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Computational Biomechanics for Patient-Specific Applications

From Finite Element Meshes to Clouds of Points: A Review of Methods for Generation of Computational Biomechanics Models for Patient-Specific Applications

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Abstract—It has been envisaged that advances in computing and engineering technologies could extend surgeons' ability to plan and carry out surgical interventions more accurately and with less trauma. The progress in this area depends crucially on the ability to create robustly and rapidly patient-specific biomechanical models. We focus on methods for generation of patient-specific computational grids used for solving partial differential equations governing the mechanics of the body organs. We review state-of-the-art in this area and provide suggestions for future research. To provide a complete picture of the field of patient-specific model generation, we also discuss methods for identifying and assigning patient-specific material properties of tissues and boundary conditions.

Keywords—Patient-specific model, Mesh generation, Finite element method, Meshless methods, Material properties, Soft tissues, Biomechanics for medicine.

INTRODUCTION

There is wide international concern about the cost of meeting rising expectations for health care, particularly if large numbers of people require currently expensive procedures such as brain surgery. At the turn of XXI century it has been envisioned that improving efficiency of health care delivery can be achieved through the use of Computer-Integrated Surgery (CIS) systems.[40,96] Such systems can overcome many limitations of the traditional surgery by extending surgeons' ability to plan and carry out surgical interventions more accurately and with less trauma.[40]

CIS systems rely on biomechanical models to estimate complex deformation fields within the human body organs undergoing surgery. This requires the transition of biomechanical research from those focusing on generic understanding of biomechanical phenomena in a human (or animal) organism to patient-specific studies addressing biomechanics of a particular individual. The key requirement is that the user—ultimately a surgeon—should not require specialist knowledge in the field of numerical computation, hence the operation of CIS systems must be robust and reliable.[78]

CIS depend crucially on the ability to develop robustly and rapidly patient-specific biomechanical models. The main requirement of the method for patient-specific computational model generation is its compatibility with a clinical workflow. This in practice eliminates approaches that require large computational power, exceedingly long calculations and specialist knowledge on the part of a user. It is not reasonable to expect hospitals worldwide to install supercomputers and employ PhDs in numerical analysis to construct patients' models.

In our judgment the minimum requirements for a patient-specific model generation method are:

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- The method would start with a standard diagnostic image (usually a magnetic resonance MR or computed tomography CT) and yield a computational grid of acceptable quality in less than 40 min.
- The method would require only the most standard computing hardware (PC, laptop or perhaps just a modern mobile phone).
- The method does not have to be fully automated but high level knowledge of numerical analysis on the user's part should not be required.

Computational biomechanics research community is rapidly closing on creating methods meeting the above requirements. This review article summarizes the state-of-the-art in this area.

We focus on the methods for generation of patient-specific computational grids subsequently used for solving partial differential equations governing the mechanics of an organ or system under investigation. Substantial progress has been achieved in this field.[51,78,114] More briefly we review methods of identifying and assigning patient-specific mechanical properties of tissues as well as boundary conditions.

This paper is organized as follows. Following the "Introduction" section, in "Geometry Extraction From Medical Images: Segmentation" section we briefly review the image segmentation and geometry extraction methods, necessary prerequisites for finite element (FE) meshing and meshless computational grid generation methods, reviewed in "Computational Grid Generation" section. "Specification of Material Properties and Boundary Conditions" section contains a short summary of methods used to assign patient-specific material properties and boundary conditions. Finally we conclude the article with "Discussion" section.

GEOMETRY EXTRACTION FROM MEDICAL IMAGES: SEGMENTATION

To make generation of patient-specific FE and meshless models truly applicable to large clinical studies, each stage of model development would ideally be automated. An area of improvement to the automated development of patient-specific biomechanical models is the identification and segmentation of the biological structures of interest. Three-dimensional (3D) imaging modalities such as CT and MR serve as the primary tools for acquiring anatomical data to serve as the basis for patient-specific models.

Automated image segmentation is a difficult task due to the complexity of medical images. Consequently, there is no universal algorithm for segmenting every medical image; the techniques available for segmentation are specific to the application, the imaging modality and anatomic structure under consideration. Some of the techniques that have been used to automate the segmentation of anatomical structures are summarized below. However, it should be noted that despite promising results, the quest for automated generation of patient-specific meshes from medical images is far from over as segmentation of images of organs with geometry/anatomy distorted by disease and pathology (such as tumors) still remains a challenge[1] and tends to rely on analyst experience and ability to manually outline boundaries of different anatomical structures in the images.

Thresholding

Thresholding based algorithms are relying on the premise that structures or organs of interest have distinctive quantifiable features such as image intensity, texture, or have a distinct boundary to separate it from surrounding structures.[88,91] The segmentation procedure is to search for voxels whose values are within the ranges established by the threshold levels. Automated approaches utilize information from the histogram to define the threshold values. Often the threshold is applied to the entire image and it can be difficult to extract/delineate the object of interest from the surrounding voxels that also meet the threshold criteria (Fig. 1a).

Region Growing

Region growing techniques overcome a number of limitations of simple threshold based segmentation by limiting the region where the threshold is applied and simplifies the extraction of multiple objects. Region growing techniques start with user defining seed voxel(s) that initiate a search of surrounding voxels that meet a threshold criterion specified by the user.[60,83] If a neighbor voxel meets the threshold criteria, it is added to the object and all of its neighbors are also searched. This process is repeated until no new voxels are added to the object of interest (Fig. 1b).

Region growing and thresholding segmentation algorithms are standard features of software packages for visualization and image analysis. This includes open source, such as 3D Slicer[33] (http://www.slicer.org) and OsiriX[87] (http://www.osirix-viewer.com/AboutOsiriX.html), and commercial, such as Mimics® (http://biomedical.materialise.com/mimics), software.

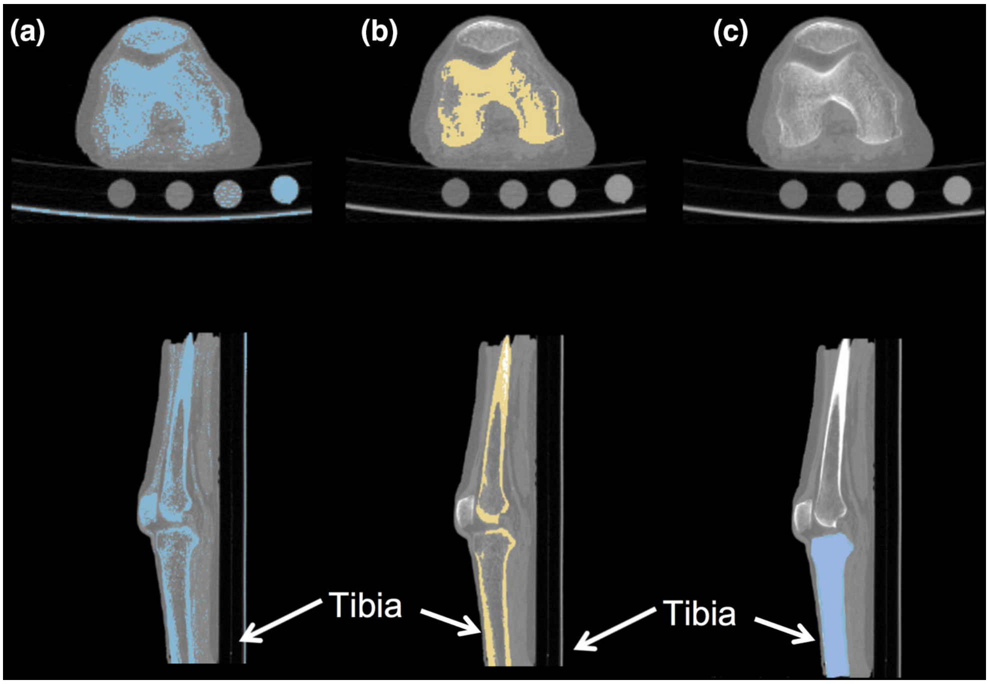

FIGURE 1. Segmentation of the tibia from CT images performed using (a) thresholding, (b) region growing, and (c) Expectation Maximization (EM) algorithm. The anatomical priors included in the EM algorithm limit the region to the tibia alone, which is difficult to achieve using the other two approaches.

Other Segmentation Approaches

Many other approaches to image segmentation have been proposed and used for a wide variety of applications. The best known examples include watershed based methods,[9] level set approach[90] and edge detection algorithms (such as edge relaxation,[43] the border detection method,[66] Canny edge detection,[19] Sobel edge detection and Laplacian edge detection[27]).

To improve the segmentation for medical images, anatomical prior information has often been introduced into several algorithms to help delineate anatomical structures. This often involves statistical based methods and machine learning approaches. We have previously used such methods (the Expectation–Maximization (EM) segmentation) to automatically delineate the femur and tibia from CT images[85] and others have applied similar approaches to the segmentation of MR images.[61] Good reliability in the segmentation of anatomical features such as the brain, femur and tibia has been achieved using these approaches (Fig. 1c).[85]

As image segmentation is a key step in obtaining information about geometry for creating patient-specific computational grids, some commercial (Mimics® http://biomedical.materialise.com/mimics) and open-source (Slicer3D http://www.slicer.org) software packages integrate image segmentation and meshing algorithms. Examples of application of these packages include models of the vasculature for evaluation of the risk of aneurysm rupture,[32] models of bones for orthopedic surgery,[53] and models of the brain and other internal organs for surgery/therapy planning and simulation.[17,107]

COMPUTATIONAL GRID GENERATION

Finite Element Meshing

3D medical images are used to locate pathologies within organs.[107] A computational grid—a mesh in the case of the FE method—must be obtained from these images in order to construct the biomechanical model. For complicated organ shapes (e.g., the brain), mesh generation is a difficult and resource-intensive process, requiring significant image processing and manual intervention—Fig. 2.

Automatic Approach: Tetrahedral Mesh Generation

Tetrahedral mesh generators are a standard feature of commonly used Computer-Assisted Engineering (CAE) packages. To achieve good mesh quality, they rely on well-established techniques and optimization schemes[20] including Delaunay triangulation method,[6] modified-octree technique,[72] and advancing front technique.[68] Tetrahedral mesh generators available in commercial CAE packages facilitate automated (with the required analyst's input typically limited to the parameters determining the element size, mesh density

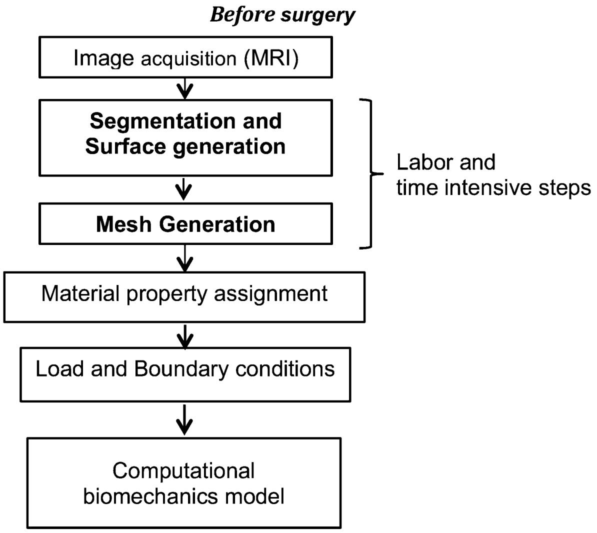

FIGURE 2. From a diagnostic image to patient-specific computational biomechanics model using finite element method.

and element quality) discretization of objects with complex geometry. They were applied in biomechanical studies to create patient-specific meshes of the human body organs and segments[37,102] together with open-source such as e.g., TetGen (http://wias-berlin.de/software/tetgen/), gmesh[39] and in-house tetrahedral mesh generators using high-quality Delaunay,[34] point-based matching (PBM) and advancing front[51] methods. Examples include meshing of bones,[53,103] musculoskeletal system,[37] blood vessels,[71] brain,[107] prostate,[107] and other internal organs.[51]

The key advantage of tetrahedral meshes in the context of patient-specific applications is that they can be generated automatically if the information about organ geometry is available as a closed surface. Consequently, they are the most common choice when creating computational grids for biomechanical models of living tissues.[18] It has been reported in the literature that high quality tetrahedral meshes can be created using readily available mesh generators.[20,34,68] However, for continua with complicated geometry, quality control of tetrahedral meshes can be a challenge[68,92] and varies according to the mesh generation method employed.[44] For instance, it has been recognized that advancing front method provides better control of the quality of generated elements than Delaunay triangulation method but suffers from slow computational speed.[20,51] Smoothing (e.g., using Laplacian method) has been proposed and used to improve tetrahedral mesh quality.[20]

The computation (CPU) time appreciably varies between different tetrahedral mesh generators. For instance, Foteinos *et al.*[34] reported that, when constructing the human brain mesh, the CPU time for Delunay-type mesh generator is around two orders of magnitude shorter than for optimization-based PBM generator. However, the key factor determining how long it takes to create a mesh for an organ of a given patient is the analyst's time spent to extract information on patient-specific geometry from medical images (often several hours or even a day[4,108]) rather than the mesh generator CPU time (hundreds of seconds for meshes consisting of several million tetrahedral elements[97,108]).

As numerous automated generators of tetrahedral meshes are available, it is tempting to conclude that they should be the method of choice when constructing patient-specific computational grids for biomechanical models. However, 4-noded tetrahedral elements exhibit artificial stiffening, known as volumetric locking, when applied in modeling of incompressible (or nearly incompressible) continua.[47] This presents a challenge in case of soft tissues such as the brain and internal organs.[109] Two types of methods to address this challenge have been used: (1) Improved linear tetrahedral elements employing a range of countermeasures to prevent locking[13,57]; (2) Higher-order and mixed-formulation elements.[7,47,86] The former includes average nodal pressure (ANP) tetrahedral element,[13] which provides much better results for nearly incompressible materials than the standard tetrahedral element with only small increase in the computational cost. Nevertheless, one problem with the ANP element implementation in a FE code is the handling of interfaces between different materials. This problem was solved by Joldes *et al.*[57] who extended the ANP formulation so that all elements in a mesh are treated in a similar way and no special handling of the interface elements is required.

Second-order 10-noded and mixed-formulation (displacement–pressure) tetrahedral elements are readily available in commercial FE codes (such as ABAQUS,[26] ANSYS,[3] RADIOSS,[2] LS-DYNA,[67] COMSOL http://www.comsol.com/products) and are effective in dealing with volumetric locking although they do not eliminate locking entirely.[86] Nevertheless, their computation cost is around four times higher than that of standard linear 4-noded tetrahedral elements.[15] This might be a limiting factor as many important applications, including image-guided surgery, require models consisting of a few hundred thousand elements to be solved in-real time (in practice tens of seconds[41]) on commodity hardware.

Hexahedral and Hexa-dominant Meshing

Mesh generation constitutes the bulk of the setup time for a problem (Fig. 2). This is especially true of anatomic hexahedral FE mesh development. For example, Ateshian *et al.*[4] stated that the process of generating a patient-specific articular contact FE model from CT arthrography image data is painfully slow, taking over 100 h for segmentation and mesh generation.

The manual generation of a 3D hexahedral mesh, although often a highly accurate method, requires significant time and operator effort to complete even a single mesh. Consequently, the majority of analyses reported in the literature refer to a single, or "average" geometry, although in many cases the anthropometric variability in size and shape should not be neglected. Furthermore, mesh refinements and convergence tasks are rarely reported for this type of mesh. As a result, additional compromises may include sub-optimal mesh refinement, homogenously modeled regions of heterogeneous structures,[81] or simplifying assumptions of symmetry.[31]

In an effort to unencumber the process, several automated meshing algorithms have been implemented.[6,103,114] They can be classified into two broad types of mesh generation schemes—routines for structured and unstructured meshes.[14,38]

The techniques for generating structured grids are based on rules for geometrical grid subdivisions and mapping techniques; producing triangular or quadrilateral elements in two-dimensional analyses, and hexahedral elements in three-dimensions. Unstructured grid generation relies on an explicit definition of the connections between nodes to form elements, in addition to the coordinates of the nodes themselves. Although largely synonymous with tetrahedral grids, unstructured grids may alternatively be composed of hexahedral elements (without directional structure).[98]

Hexahedral elements are preferred for many applications. A mathematical argument in favor of the hexahedral element is that the volume defined by one such element must be represented by at least five tetrahedral elements, which in turn yields a system matrix that is computationally more expensive, in particular if higher order elements are used. Moreover, under-integrated hexahedral elements do not exhibit volumetric locking[26,57] and are by far the most efficient when explicit time integration schemes are used.[110,112] Despite decades of intense effort and successful application of semi-automated approaches in patient-specific meshing of selected anatomical structures (such as key parts of the vasculature[28,29]), there are no automatic hexahedral meshing algorithms available which would work for complicated shapes routinely encountered when modeling human organs. Automated hexahedral meshing methods such as plastering,[12] whisker weaving,[94] and octree-based[50] techniques have been reported. Although such techniques yield meshes of high quality, element size and orientation control remains a challenge. Moreover, they have proven to be not always robust.

Structured grid generators are commonly used when strict elemental alignment is mandated by the analysis code or when necessary to capture physical phenomenon. Structured meshing algorithms generally involve complex iterative smoothing techniques that attempt to align elements with boundaries or physical domains. Where non-trivial boundaries are required, "block-structured" techniques can be employed which allow the user to break the domain up into topological blocks (e.g., TrueGrid http://www.truegrid.com/, Ansys ICEM CFD[3] and IA-FEMesh[42]). These multiblock grids are a powerful extension of the structured mesh approach. Structured meshing techniques are applied to a series of interconnected sub-grids or "blocks". While the individual blocks remain structured, the blocks fit together in an unstructured manner. As a result, the multiblock technique affords geometric flexibility while retaining computational efficiency (Figs. 3 and 4).

When traditional commercial FE programs are applied to anatomic structures, the geometry thereof is often simplified. In addition, several different packages are often required to develop a single model.[89] Various custom-written codes have been reported. Unfortunately, they tend to have limited availability, are poorly documented, are inadequate for producing a mesh of high quality in a rapid manner, or simply do not meet the needs of the problem under consideration.

Isogeometric Analysis and High Order Elements

As discussed in the previous sections, the current approach (Fig. 2) for creating patient-specific FE meshes includes extraction of patient-specific geometry from medical images through image segmentation and then generation of the actual mesh. In general (with exception of voxel-based meshes), geometry representation obtained through segmentation differs from that in the FE analysis. This not only makes mesh generation difficult and often tedious, but also leads to inaccuracies as mesh only approximates geometry extracted from the images. This problem is not limited to computational grids for patient-specific biomechanical simulations. According to Hughes[48] differences in geometry representation in the computer aided design (CAD) systems and FE analysis lead to excessively long time (up to 80% of the entire analysis time) devoted to mesh generation in major engineering applications.

The isogeometric analysis proposes to solve this problem by eliminating the FE polynomial representation of geometry and replacing it with the representation based on Non-Uniform Rational B-Splines (NURBS)[48] which is a standard technology used in CAD systems. This implies creation of NURBS elements that exactly represent the geometry and facilitate direct translation of CAD geometric model to computational model. So far NURBS-based isogeometric

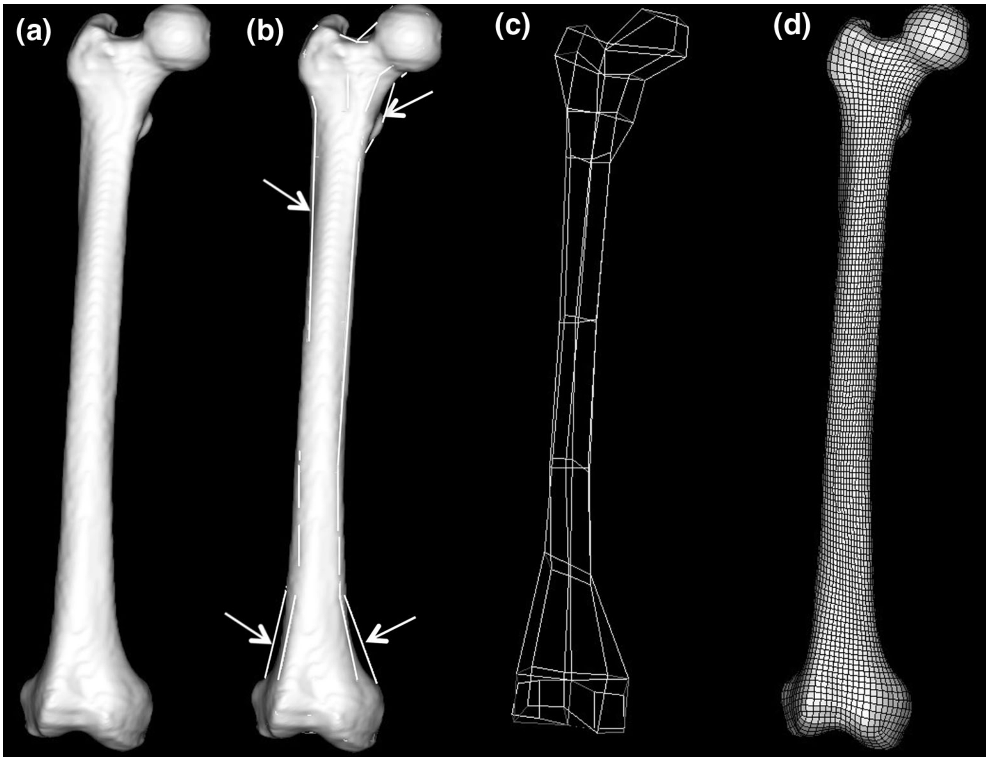

FIGURE 3. Generation of subject-specific hexahedral mesh of human femur using a multiblock technique. (a) Discretized (triangulated) representation of the femur surface obtained from segmentation of the CT image; (b) Grid of interconnected blocks (thin white lines indicated by arrows) breaking the domain of interest into topological block overlaid on the femur surface. (c) Each block is defined by eight vertices, which allows application of structured meshing techniques; (d) Hexahedral mesh obtained by applying structured meshing on the grid interconnected block and closest point projection onto femur surface. Detailed description of this process is provided in Grosland *et al.*[42] High quality hexahedral mesh can be generated but significant operator input may still be required when creating a grid of structured blocks.

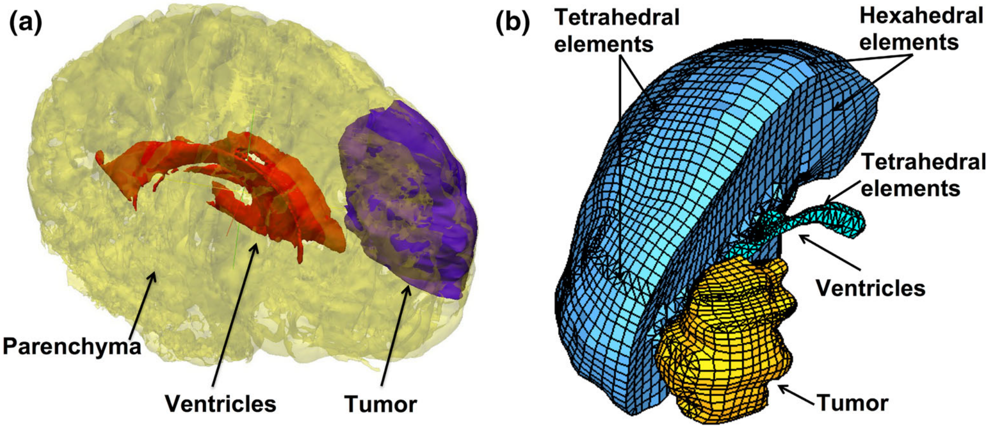

FIGURE 4. Patient specific hexa-dominant mesh generation. (a) Definition of patient specific problem geometry—discretized representation of the parenchyma, ventricles and tumor surfaces used in Miller *et al.*[76] and Wittek *et al.*[108] (b) Hexa-dominant mesh created using a multiblock technique for the patient specific geometry shown in (a). The mesh was applied for computing the brain deformations due to craniotomy induced brain shift.[108] Poor quality hexahedral elements were replaced by tetrahedral elements. Because of irregular/complex geometry of ventricles and tumor, tetrahedral elements dominate the mesh of ventricles, tumor and parenchyma areas adjacent to the tumor and ventricles. Adapted from Wittek *et al.*[108]

analysis has found only very limited application in biomechanics. Patient-specific modeling of blood flow[8,113] is one of the best known examples.

Isogeometric analysis is a relatively recent development to address shortcomings of low-order polynomial interpolation in FE analysis in biomechanical computations. Alternative solutions have been proposed. In late 1980s of XX century, Hermite interpolation functions were introduced by Hunter and Smaill[49] to model the heart muscle electromechanics and non-linear stress and strain analysis of the heart (myocardium).[23] Application of Hermitian elements has been later extended to pulmonary system[95] and multi-scale heart modeling.[16]

Isogeometric method and Hermitian elements discussed in this section provide interesting alternatives to commonly used FE analysis with proven success in selected applications. Nevertheless, the current practice of patient-specific model generation still involves image segmentation and FE meshing, both of which are formidable problems that are very difficult to automate. Therefore, the need for entirely new approaches has been suggested in recent studies.[78]

Beyond Finite Element Meshes: Meshless Methods and Models as Clouds of Points

Many decades of computational biomechanics research revealed important weaknesses of the FE method:

- A good quality mesh is needed in order to obtain accurate results. Such a mesh is difficult to build for complicated organ shapes (such as e.g., the brain), and requires significant processing of images. Creation of patient-specific FE models is expensive, time consuming and inherently incompatible with existing clinical workflows.
- Even when a good quality mesh is created, the FE solution method often fails in the case of large deformations, due to problems such as element inversion. Tissue cutting simulation is also difficult, as small and poorly shaped elements can be created during the cutting process.[24,54]

Meshless methods of computational mechanics have been recognized as one possible solution for some of these challenges.[30] In particular, several meshless methods for surgical simulation have been developed, implemented and tested at the Intelligent Systems for Medicine Laboratory at the University of Western Australia.[46,54,58]

In meshless methods, the field variable interpolation is constructed without the use of a predefined mesh. These methods use a set of nodes scattered within the problem domain and on its boundary (Fig. 5), which is easier than creating a good quality mesh. Because more nodes are involved in the creation of shape functions as compared to FE method, meshless methods are more robust in handling large deformations.[80,84] However, meshless methods currently available in the literature (including those developed by the authors), suffer from a number of deficiencies that preclude their use by a non-specialist in the clinical environment:

- Inability to create shape functions for arbitrary grids. Only "admissible node distributions" can be used.[63] The user must have sufficient knowledge and experience to understand what constitutes an "admissible" grid, and what modifications are necessary if the grid is not "admissible".
- Lack of theoretical error bounds on numerical integration due to the non-polynomial nature of integrands. Without rigorously established error bounds the solution methods cannot be used in sensitive applications like computational biomechanics for medicine.

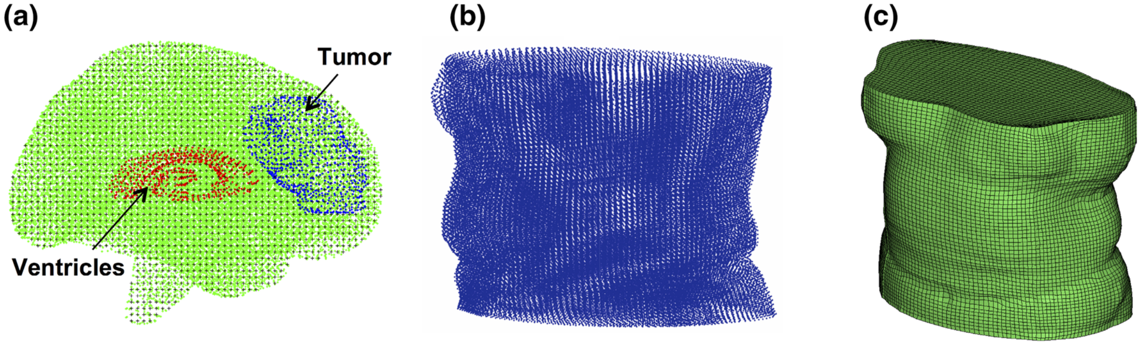

FIGURE 5. Meshless discretization—biomechanical model as a cloud of points. (a) Three dimensional patient-specific meshless model applied in Miller *et al.*[76] to compute the brain deformations due to craniotomy-induced brain shift (the problem geometry is shown in Fig. 4a). Dots are the model nodes, and black crosses are the background integration points. The figure was created by Mr Ashley Horton of the Intelligent Systems for Medicine Laboratory, The University of Western Australia. (b) Patient-specific meshless model for computing organ/tissue deformation for whole-body image registration. Dark blue dots are the model nodes. Adapted from Li *et al.*[65] (c) Finite element model for computing organ deformations for the patient analyzed using the meshless model shown in (b). Included for the purpose of comparison with model (b). Adapted from Li *et al.*[64]

Recent developments in meshless algorithms eliminate some of these deficiencies and make meshless methods even more suitable for computational biomechanics applications. They include a more efficient method for handling discontinuities,[45] modified moving least squares approximation which can handle more nodal distributions without loss of accuracy[21,59] and incorporation of fuzzy tissue classification method within the meshless computational framework which makes it possible to assign material properties at integration points of a computational grid directly from the medical images without segmentation. Assignment of material properties directly from the medical images using fuzzy tissue classification was successfully applied in the context of computation of the brain and abdominal organ deformations when treating soft tissues as a hyperelastic neo-Hookean material.[64,115]

SPECIFICATION OF MATERIAL PROPERTIES AND BOUNDARY CONDITIONS

We discuss these two clearly separate issues in a single subsection because in our opinion they share a common feature. In contrast to computational grid generation discussed in the previous sections, it appears that little progress has been achieved in developing methods for identification of patient-specific mechanical properties and boundary conditions that would be useful in a clinical setting.

Specification of Material Properties

Mechanical Testing

Mechanical experiments on tissue samples are a key source of knowledge of material properties of living tissues. Due to ethical and technical constraints they are of little practical importance for patient-specific applications. Nevertheless, *in vivo* methods for determining patient-specific tissue properties by directly exerting force (mainly through aspiration/suction) on the body organs have been proposed[104] and validated during surgery.[70] However, the usage of such methods remains limited.

Elastography

In elastography, measurements of tissue mechanical properties is performed indirectly by imaging of either changes in tissue displacements/deformations due to slight compression by the ultrasound transducer (strain elastography) or low-frequency mechanically excited shear waves within the tissue of interest (shear wave elastography). The observation of tissue deformations and shear waves can be conducted using ultrasound,[82,100] MR[11,93] and optical[62,105] imaging.

Ultrasound and MR elastography have been used as non-invasive methods for creating maps of relative tissue stiffness within the organ for diagnosis for over 20 years[82] with detection of cancers of prostate, thyroid and breast and liver pathologies as key applications.[36,93] Steady progress has been made to quantify elastography in terms of the tissue stress parameters and viscoelastic properties.[11] As discussed by Bilston,[11] one of the key challenges is that MR elastography determines tissue properties only for small deformations within the linear range. As soft tissues exhibit non-linear stress–strain behaviour,[35,75] responses at larger deformations cannot be inferred from elastography alone.

Nevertheless, it is now known that a lot can be achieved even without the knowledge of patient-specific properties of tissues. 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. Already two types of such problems have been found to possess relevance for computational biomechanics:

1. Dirichlet-type problem, sometimes called pure-displacement,[22] and displacement-zero traction problems[79] whose solution in displacements are weakly sensitive to mechanical properties of the considered continuum.
2. Problems that are approximately statically determinate and therefore their solutions in stresses are weakly sensitive to mechanical properties of constituents.[56,69,77]

In 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, and have 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.[64,79,108] The second type of problems has been identified in the field of biomechanics of intracranial aneurysms that can be approximately modeled as pressure vessels that are known to be statically determinate. If we formulate the boundary value problem inversely, we are able to determine the aneurysm wall stress distribution without knowledge of patient-specific mechanical properties of the tissues comprising the wall. This reasoning applies to many structures in a human body which can be approximated as vessels loaded by internal pressure.[56,73]

Boundary Conditions

Textbooks[7] and review articles[5] on methods of computer simulation in engineering and science recognize representation of boundary conditions and collection of data about boundary conditions as key components of the process of formulating computational models together with geometry, materials properties and loading. The importance of representation of boundary conditions has been confirmed e.g., by studies using FE analysis for investigation of biomechanics of brain injury[25] and prostate surgery simulation.[52] However, it appears that only very few studies using experimental or clinical data (all in the brain[55,74] and heart[10,111] biomechanics) have been conducted with the purpose of obtaining quantitative data for determining boundary conditions of the human body organs. Only some of them[10] aim at patient-specific applications.

DISCUSSION

Patient-specific biomechanical computations have been dominated by FE analysis as confirmed by the following articles published in this Special Issue of *Annals of Biomedical Engineering*.[99,101,106,116] However, this review indicates that despite many years of research and development in academia and software industry, generation of patient-specific FE meshes using medical images as a source of information about organ geometry still requires input from an experienced analyst with expert knowledge of image processing and mesh generation. As discussed in sections "Isogeometric Analysis and High Order Elements" and "Beyond Finite Element Meshes: Meshless Methods and Models as Clouds of Points" methods combined with tissue classification eliminate key disadvantages associated with FE method's reliance on low-order polynomial interpolation and pave a way for automating computational grid generation. However, there are still numerical constraints and requirements the grids used in meshless methods need to satisfy. Nodes placement cannot be completely arbitrary. Only "admissible node distributions",[63] for which shape functions can be created, can be used.

A challenge is to create model generation methods that are sufficiently flexible and robust so that they can be used by a non-specialist. Such methods are capable of forming the foundation of biomechanics-based CIS systems which ultimately will be used by medical specialists in a clinical environment, and not by engineers or numerical analysts in their laboratories. A modified moving least squares approximation which can handle more nodal distributions without loss of accuracy is an example of a recent step in this direction.[21,59]

Determining patient-specific material properties has been a subject of research effort in the last 20–30 years.[36] However, despite substantial progress, including recent advances in MR elastography,[11,93] *in vivo* quantification of soft tissue material properties still remains an unsolved challenge. Nevertheless it is now known that a lot can be achieved even without the knowledge of patient-specific properties of tissues. For applications (such as image-guided surgery) that can be formulated as Dirichlet-type problems, it is possible to determine deformations of soft organs during surgery without exact knowledge of patient specific properties of soft tissues.[64,76,77,108] Using sophisticated inverse solution procedures it is also possible to compute wall stresses of aneurysms and other approximately statically determinate structures without the knowledge of the tissue properties.[56]

Representation of boundary conditions is a key component of computational model formulation. However, it has attracted much less attention and research effort than methods for the grid generation and determination of patient-specific material properties. Despite the fact that studies of the brain and heart biomechanics[10,55,74,111] indicated the importance of boundary conditions for predicting the organ responses, quantitative knowledge of such properties is very limited.

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CONFLICT OF INTEREST

We have no conflict of interest to report in relation to this review.

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