage differences in the first principal stress between materials B and A are presented in Fig. 8. The average differences from the inverse analysis are 1.1%, 3.9%, and 2.3%, respectively, in each aneurysm. In forward solutions the average difference elevate to 20.1%, 24.3%, and 22.6%. In all other material models, the forward analysis resulted in larger spreads of stress values, as indicated in Table 3. Details are omitted

4. Discussion and conclusions

Therapeutics, devices used during surgery to restore health, encompasses a very broad area of instrumentation. Examples of therapeutic technologies that are entering the medical practice now and will be employed in the future include gene therapy, stimulators, focused radiation, lesion generation, nanotechnology devices, drug polymers, robotic surgery and robotic prosthetics (Bucholz et al., 2004). One common element of all of these novel therapeutic devices is that they have extremely localized areas of therapeutic effect. As a result, they have to be applied precisely in relation to the current (i.e., intra-operative) patient's anatomy, directly over the specific location of anatomic or functional abnormality (Bucholz et al., 2004). Nakaji and Speltzer (2004) list the “accurate localization of the target” as the first principle in modern surgical approaches. As only the preoperative anatomy of the patient is known precisely from medical images (usually magnetic resonance images—MRI), it is now recognized that the ability to predict soft organ deformation (and

therefore intraoperative anatomy) during the operation is the main problem in performing reliable surgery on soft organs.

In this article we offer an appealing prospect of accurately computing these deformations without knowing patient-specific properties of tissues. This can be achieved by defining the model loading as enforced motion of boundaries and consequently formulating the solid mechanics equations in a format of pure displacement or displacement-zero traction problem.

Of course it needs to be recognized that such an approach would fail if we required information about internal or reaction forces—the knowledge of tissue properties is inescapable in such cases. Also, the use of the proposed methods would not be appropriate if the volumetric response of the continuum were complicated, e.g., described by a variable or inhomogeneous Poisson's ratio.

The example of aneurysm stress analysis underlines the significance of static determinacy in analysis. The example demonstrates that, if we formulate the aneurysm stress analysis inversely as it should be, we can obtain wall tension solutions that are insensitive to the material description. In other words, we are able to predict the tension more reliably. In the conventional forward approach, we have to make necessary assumptions about the tissue properties and that inevitably brings in a certain level of uncertainty to the stress solution. This inverse paradigm is also natural for image-based *in vivo* analysis, because *in vivo* geometries of aneurysm are always deformed. It should be noted, though, that the actual wall stress depends on the wall thickness which is also difficult to obtain *in vivo*.

Another implication of membrane static determinacy relates to the design of innovative experimental methods for characterizing thin tissues. Recently, Lu's group proposed the so-called point-wise identification method (Lu and Zhao,

2009; Zhao et al., 2009, 2011a, 2011b) which is a whole-organ inflation test for membrane tissues. The method hinges critically on the ability to obtain stress distributions without reference to the properties of the material in question. The key idea is to compute the stress distribution in each of the pressurized state using the inverse method. The point-wise stress data, together with the strain data acquired separately, characterize the local property of the tissue. The advantage of this method lies in that it can sharply delineate heterogeneous properties. Also, by solving the regression problem locally, large scale optimization problems are avoided. The method is still in its infancy, but existing studies (Zhao et al., 2011a, 2011b) clearly demonstrate its potential.

Human soft tissues are highly variable, and despite recent progress in magnetic resonance (MR) and ultrasound elastography (Bilston, 2011), their in-vivo properties are difficult to obtain (Miller, 2011). We envisage that substantial progress will be achieved by reformulating computational biomechanics problems away from the traditional force/stress/strain focus to either a kinematics-based emphasis that considers motion and strain as variables of primary interest or static force/stress description that takes advantage of the features of statically determinate structures.

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