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Computational Biomechanics for Patient-Specific Applications

Influence of Geometry and Mechanical Properties on the Accuracy of Patient-Specific Simulation of Women Pelvic Floor

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Abstract—The woman pelvic system involves multiple organs, muscles, ligaments, and fasciae where different pathologies may occur. Here we are most interested in abnormal mobility, often caused by complex and not fully understood mechanisms. Computer simulation and modeling using the finite element (FE) method are the tools helping to better understand the pathological mobility, but of course patient-specific models are required to make contribution to patient care. These models require a good representation of the pelvic system geometry, information on the material properties, boundary conditions and loading. In this contribution we focus on the relative influence of the inaccuracies in geometry description and of uncertainty of patient-specific material properties of soft connective tissues. We conducted a comparative study using several constitutive behavior laws and variations in geometry description resulting from the imprecision of clinical imaging and image analysis. We find that geometry seems to have the dominant effect on the pelvic organ mobility simulation results. Provided that proper finite deformation non-linear FE solution procedures are used, the influence of the functional form of the constitutive law might be for practical purposes negligible. These last findings confirm similar results from the fields of modeling neurosurgery and abdominal aortic aneurysms.

Keywords—Pelvic system, Material behavior, Geometrical reconstruction, FE models.

INTRODUCTION

Pelvic organ prolapse (POP) is a disorder of the mobility of female genital organs, resulting from a deficiency of organ suspension, causing anatomical and mechanical dysfunction of pelvic system. POP concerns approximately one in three women of all ages and more than 60% of women over 60.[33] The most common treatment option is surgery, however, these interventions have a failure rate reaching 40%.[1,3] High failure rate is considered to be caused by a complex and not fully understood physiopathology, linked to intricate anatomical suspension structures. A significant increase in the descent of the pelvic organs is also observed during pregnancy causing a change in the POP-Q score.[26] A spontaneous regression was observed in the year following childbirth especially delivered by cesarean section.[8] Pregnancy and childbirth are identified and recognized risk factors for pelvic pathologies. In this context, current research aims to better understand this complex pathophysiology by studying the pelvic support elements that create physiological conditions. Numerous simulations of childbirth were performed and aimed to analyze the strain on the pelvic system during childbirth and improve our understanding of these complex processes.[2,27]

During the past decade the advances in mathematical modeling and computer simulation made it possible to develop patient-specific functional models of the pelvic system. The finite element (FE) method is commonly used to investigate organ mobility and the mechanisms involved, and to provide better understanding of the important patient-specific aspects of the problem.

To develop numerical models of the pelvic system, research has concentrated on the anatomical structures easily identifiable with anatomical knowledge[10,11,29] and in medical images.[18,21,35] Such numerical models are

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improved by the introduction of structures that are not observable through medical imaging, such as fasciae and ligaments.[7,17,22,23,30,35]

For patient-specific model geometry definition usually magnetic resonance images are used. However their resolution (usually the voxel size is of the order of $0.7 \times 0.7 \times 4$ mm) is insufficient to construct the geometry of the biomechanical models with high precision. Moreover, the resolution of clinical scans does not allow accurate reconstruction of geometries of important structures such as ligaments and fasciae. Due to this lack of imaging precision, geometry of fasciae and ligaments is usually defined manually, based on the anatomical knowledge of an analyst. Analysis of the displacement fields measured using dynamic MRI and digital image correlation[18,21] confirms that the geometry construction based on medical imaging combined with anatomical knowledge improves the bio-fidelity of FE models.[23,35]

In the next step in creating a truly personalized model, patient-specific geometry needs to be supplemented with patient-specific mechanical properties of soft connective tissues of the pelvic area. There is strong experimental evidence for a large inter-subject variability.[6] Additional variability in tissue properties is introduced by differences in age and pathology.[6,9,14,31]

Thus the simulation results obtained by means of a patient-specific numerical model: displacements, strains and stresses, depend on a huge number of parameters. Motivated by recent somewhat controversial suggestions that the influence of the variability in the mechanical properties of tissues is smaller than most researchers assume,[24,25,36] the purpose of this paper is to analyze the relative influence of the imprecision of description of geometry and the choice of constitutive behavior laws and material parameters.

We acknowledge here that the uncertainty in the patient-specific description of boundary conditions and loading may have a non-negligible impact on the simulation results, however this important matter is not considered in this manuscript.

This paper is organized as follows. In the next section we provide details of the FE models used in this study, followed by the description of parametric studies employed to assess the relative importance of the precision in geometry description and mechanical behavior of soft tissues. Next we provide results and finally we discuss our findings and offer conclusions.

MATERIALS AND METHODS

Patient-Specific Model of Geometry

The digitized geometry of the pelvic system is defined based on a patient's magnetic resonance image (MRI) obtained using 3 Tesla MR (Philips Achieva 3.0T TX) through 3 sequences of 2D images on the axial, coronal and sagittal incidences (resolution 512×512, pixel size: 0.7 mm). Figure 1a presents the sagittal view of pelvic organs, with a representation of a zone of interest corresponding to the vaginal thickness. The resolution of the clinical scans is insufficient to detect the exact contours of organs because imprecision is between two to six pixels. The images are used to generate a 3D representation of the pelvic system. The contour of each organ is defined on MR slices semi-manually (Fig. 1b) with Aviso Standard Edition 7 software (Visualization Sciences Group VSG, SAS). In order to mark the position of anatomical structures, a contrast gel is injected into the vagina and rectum. Threshold value is defined on the image to select zones

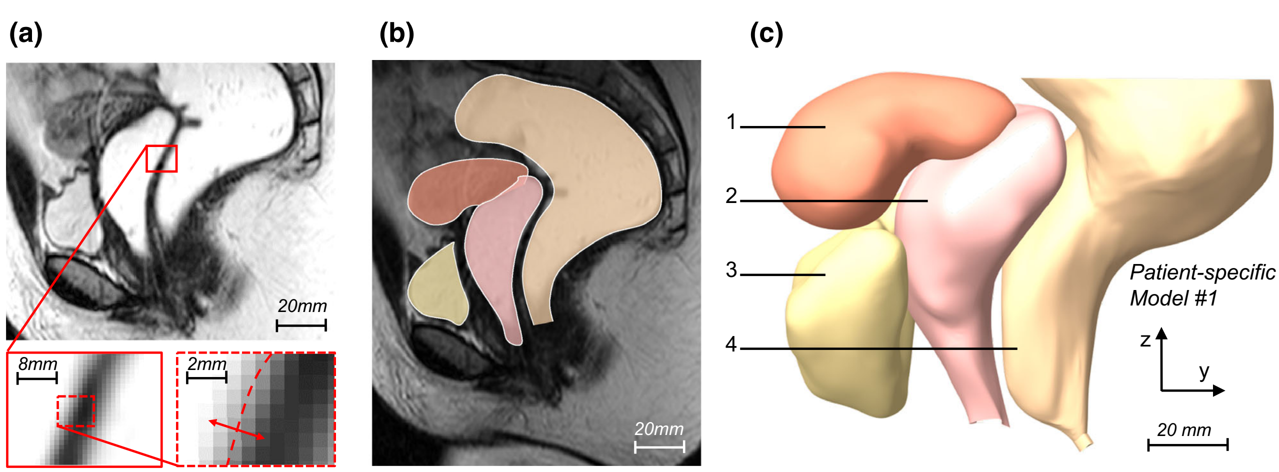

FIGURE 1. MRI to patient specific 3D model, (a) sagittal plane of pelvic system with illustration of the pixel size, (b) organ contours definition with Aviso software, (c) 3D reconstruction of organs including 1: uterus, 2: vagina, 3: bladder and 4: rectum.

of interest and generate a 3D model with a slice superimposition for vagina (VA), rectum (RE), bladder (BL) and uterus (UT).

All reconstructions are represented by clouds of points. B-spline curves are designed to specify 3D models (Fig. 1c). The geometries of the four organs (vagina, uterus, bladder and rectum) are represented by surface models and then exported for simulation into Abaqus/CAE 6.12-2 software (Dassault Systèmes Simulia Corp.). This protocol has been applied on four volunteers presenting no pelvic pathology (institutional ethical approval CEROG OBS 2012-05-01 R1).

Anatomical supporting structures such as ligaments and fasciae, which are not visible on the clinical images, are introduced in the 3D model in accordance with anatomic literature[10,11,29] and an iterative optimization process[23,30,35] in order to obtain numerical simulation in agreement with MRI-analysis of the displacement and strain fields.[18,21] We used digital image correlation to estimate the organ displacement fields.

The cardinal ligament and uterosacral ligaments represent the two structures supporting the cervix. The paravaginal ligaments form the third structure supporting the vagina, located on both sides of it and linked to the pelvic sidewall. To complete the geometrical model, the fasciae are inserted between organs. The first one is the fascia between the rectum and the vagina. The second one is placed between rectum and pelvic floor. Finally, the fasciae between bladder and vagina represents the last structure.

Generic Model of Geometry

The disadvantage of our protocol is that vagina and rectum are injected with a gel to increase the visibility of organ edges on MRI. These injections modify the geometries of vagina, departing from the true anatomical representation. Additionally, the injection enhances the asymmetry of organs (Fig. 2).

This brings in difficult to control parameters in the analysis of the relative influence of geometry and mechanical properties. To alleviate this difficulty we created a ''generic'' symmetric model of geometry representative of the four subjects considered in this study (Fig. 3). This generic model allows us to avoid difficulties stemming from substantial differences between patients (Fig. 2), which are consequences of inter subject variability and asymmetry, and focus on the impact of the inaccuracies n geometry reconstruction.

To create our generic symmetrical model, we averaged the left and right sides of each patient-specific model. Additionally, following discussions with anatomists and surgeons, we found that the injected gel, allowing us to perform initially a better edge detection during our displacement fields protocol on dynamic MRI, affects the geometry of organs, especially of the vagina. Consequently, with the help of anatomists and surgeons, we have rectified the geometry of the vagina, flattened by the injected gel. Analysis of the mobility of our four patients with dynamic MRI allowed us to measure an average displacement of the cervix to be about 7 mm. This displacement is also found in our simulation of the generic model.

FE Mesh

The FE model of organs uses shell elements with a constant thickness, except for uterus which is discretized by hexahedral elements. The paravaginal and cardinal ligaments are meshed with shell elements. The pelvic floor is defined by a representative surface. Beam

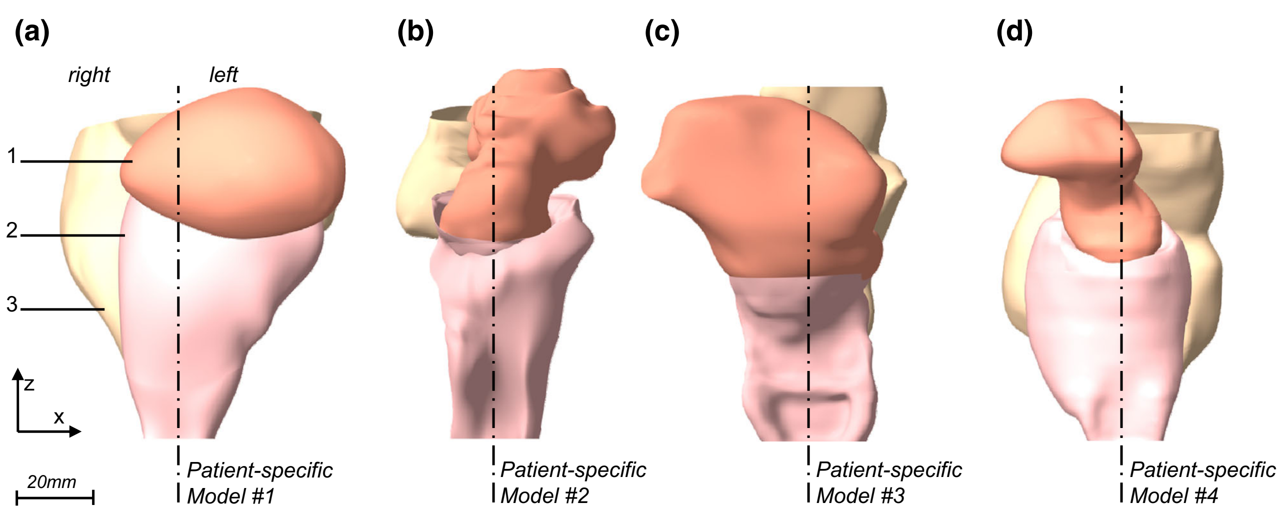

FIGURE 2. Illustration of four patient-specific models with pronounced asymmetry of organs (1: uterus, 2: vagina and 3: rectum).

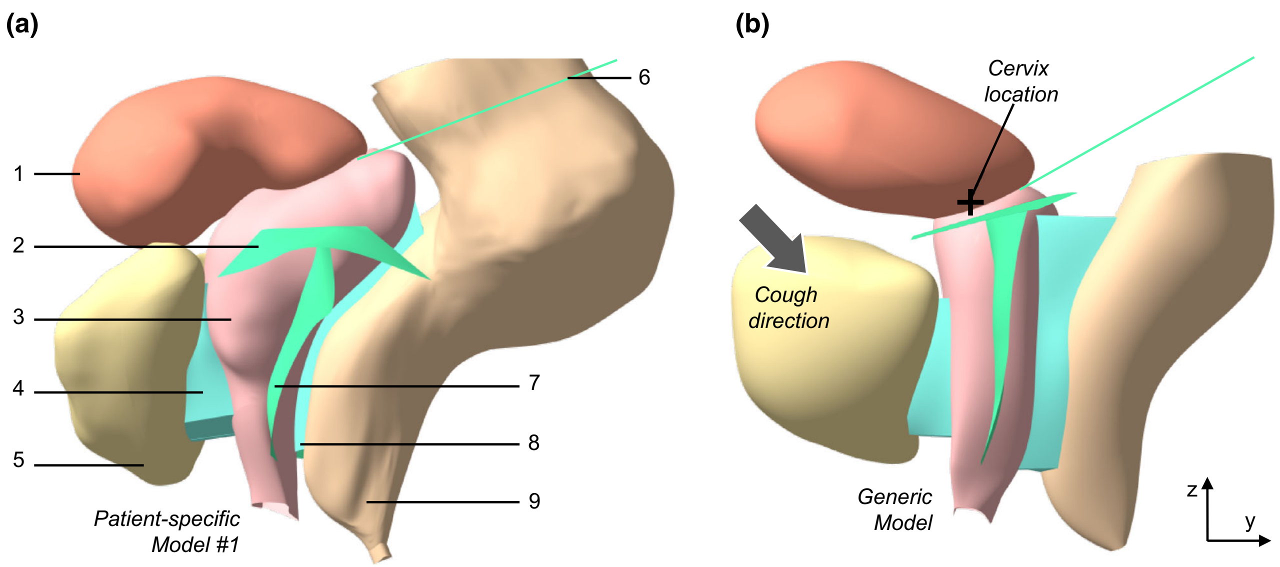

FIGURE 3. Comparison between patient-specific (a) and generic symmetrical model (b) of the pelvic system. (1: uterus, 2: cardinal ligament, 3: vagina, 4: fascia between bladder and vagina, 5: bladder, 6: uterosacral ligament, 7: paravaginal ligament, 8: fasciae between vagina and rectum, 9: rectum).

elements are used to mesh uterosacral ligaments, allowing the suspension of the cervix. We have taken care to ensure that this supportive structure works only in tension.[5] To reduce the number of DOFs we have chosen to represent the other ligaments, which are surface-like, with shell elements. In our models loaded by the caught these structures work also in traction. The fasciae between organs are discretized using 3D elements (Table 1). Their geometry is characterized by more massive structures so we use hexahedral elements, most suitable to represent deformation mechanisms. The bone structures are considered rigid as their stiffness is much larger than that of soft tissues in the model. We used B31 element type for 1D beam (3D, 1st order interpolation), S4R for 2D shell (quadrilateral element, 4 nodes with reduced integration) and C3D10 for 3D solid (10 nodes, 2nd order tetrahedral element), all taken from the standard library of Abaqus/CAE 6.12-2, Fig. 4. Since bladder is filled partially during physiologic situation, an incompressible fluid has been modeled inside the bladder to provide a better representation of organ mobility. The use of an incompressible fluid allows us to keep a constant volume in the bladder during simulation which has been noticed on MRI observation.

The FE mesh of our complete structure, composed by organs, ligaments, fasciae and pelvic floor, consist of approximately 50,000 elements. To ascertain sufficient mesh quality we conducted an h-convergence study. The difference in displacements and strains computed with the discretization shown in Fig. 4 and the mesh with six times more elements is less than 0.5%, and the difference in maximum stress is less than 1.5%. We considered these small differences as an evidence that the mesh has converged because the comparison with the mesh twice courser showed the differences in computed variables of 4.6%. The number of elements, the corresponding element type and the thickness of the shell are given in Table 1. Because we introduced anatomical supportive structures such as fasciae in the model there is no need for contact models between organs. The presence of connective tissues between organs, observable during cadaver dissections performed by our group, is sufficiently marked to conclude that there is no direct contact between organs. We introduce anatomical supportive structures which clearly separate the organs.

TABLE 1. FE element type, thickness and number for each anatomical structure.

Anatomical structure	Elt type	Thickness (mm)	Elt Nb
Vagina	S4R	3	5000
Uterus	C3D10	na	6000
Bladder	S4R	2	3500
Rectum	S4R	2	3000
Fluid	C3D10H	na	7500
Pelvic floor	S4R	2	3500
Uterosacral ligament	B31	na	30
Cardinal ligament	S4R	1	270
Paravaginal ligament	S4R	1	200
Bladder/vagina fascia	C3D10	na	7000
Vagina/rectum fascia	C3D10	na	8000
Pelvic floor/rectum fascia	C3D10	na	6000
Total			50,000

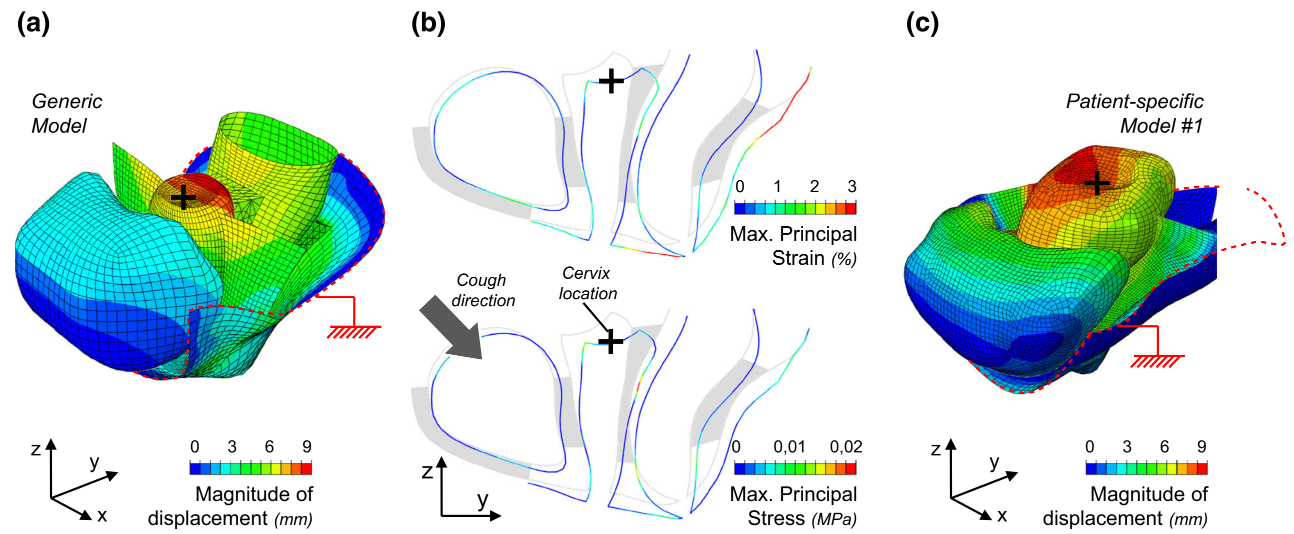

FIGURE 4. Finite element mesh, (a) magnitude of displacement (generic model), with boundary condition located on the pelvic floor (red dotted line), (b) max. principal strain in the sagittal plane with initial position (gray) and max. principal stress in the sagittal plane with initial position (gray), (c) magnitude of displacement for patient specific case 1.

Mechanical Properties

To be patient-specific, FE simulation requires patient-specific mechanical properties. Such requirement brings in the need for non-destructive method of material characterization. Unfortunately the existing probes[16] provide, in the pelvic system, qualitative rather than quantitative information, since each tissue is connected by fasciae.

Most of the mechanical properties of soft tissues in the pelvic area were obtained using destructive *in vitro* mechanical tests.[15,28,34] The hyperelastic behavior of these soft tissues has been highlighted[31] and a map of the mechanical properties of the entire pelvic floor soft tissues has been provided.[6,32] Previous research[9] has shown that from the statistical point of view, at least for vagina, bladder and rectum, tissues are not anisotropic. We assume, mainly because of the lack of experimental evidence, that the other considered tissues are also isotropic.

For this reason some authors[6,9,32] introduced a second order Yeoh model.[37] In this model the strain energy function depends only on the first invariant, I_1, of the Cauchy-Green strain tensor and is given as:

$$W(I_1) = C_0(I_1 - 3) + C_1(I_1 - 3)^2 \quad (1)$$

Such strain energy density is defined by a C_0 parameter, which at low strain represents the initial stiffness modulus, and a C_1 parameter which allows the high increase in stiffness at large strains.

Even for a young population (less than 40 years-old) without noticed pathology, a strong inter-subject variation of mechanical properties is revealed. We consider minimum, median and maximum values of C_0 and C_1 coefficients for each organ. The box-plot and whiskers representation shows significant variations in the vagina and other organs (Fig. 5).

As we do not know precisely the values of these material parameters for a given patient it is important to understand the influence of this uncertainty on the overall results of the simulation. Insofar as the variations are very large and since the influence of the C_1 parameter of the Yeoh strain energy density, Eq. (1), is noticeable only for large strains that might not be present in physiological cases, let us assume that the C_1 parameter contribution can be neglected and that the Yeoh strain energy density, Eq. (1), can be reduced to the Neo-Hookean strain energy density:

$$W(I_1) = C_0(I_1 - 3) \quad (2)$$

This simplest hyperelastic case is the second we considered.

Patient-specific simulations are frequently developed to help surgeon during surgery. In such a case, real-time simulation is required. In this context, some authors, to satisfy the real-time simulation constraint, choose to reduce the complexity of the problem and assume linear elastic material behavior, small strain but possibly finite rotation.[12,13,30] In such a case the linear Hooke's Law holds, with a Young's modulus

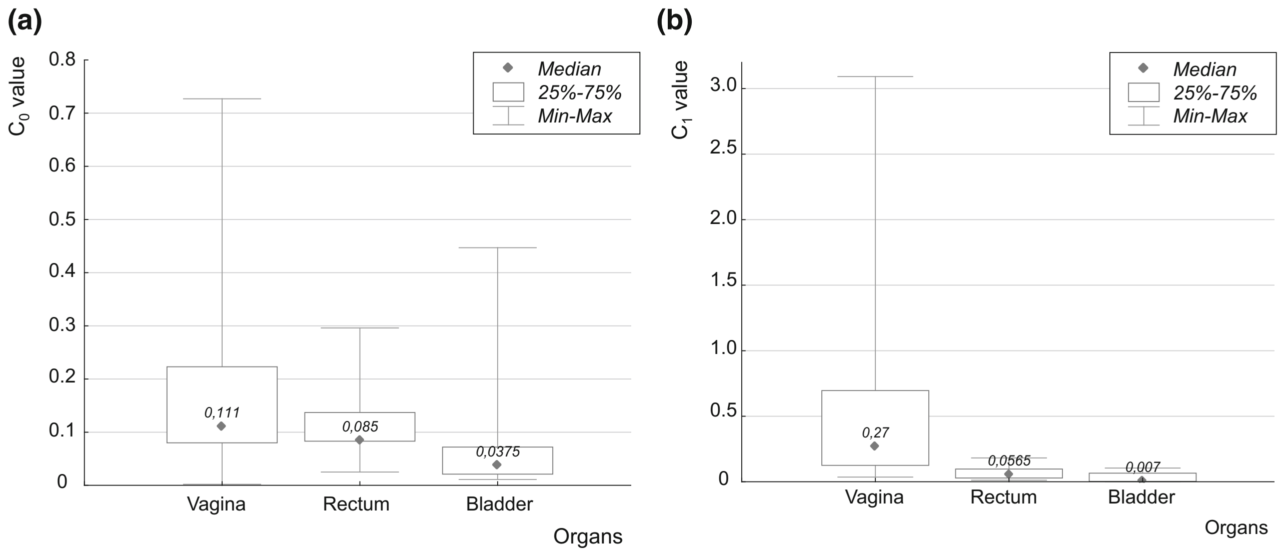

FIGURE 5. Material property variations of each organ, (a) C_0 value, (b) C_1 value.

$E = 6C_0$. This last equality follows from the linearization of Eq. (2). In the linear elastic case, to model close-to-incompressible behavior of tissues usually high Poisson's ration of at least 0.49 is used. The linear elastic material behavior together with small strain co-rotational formulation, is the third case we consider.

To study the influence of the material constants on the simulation results, we chose to consider the first (q1) and third (q3) quartiles of parameter values. The values included between q1 and q3 represent 50% of the measurements.

Loading and Boundary Conditions

The applied loading corresponds to the one inducing the largest organ displacements noticed: the cough. Preliminary studies showed that cough effort is oriented at 45 degrees with respect to horizontal axis, from anterior to posterior direction (Fig. 3b), and with an intensity about 10^{-3} MPa.[4,20] This loading condition is modeled by a surface traction load, applied on the upper surface of the bladder.[36]

The pelvic floor modeled through a representative surface sustaining organs and equivalent to the pelvic muscles. This surface is fixed on its edges to mimic the junction to the bones structures of the pubis, the arcus tendineus musculi levatoris, the sacrospinous ligaments and the sacrum.

The presence of connective tissues between organs is sufficiently marked to conclude that there is no direct contact between organs. The modeling approach we follow does not allow the inter-patient variability in boundary conditions and therefore this potentially important issue is not addressed in this paper.

RESULTS

Influence of the Choice of the Functional Form of the Constitutive Model

As explained in "Materials and Methods" section we consider three different constitutive behavior models in our models of the pelvic-soft tissue displacements under abdominal pressure loading: (i) Hooke's linear elastic law under small strain, possible finite rotation; (ii) Neo-Hookean strain energy density or (iii) Yeoh strain energy density, the last two under finite deformation and large strain. Figure 6b shows for each modeling approach the cervix displacement (see Fig. 3b for the exact location) at equivalent pressure intensity corresponding to cough. The numerical simulations have been performed using our generic model with median values of C_0 and C_1 parameters for Yeoh model, the same C_0 parameter for Neo-Hookean model and $E = 6C_0$ for linear elastic model.

One may notice on Fig. 6b that each approach provides virtually the same results and that the noticed differences are below the resolution of MR images and therefore impossible to detect in practice. This finding allows us to conclude that the choice of the constitutive behavior law has little influence on organ mobility.

However, on a local scale, the mechanical response in terms of strains or stresses could be affected by the type of constitutive behavior law. Experimental tests on pelvic organs have shown an influence of strain level on the material damage.[32] It is then necessary to analyze the impact of constitutive behavior law on local quantities such as strain and stress. Figure 7

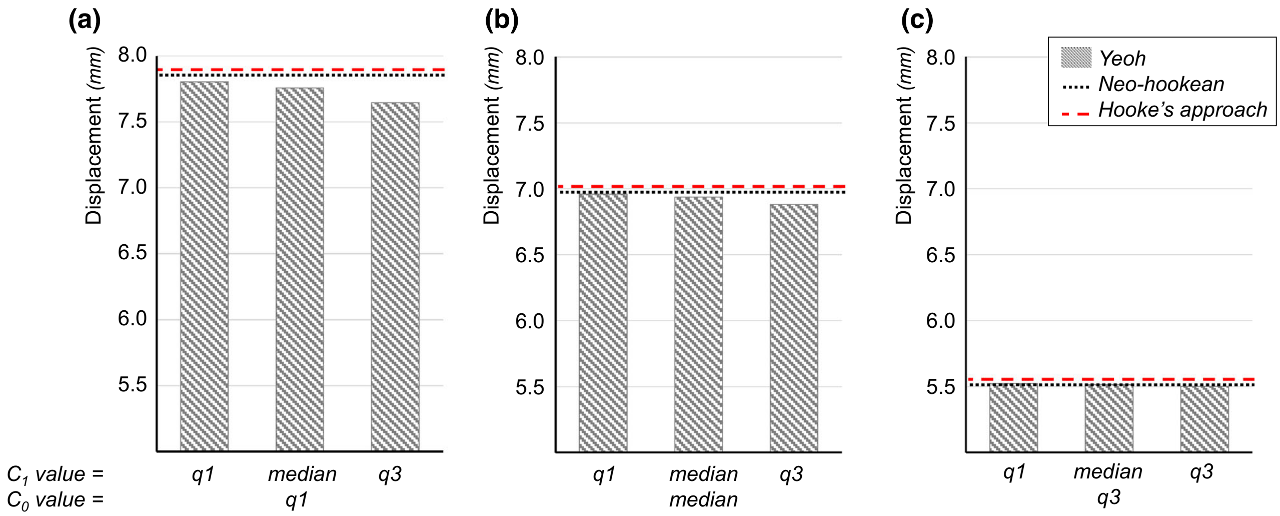

FIGURE 6. Analysis of cervix displacement at fixed pressure (10^{-3} MPa) and in function of the C_1 coefficient dispersion with (a) C_0 = q1 value, (b) C_0 = median value and (c) C_0 = q3 value.

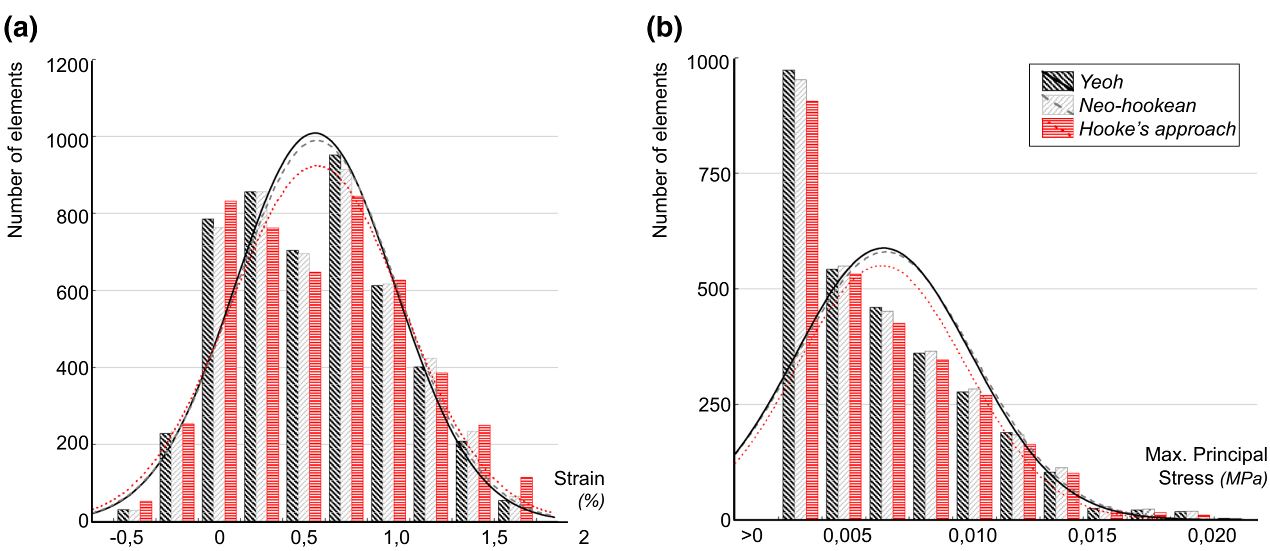

FIGURE 7. Comparison of constitutive behavior law approaches (a) on the max. principal strains of vagina and (b) on the max. principal stresses of vagina.

presents the estimated maximal principal stresses and strains for a given value of the applied abdominal pressure corresponding to cough, with value of 10^{-3} MPa.[4]

One may notice on Fig. 7 that the small strain approach coupled to a Hooke's law behavior is underestimating maximum strains and stresses in the soft tissues, with about 8% deviation when compared to the non-linear analysis using Yeoh's constitutive law, while Neo-Hookean and Yeoh laws have less than 2% difference between them.

Influence of the Choice of the Material Constants

As explained in the previous section the co-rotational small strain approach coupled to the linear elastic Hooke's law was underestimating the maximum strains and stresses. Such an approach is thus no longer taken into account in the further analysis, especially that non-linear models with ca. 50,000 elements can be solved nowadays very rapidly.[19]

Literature reveals large dispersion of the mechanical properties among patients (Table 2 above). Figures 6

TABLE 2. Material properties of organs with the inter-individual dispersion.

	C_0q1	C_0med	C_0q3	C_1q1	C_1med	C_1q3
Vagina	0.08	0.111	0.224	0.135	0.27	0.695
Rectum	0.083	0.085	0.138	0.025	0.0565	0.098
Bladder	0.021	0.0375	0.073	0.005	0.007	0.065

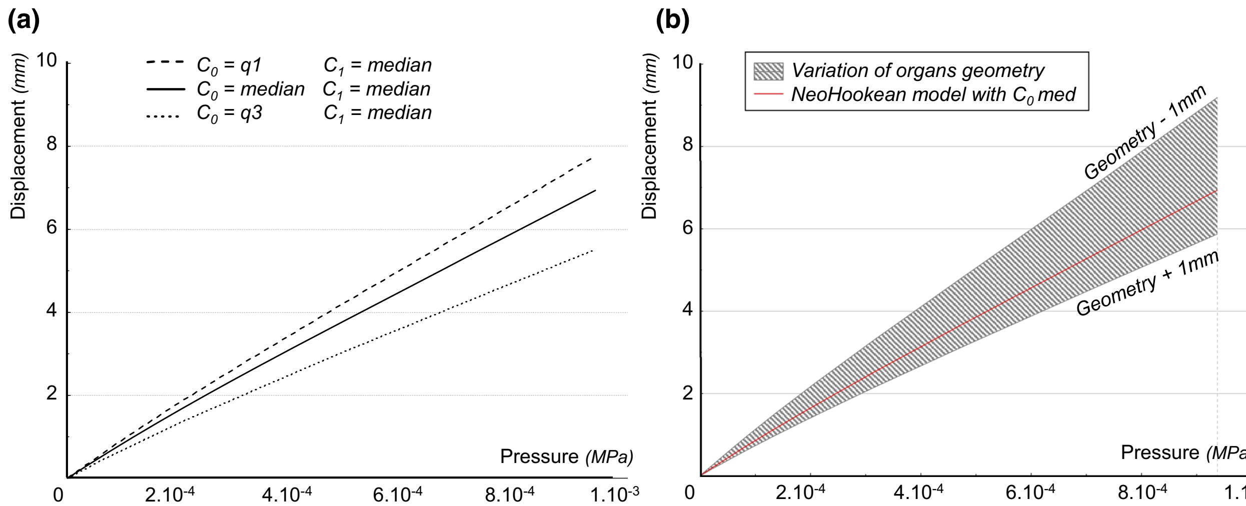

FIGURE 8. (a) Analysis of cervix displacement with respect to C_0 coefficient dispersion (Yeoh's approach). Applied pressure corresponding to cough on horizontal axis and magnitude of cervix displacement on the vertical axis. (b) Influence of the geometrical parameter.

and 8a present the impact of the inter-subject variability, plotted against applied abdominal pressure.

Figure 8a reveals noticeable influence of the stress parameter C_0 with the difference in computed cervix displacement at maximum abdominal pressure load up to 2.3 mm for C_0 values corresponding to the first and third quartile (Table 2). Figure 6 shows that indeed there is little practical difference between the Neo-Hookean and Yeoh laws as the influence of the parameter C_1 is minimal.

Our results suggest that the second order constitutive law such as Yeoh's brings little benefit in the study of biomechanics of pelvic floor. It appears that for the physiological range of abdominal pressures the increase in tissue stiffness that C_1 is modeling does not occur. For such pressure range, the Neo-Hookean behavior law seems sufficient. Consequently, one needs to take into account only the variability in the coefficient C_0.

Influence of the Accuracy of the Geometry Description

Our FE models allow us to consider geometric parameters such as the thicknesses of organs. As presented above, the limited resolution of medical imaging introduces uncertainty in estimating contours during the numerical model generation. For example the reconstruction of the vaginal wall leads to uncertainties between two and six pixels. Therefore we analyze how the variations in organ thickness influence the model response. Consequences of such variation have been simulated using our generic model and results are presented in Fig. 8b. Even a very small change in the input geometry—by 1 mm which is of the order of a single pixel—leads to substantial change in the predicted mobility of the uterus, substantially larger than this effected by a large change in the stress parameter C_0. The variation in geometry description seems to have a dominant influence on organ displacement.

Simulation with Asymmetric Patient-Specific Models

To strengthen the conclusions of our study we repeated the parametric studies described in "Influence of the Choice of the Functional Form of the Constitutive Model", "Influence of the Choice of the Material Constants" and "Influence of the Accuracy of the Geometry Description" sections using four patient specific models initially used to produce an average "generic model". Results are presented in Fig. 9 and show that our conclusions are unchanged for each case and do not appear to depend on particular features of a model used—as seen in Fig. 2 these patient specific models differ significantly. The comparison between

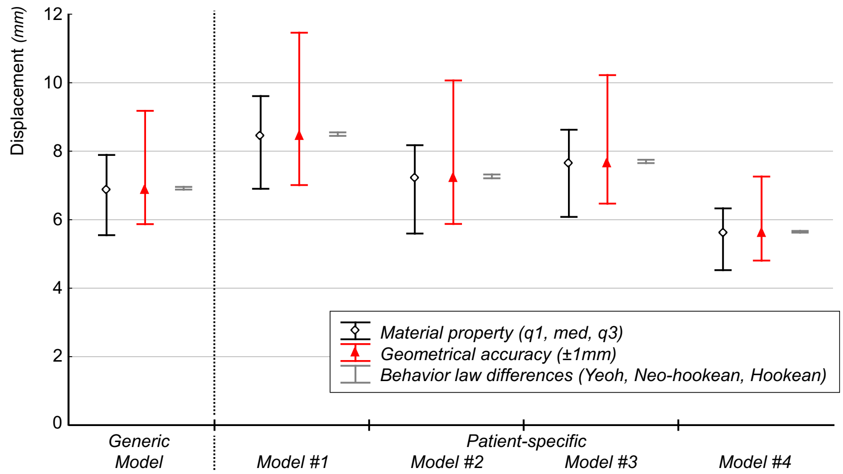

FIGURE 9. Displacements observed on four non-pathological patients with the influence of every model parameter (behavior law type, variation of the mechanical properties and geometric variations).

the four patients shows different displacement fields under the same abdominal pressure loading, resulting from the inter subject variability, but the influence of each studied parameter is similar to that seen when using the generic model.

DISCUSSION AND CONCLUSIONS

In this paper we analyzed the effects of material modeling and geometry description of the pelvic system on the results of comprehensive FE simulations of the pelvic floor organ mobility.

Our results show that simulating the pelvic mobility with a linear elastic approach under small strain and large rotation assumptions (so called co-rotational approach) provides displacement filed that is similar to that obtained with non-linear finite deformation solution procedure and hyperplastic material description. Thus if the requirements of the patient-specific simulation are only to estimate the displacements, the linear elastic approach under small strain and large rotation is sufficient and can lead to optimized FEM software that can be used in the operating theater in real time.

However, when more accurate estimates of strains and stresses are required, for example to assess the potential of tissue damage, a fully non-linear mathematical formulation is necessary. However our analysis demonstrates that when using a proper large deformation FE solution procedure, for practical purposes the choice of the hyperelastic law appears to be immaterial and we recommend the use of the simplest one—the Neo Hookean constitutive law.

The large observed inter-subject variability in the tissue stiffness, described by the parameter C_0 was investigated and our results show its moderate influence on the organ mobility.

In this work we also considered the influence of the accuracy of the geometry description. A significant difference in computed organ displacement is observed despite allowing only small (±1 mm) variations in organ thickness resulting from medical imaging imprecision. We find that the imprecision in geometry description has significantly larger influence on the computed organ mobility than imprecision in the constitutive model and material parameter choice. Our FE models employed a constant thickness for each organs, even though it is variable in reality, albeit this thickness variability is very difficult to measure *in vivo*. Our results show that the geometrical inaccuracy is significantly affecting the pelvic mobility simulation results, and therefore future biofidelic models need to take into account these local geometry differences.

The bladder and the rectum are permanently, but only partially, filled which leads us to suggest that they will not collapse in physiological situations. However, in physiological situation vagina is indeed collapsed. Our model is not considering collapsed vagina because during MRI observation fluid has been introduced inside it as a necessary step to observe it. This is indeed a limitation of our study that can be rectified only by much more powerful imaging. Another limitation of our model is that the pressure drop in the abdominal cavity, during coughing for instance, is not taken into account.

Our findings with regard to the relative unimportance of the choice of the constitutive law and limited importance of the stress parameter for the predictions of pelvic organ mobility is in concord with recent, often considered somewhat controversial suggestions that accurate mechanical characterization of soft tissues is relatively unimportant when large, comprehensive simulations are performed.[19,25,36] Nevertheless our work is in agreement with the recent study[23] which also highlights the key role of the precise description of geometry on organ displacement predictions.

Finally, when assessing the applicability of the results presented here one needs to consider that in some cases very large increase (by a factor of three) in the stiffness parameter is observed. Such an increase can be attributed to aging[6] or pathology occurrence.[9]

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CONFLICTS OF INTEREST

None.

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