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(56) Documents Cited:

Peirlinck M., "A modular inverse elastostatics approach to resolve the pressure-induced stress state for in vivo imaging based on cardiovascular modeling", 2018, Journal of the Mechanical Behavior of Biomedical Materials, vol 85, pages 124-133
Raghavan M. L., "Non-Invasive Determination of Zero-Pressure Geometry of Arterial Aneurysms", 2006, Annals of Biomedical Engineering, vol. 34, pages 1414-1419
Sellier M., "An iterative method for the inverse elastostatic problem", 2011, Journal of Fluids and Structures, vol. 27, pages 1461-1470

(58) Field of Search:
INT CL **G06T**
Other: **WPI, EPODOC, INSPEC**

(54) Title of the Invention: **Deformation gradient-based zero-pressure configuration recovery for vessels**
Abstract Title: **Zero Pressure Configuration Recovery for Blood Vessels**

(57) Determining an unpressurised blood vessel configuration (e.g. coronal or carotid artery, vein), comprises providing (S104) an initial (i.e. a 'normal' start state) configuration model $S^{(k=1)}$ of the vessel comprising a mesh of N nodes (e.g. originally derived from segmented imaging of the vessel (S101), using MRI, CT, ultrasound), and applying (S105) a pressure (e.g. systolic or diastolic average) to the model $S^{(k)}$ to obtain a pressurised configuration model $D^{(k)}$. A deformation gradient $F^{(k)}$, wherein $D^{(k)} = F(S^{(k)})$, is determined (S106), and for each node, a displacement $E^{(k)}$ is calculated (S107) representing the difference between the pressurised configuration model and the configuration model at each node. An updated configuration model $S^{(k+1)} = D^{(k)} - F^{-1(k)} \odot E^{(k)}$ is calculated (S108), wherein $F^{-1(k)}$ is the inverse of the deformation gradient and $\odot$ is an elementwise product. If a difference between the maximum value of $E^{(k)}$ and $E^{(k-1)}$ is more than an error threshold (Y), the pressurising, deformation gradient determination, displacement calculation and updated model calculation steps are repeated, otherwise (N) $S^{(k)}$ (as iterated) is output as the unpressurised blood vessel configuration (S109). Use of the deformation gradient accelerates convergence. Zero pressure geometry required by Finite Element Analysis (FEA) of vessels is improved.

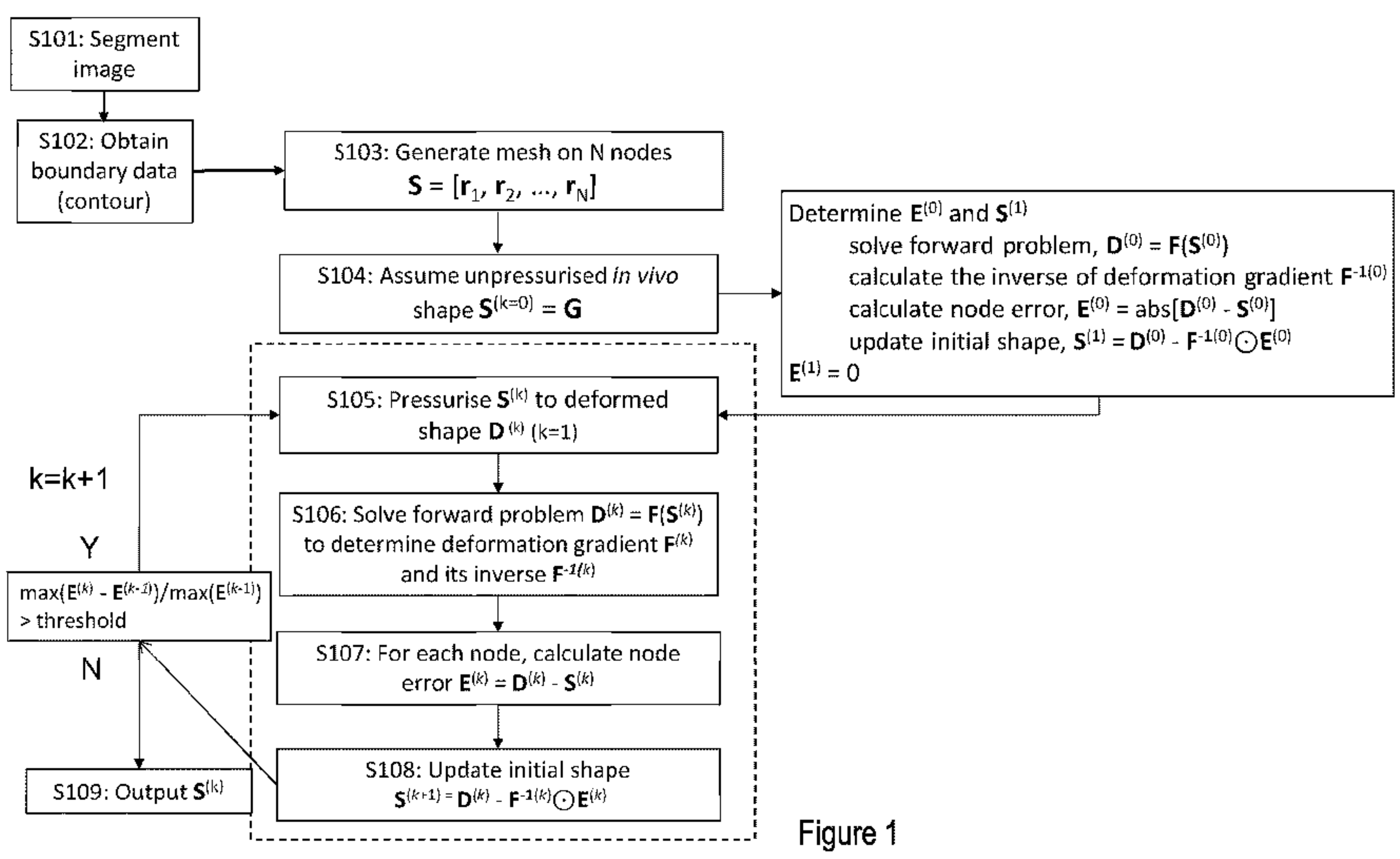

Figure 1

At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

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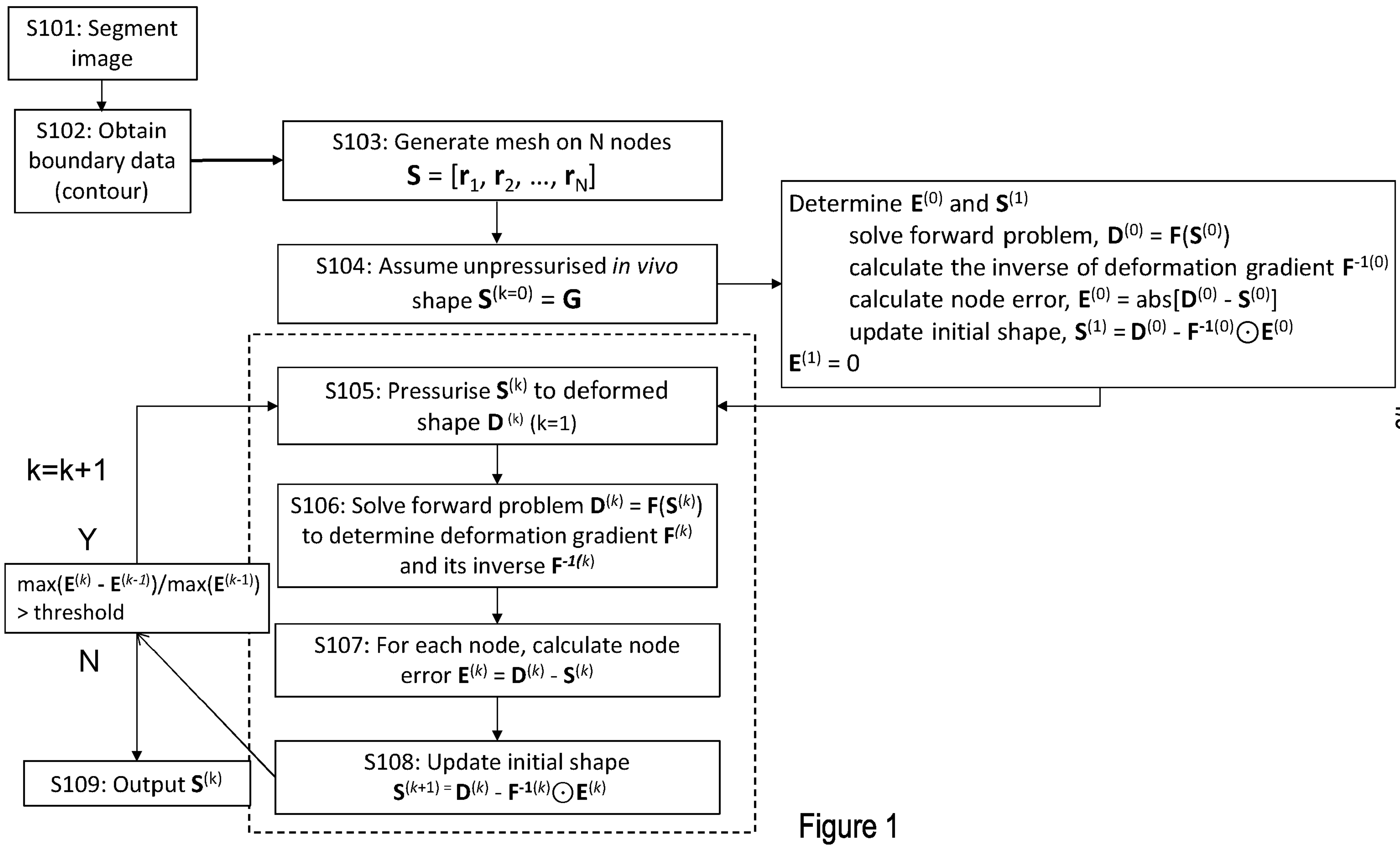
S101: Segment image
S102: Obtain boundary data (contour)
S103: Generate mesh on N nodes
S = [r1, r2, ..., rN]
S104: Assume unpressurised in vivo shape S(k=0) = G
Determine E(0) and S(1)
solve forward problem, D(0) = F(S(0))
calculate the inverse of deformation gradient F-1(0)
calculate node error, E(0) = abs[D(0) - S(0)]
update initial shape, S(1) = D(0) - F-1(0)⊙E(0)
E(1) = 0
S105: Pressurise S(k) to deformed shape D(k) (k=1)
S106: Solve forward problem D(k) = F(S(k)) to determine deformation gradient F(k) and its inverse F-1(k)
S107: For each node, calculate node error E(k) = D(k) - S(k)
S108: Update initial shape
S(k+1) = D(k) - F-1(k)⊙E(k)
k=k+1
Y
max(E(k) - E(k-1))/max(E(k-1)) > threshold
N
S109: Output S(k)

Figure 1

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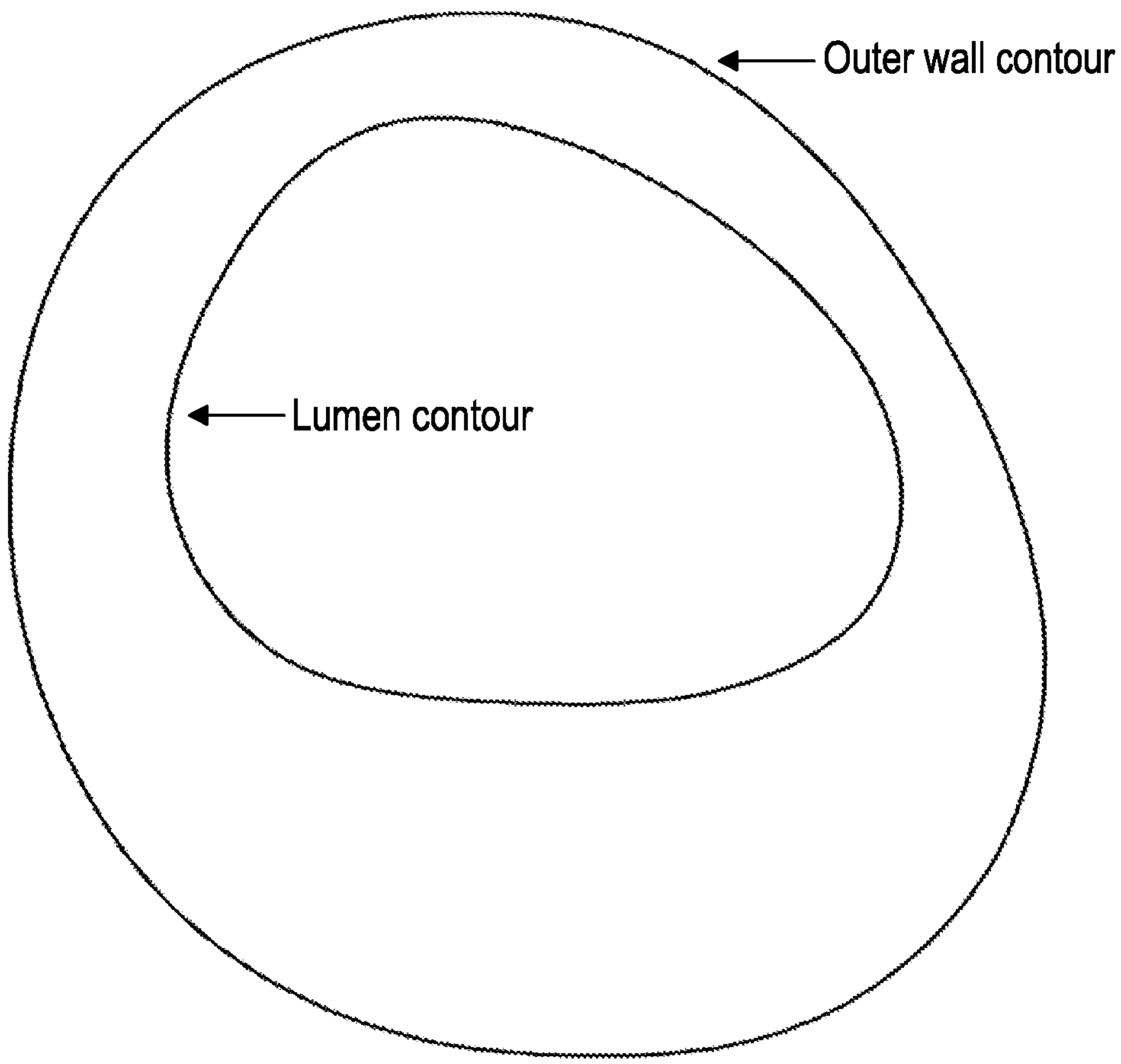

In vivo configuration G (initial shape guess)

Figure 2

Meshed in vivo configuration

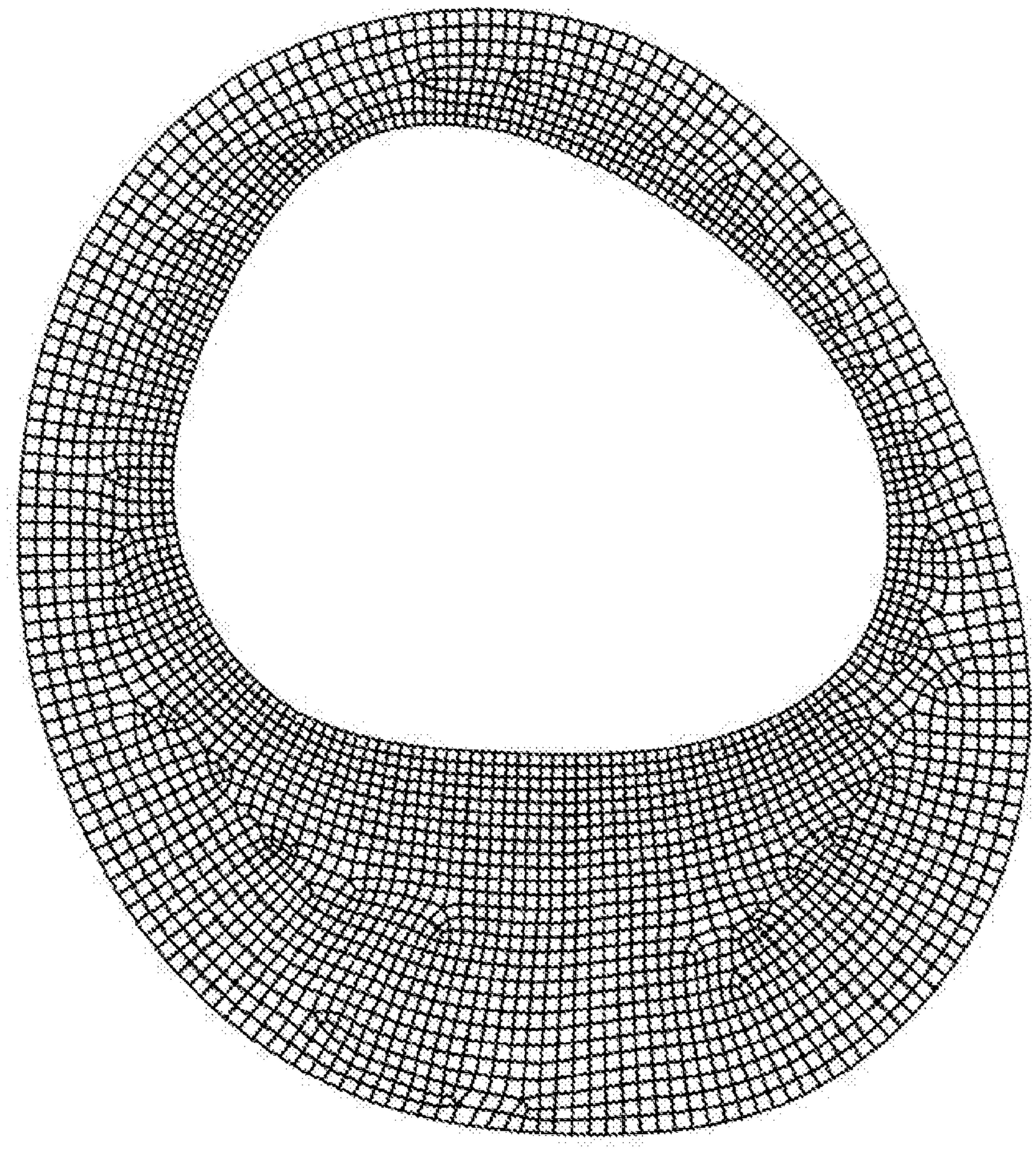

Figure 3A

Pressurized geometry based on in vivo configuration

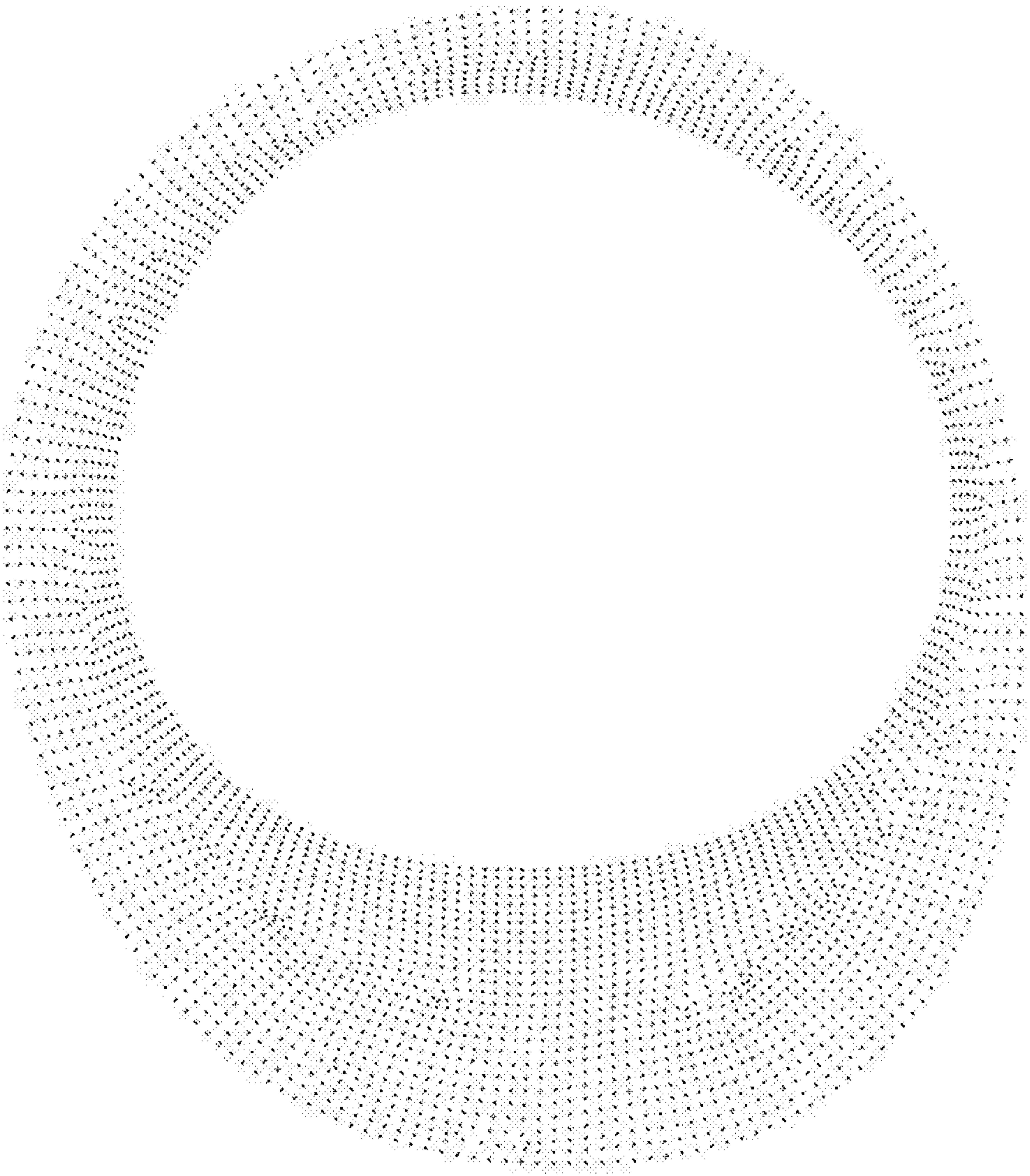

Figure 3B

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The difference between pressurized and in vivo configuration

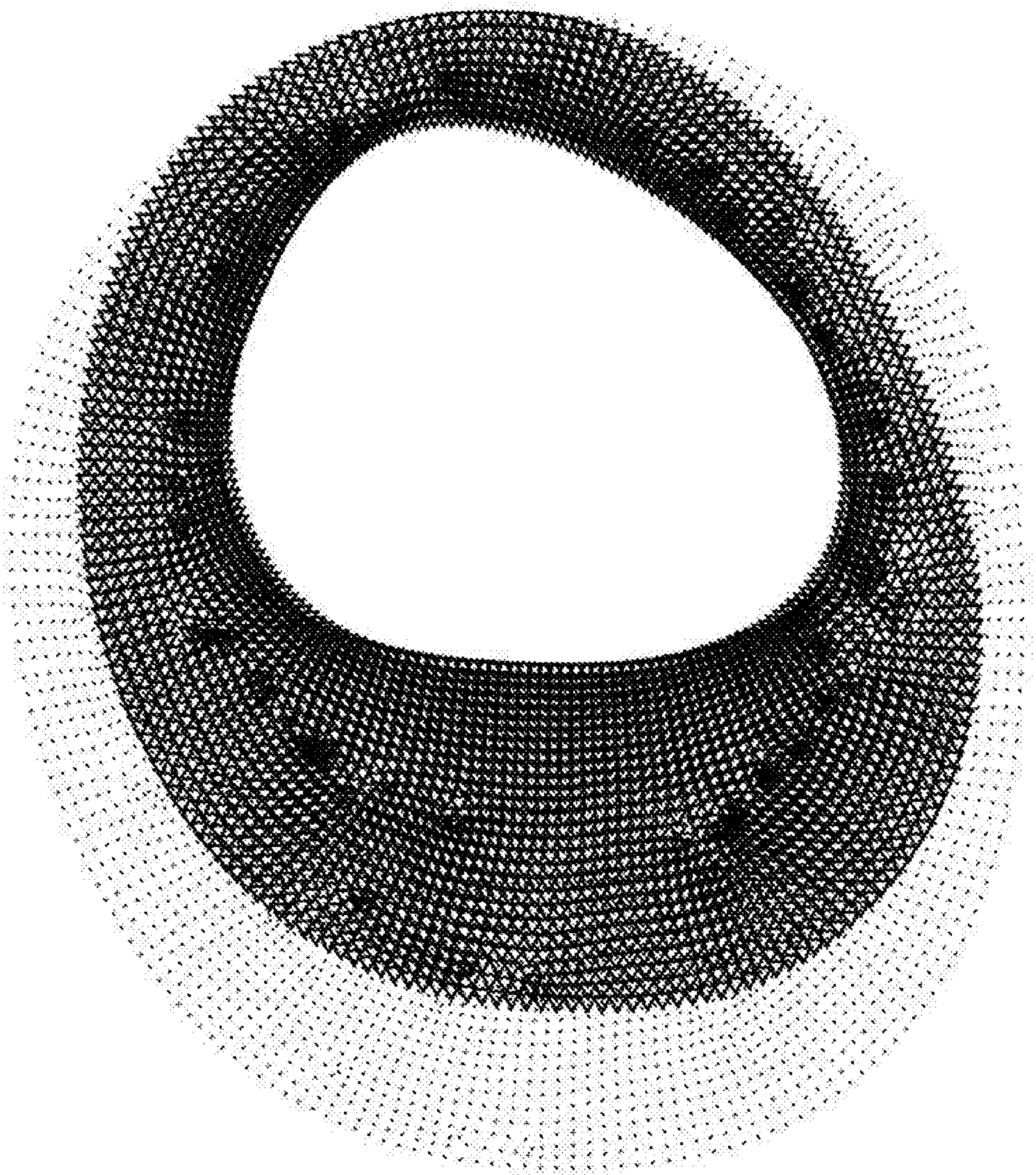

Figure 3C

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Meshed predicted zero-pressure configuration

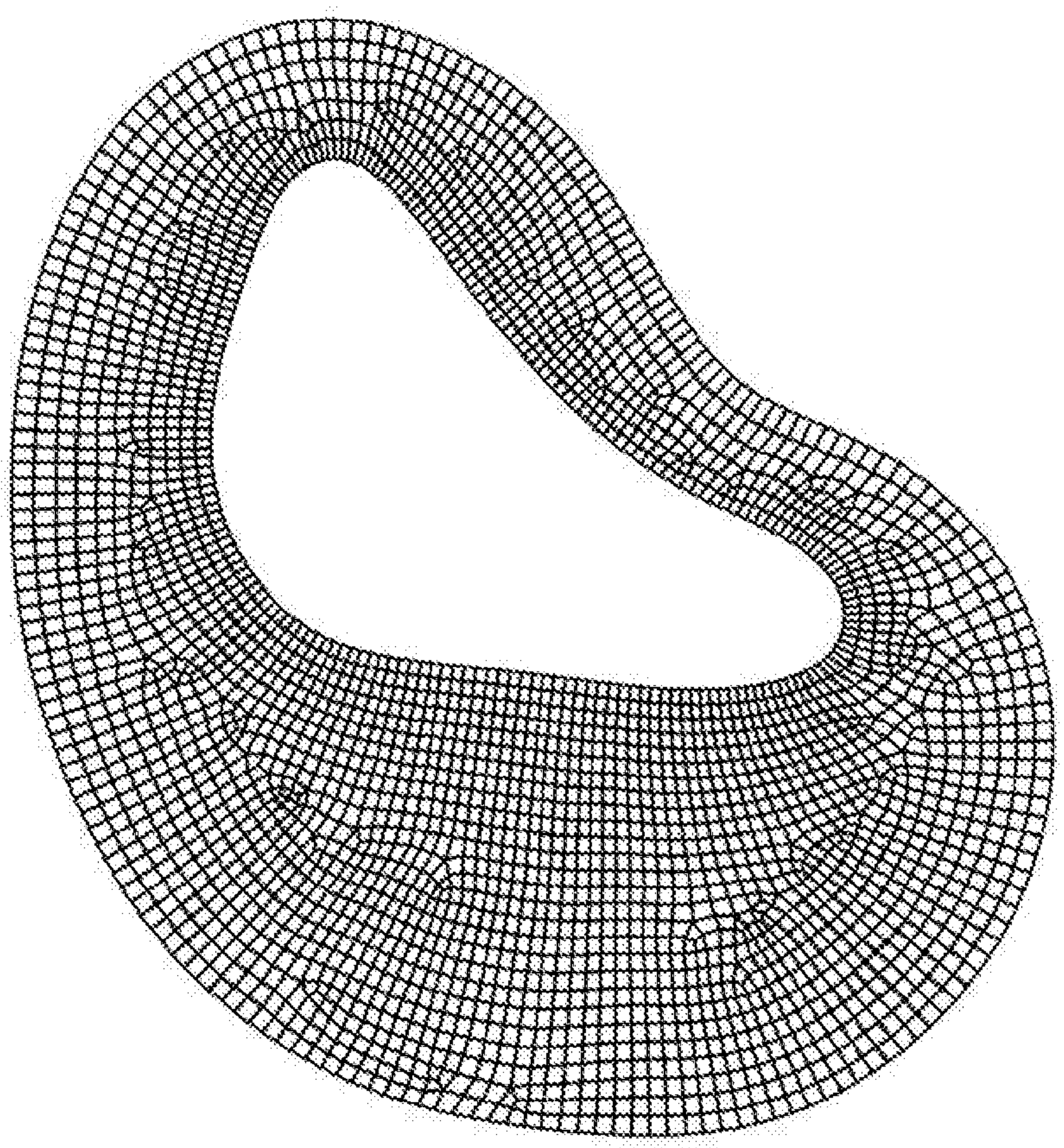

Figure 4A

Recovered in vivo configuration based on the estimated zero-pressure geometry

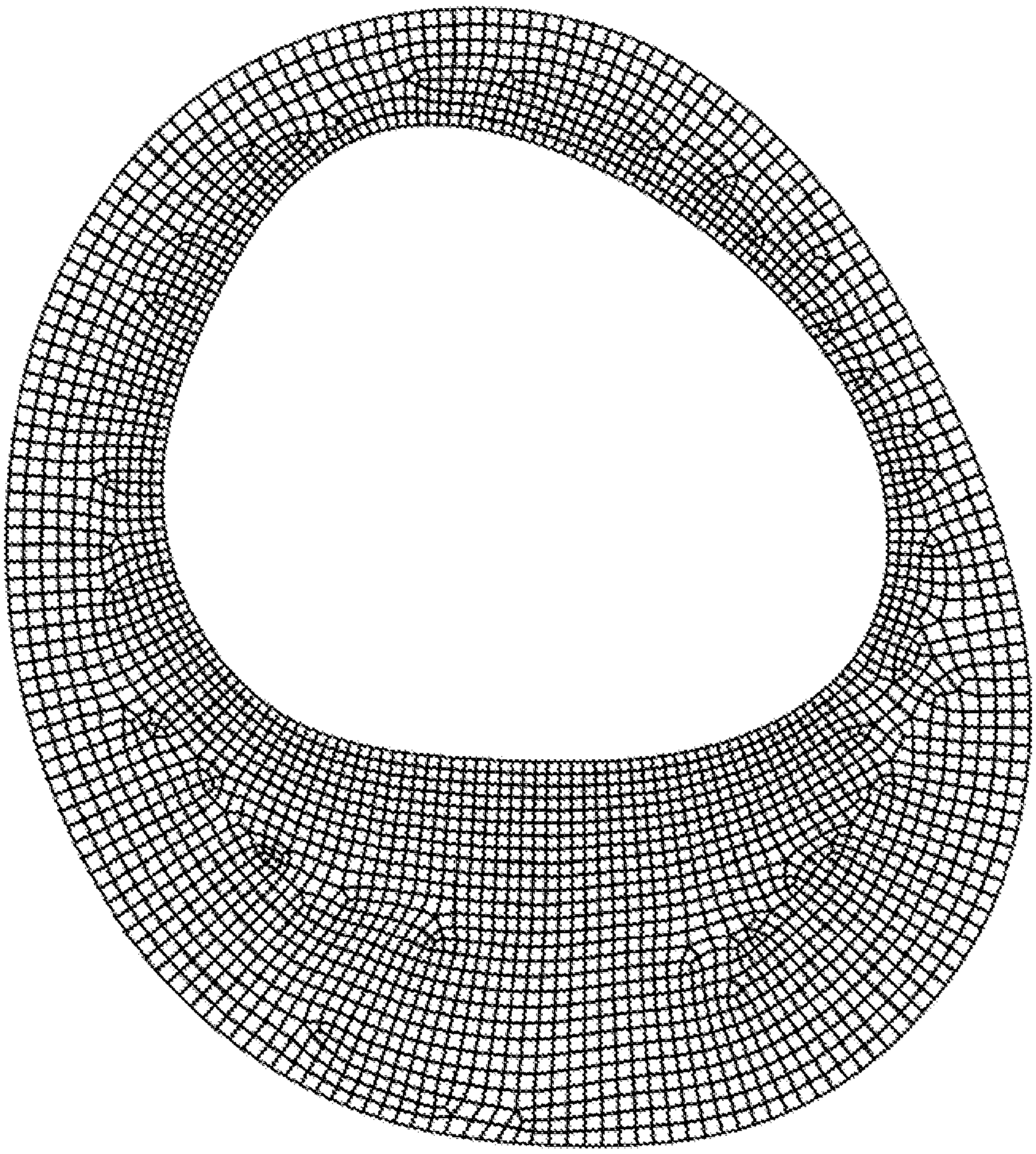

Figure 4B

Comparison between recovered and in vivo configurations

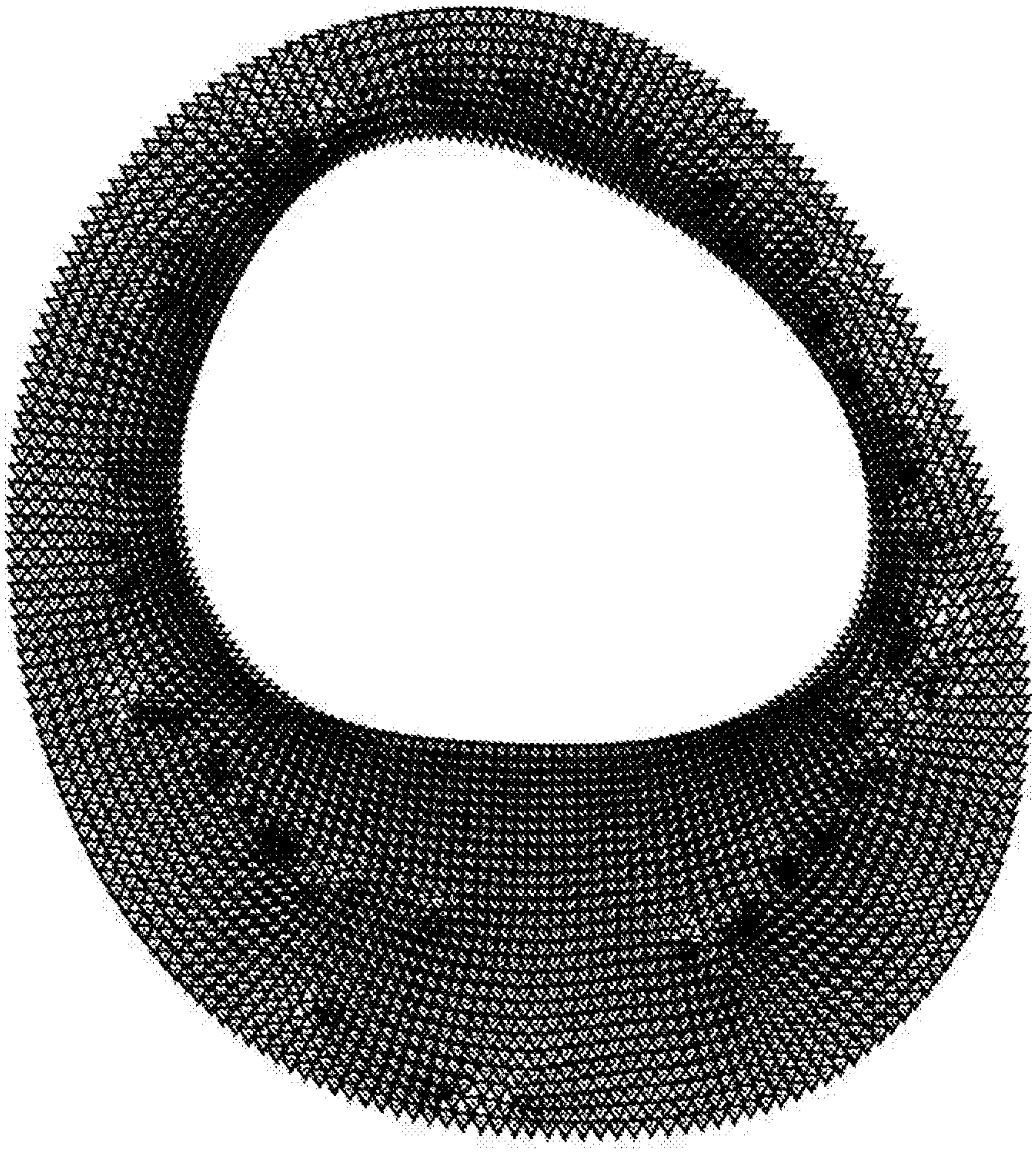

Figure 4C

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Deformation gradient-based zero-pressure configuration recovery for vessels

Technical Field

Aspects of the present invention generally relate to medical image-based geometry reconstruction. In particular, aspects of the present invention relate to *in vivo* imaging-based analysis to assess mechanical loading of arterial lesions and evaluate the risk of lesion rupture.

Background

Under physiological conditions, arterial lesions, including atherosclerosis and aneurysm, are subject to mechanical loading due to blood pressure and flow.

Lesion may rupture if such loading exceeds its material strength, causing symptoms such as stroke and heart attack.

Image-based finite element analysis (FEA) provides a method to estimate the mechanical loading within the lesion *in vivo*, which shows potential in assessing the lesion vulnerability and risk. While the acquired image provides the anatomical information under physiological blood pressure, FEA requires a zero-pressure geometry as the computational starting shape. Therefore, a “shrinkage” procedure which recovers the zero-pressure shape should be performed before the mechanical simulation.

Given the pressurised configuration and corresponding boundary conditions, for a given constitutive relation, the unpressurised configuration can be recovered using inverse methods. At present, there are two main types of approaches:
1) direct methods, in which the displacement field is directly obtained by solving inverse differential equations and is used to recover the unpressurised shape; and
2) iterative methods, in which the initial shape is updated to minimise the difference between the pressurised shape and *in vivo* shape.

Direct methods can find a unique solution by solving the inverse equations in Eulerian weak form, however, the derivation of the equations is cumbersome and dependent on the constitutive model, which is not easily implemented with a commercial solver package. In contrast, iterative methods are easy to implemented in established FEA packages with simple algorithms, and applicable to various constitutive models. However, the iterative procedure involves a series of FEA, which is often time-consuming.

Aspects of the present invention provide methods and systems to address this problem, amongst others.

Summary of the invention

According to a first independent aspect of the invention, there is provided a method for determining an unpressurised configuration of a blood vessel, the method comprising the steps of:

(a) providing a configuration model $S^{(k=1)}$ of the blood vessel comprising a mesh of N nodes;

(b) applying a pressure p to the configuration model $S^{(k)}$ to obtain a pressurised configuration model $D^{(k)}$;

(c) determining a deformation gradient $F^{(k)}$, wherein $D^{(k)} = F(S^{(k)})$;

(d) for each node, calculating a displacement $E^{(k)}$ representing the difference between the pressurised configuration model $D^{(k)}$ and the configuration model S at the each node;

(e) calculating an updated configuration model $S^{(k+1)} = D^{(k)} - F^{-1(k)} \odot E^{(k)}$, wherein $F^{-1(k)}$ is the inverse of the deformation gradient and $\odot$ is an elementwise product;

(f) if a maximum value of $E^{(k)}$ is less than a predetermined error threshold, repeat steps (b) to (e), wherein k=k+1; else output $S^{(k)}$ as the unpressurised configuration of the blood vessel.

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For example, the blood vessel may be an artery or a vein. This is an optimised iterative method which determines the unpressurised configuration of the blood vessel, using information from deformation gradient, to accelerate convergence.

When carrying out the initial step of providing a configuration model S of the blood vessel comprising a mesh of N nodes, the assumption is that the configuration model (as provided in the initial step) corresponds to an unpressurised *in vivo* shape G. The configuration or shape model is a structural model, the term referring to the geometry of the blood vessel, including a mesh which is a collection of N nodes, as generated for example by a numerical solver.

In a dependent aspect, step (f) comprises determining a relative difference between a maximum value of $E^{(k)}$ and a maximum value of $E^{(k-1)}$ and comparing the relative difference to a predetermine relative error threshold.

In a dependent aspect, providing a structural model comprises the steps of:

providing a segmented image of the blood vessel;

obtaining contour data for the segmented image; and

using the contour data to generate the structural model.

In a dependent aspect, the segmented image is obtained according to an imaging technique. In further dependent aspects, the imaging technique is magnetic resonance imaging (MRI), computed tomography (CT) or ultrasound.

In a dependent aspect, in step (b), pressure p is measured at the time at which the segmented image is provided. More preferably, pressure p is measured as a systolic or diastolic mean blood pressure.

It will be appreciated that the described methods may be performed on any suitable processing system, including hardware or firmware. In some cases, each step may be performed by a module in a system.

Additionally or alternatively, any of the described methods may be embodied as instructions on a non-transitory computer-readable medium such that, when the instructions are executed by a suitable module within the system (such as a processor), cause the module to perform a described method.

According to a second independent aspect of the invention, there is provided a system comprising a processor, the processor being configured to:

(a) provide a configuration model $S^{(k=1)}$ of the blood vessel comprising a mesh of N nodes;
(b) apply a pressure p to the configuration model $S^{(k)}$ to obtain a pressurised configuration model $D^{(k)}$;

(c) determine a deformation gradient $F^{(k)}$, wherein $D^{(k)} = F(S^{(k)})$;

(d) for each node, calculate a displacement $E^{(k)}$ representing the difference between the pressurised configuration model $D^{(k)}$ and the configuration model S at the each node;

(e) calculate an updated configuration model $S^{(k+1)} = D^{(k)} - F^{-1(k)} \odot E^{(k)}$, wherein $F^{-1(k)}$ is the inverse of the deformation gradient and $\odot$ is an elementwise product;

(f) if a maximum value of $E^{(k)}$ is less than a predetermined error threshold, repeat steps (b) to (e), wherein k=k+1; else output $S^{(k)}$ as the unpressurised configuration of the blood vessel.

Preferred features of either one of the independent aspects are provided in the dependent claims.

Brief Description of the Drawings

Aspects of the present invention will now be described, by way of example only, with reference to the accompanying figures, in which:

Figure 1 shows is a flow diagram of an embodiment of the invention;

Figure 2 shows an *in vivo* configuration of a lumen with boundary contours (initial shape guess G);

Figure 3A shows the meshed *in vivo* configuration;

Figure 3B shows a pressurised geometry based on the *in vivo* configuration;

Figure 3C shows the difference between the pressurised and the *in vivo* configuration;

Figure 4A shows the meshed predicted zero-pressure configuration;

Figure 4B shows the recovered *in vivo* configuration based on the predicted zero-pressure configuration; and

Figure 4C shows a comparison between the recovered and *in vivo* configurations.

Detailed Description

Figure 1 is a flow diagram of an embodiment of the invention, which is process that determines a zero-pressure ("unpressurised") configuration from an *in vivo* image data corresponding to an image of a blood vessel. The blood vessel may be an artery such as a coronal or carotid artery.

At step S101, image segmentation is performed for mechanical analysis. This can be done via known manual, semi-automatic or fully automatic procedures. Image segmentation starts with the identification of the lumen and outer arterial or venous wall. The arterial or venous wall is segmented based on medical images acquired by a suitable method such as magnetic resonance (MR), computed tomography (CT) or ultrasound (i.e. intravascular ultrasound, "IVUS"). The components between the lumen and outer wall, if presented, should be segmented as well.

Interpolation and contour smoothing may be performed to bridge gaps and to correct for irregular shapes caused by image and segmentation distortion. At step S102, data points corresponding to a contour of the segmented image are determined (boundary data). In an example, as shown in Figure 2, the boundary (contour) or area of the lumen can be determined according to the signal intensity in multi-contrast MR images or according to the value of each pixel in quantitative mapping images, acquired by proton density (PD), T1, T2, and/or T2* mapping sequences.

The motion of the arterial wall was governed by the following equation:

$$\rho_w v_{i,tt} = \sigma_{ij,j}, \quad i, j = 1,2,3; \text{ sum over } j,$$

with boundary condition,

$$\sigma_{ij,j} \cdot n_j \big|_{outer\ wall} = 0$$

in which $\boldsymbol{v}$ is the displacement vector, $\boldsymbol{\sigma}$ is the stress tensor, and t denotes time. Different constitutive law can be used to characterize the material properties, e.g., the modified Mooney-Rivlin model,

$$W = c_1(I_1 - 3) + D_1\left[exp\left(D_2(I_1 - 3)\right) - 1\right] + \kappa(J - 1)$$

where I_1 is the first invariant of deformation tensor, J is the determinant of deformation gradient, c_1, D_1 and D_2 are material parameters and κ is the Lagrangian multiplier for incompressibility.

At step S103, the boundary data (representing contours of the lumen, the outer wall and components if presented) are imported into a numerical solver to generate a mesh, resulting in N nodes (Figure 3A). For example, a numerical solver such as the commercial finite-element package ADINA® version 9.2 (ADINA R&D, Inc., Watertown, Mass., USA) may be used.

The coordinates of the *i*-th node are $\mathbf{r}_i = [x_i, y_i]^T$. The collection of all nodes is $\mathbf{S} = [\mathbf{r}_1, \mathbf{r}_2, \ldots, \mathbf{r}_N]$.

The *in vivo* shape **G** is the pressurised under blood pressure, *p*. Ideally the pressure corresponds to the pressure at the time at which the *in vivo* image is acquired, which can be difficult to achieve. In practice, blood pressure *p* can be a systolic or diastolic blood pressure measured on a patient over a period of time and averaged over that period of time (mean blood pressure).

At step S104, an initial shape guess $\mathbf{S}^{(1)} = \mathbf{G}$ (Figure 3B) is made. The unpressurised shape is then recovered through an iteration process. as shown in the table below, in pseudo-code:

Algorithm Recover zero-pressure configuration using optimised backward displacement

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initialise $\mathbf{S}^{(0)} \leftarrow \mathbf{G}$

Determination of $\mathbf{E}^{(0)}$ and $\mathbf{S}^{(1)}$:

  solve forward problem, $\mathbf{D}^{(0)} = \mathbf{F}(\mathbf{S}^{(0)})$

  calculate the inverse of deformation gradient $\mathbf{F}^{-1(0)}$

  calculate node error, $\mathbf{E}^{(0)} = \text{abs}[\mathbf{D}^{(0)} - \mathbf{S}^{(0)}]$

  update initial shape, $\mathbf{S}^{(1)} = \mathbf{D}^{(0)} - \mathbf{F}^{-1(0)} \odot \mathbf{E}^{(0)}$

set $k = 1$ and $\mathbf{E}^{(1)} = 0$

while $\max(\mathbf{E}^{(k)} - \mathbf{E}^{(k-1)})/\max(\mathbf{E}^{(k-1)}) > x\%$ (x can be a predefined

  solve forward problem, $\mathbf{D}^{(k)} = \mathbf{F}(\mathbf{S}^{(k)})$

  calculate the inverse of deformation gradient $\mathbf{F}^{-1(k)}$

  calculate node error, $\mathbf{E}^{(k)} = \text{abs}[\mathbf{D}^{(k)} - \mathbf{S}^{(k)}]$

  update initial shape, $\mathbf{S}^{(k+1)} = \mathbf{D}^{(k)} - \mathbf{F}^{-1(k)} \odot \mathbf{E}^{(k)}$

  update counter, $k = k + 1$

end while

output zero-pressure shape, $\mathbf{S}^{(k)}$

At step S105, in the k-th step, the starting shape, $\mathbf{S}^{(k)}$, is pressurised to the correspondingly deformed shape $\mathbf{D}^{(k)}$ through FEA. Pressure p is applied on the lumen, and degree of freedom (DOF) policies are applied on two nodes to eliminate rigid translation and rotation. The x-axis DOF is fixed on node A whose y-axis coordinate is the maximum. The y-axis DOF of x-axis direction is fixed on node B whose x-axis coordinate is the minimum.

At step S106, the forward problem $\mathbf{D}^{(k)} = \mathbf{F}(\mathbf{S}^{(k)})$ is solved to determine the deformation gradient $\mathbf{F}^{(k)}$ is output and the inverse of the deformation gradient $\mathbf{F}^{-1(k)}$ is calculated.

At step S107, the difference between the pressurised shape $\mathbf{D}^{(k)}$ and *in vivo* shape $\mathbf{G}$ is calculated at each node, resulting in $\mathbf{E}^{(k)} = \mathbf{D}^{(k)} - \mathbf{S}^{(k)}$ (e.g., Figure 3C). Advantageously, displacement information is thus provided at each node. Unlike prior art methods, this guarantees that the shape will eventually converge towards the recovered zero-pressure configuration.

At step S108, the starting shape is set as: $\mathbf{S}^{(k+1)} = \mathbf{D}^{(k)} - \mathbf{F}^{-1(k)} \odot \mathbf{E}^{(k)}$, where $\odot$ is the elementwise product. The iteration ends when the relative difference between the maximum value of $\mathbf{E}^{(k)}$ and that of $\mathbf{E}^{(k-1)}$ is less than a predefined threshold, e.g., 1% (Figure 4C). The starting shape output in the final step (S109) is the recovered zero-pressure configuration (Figure 4A).

Interpretation

It will be appreciated that the order of performance of the steps in any of the embodiments in the present description is not essential, unless required by context or otherwise specified. Thus most steps may be performed in any order. In addition, any of the embodiments may include more or fewer steps than those disclosed.

Additionally, it will be appreciated that the term “comprising” and its grammatical variants must be interpreted inclusively, unless the context requires otherwise. That is, “comprising” should be interpreted as meaning “including but not limited to”.

Moreover, the invention has been described in terms of various specific embodiments. However, it will be appreciated that these are only examples which are used to illustrate the invention without limitation to those specific embodiments. Consequently, modifications can be made to the described embodiments without departing from the scope of the invention.

Claims

1. A method for determining an unpressurised configuration of a blood vessel, the method comprising the steps of:
   (a) providing a configuration model $S^{(k=1)}$ of the blood vessel comprising a mesh of N nodes;
   (b) applying a pressure p to the configuration model $S^{(k)}$ to obtain a pressurised configuration model $D^{(k)}$;
   (c) determining a deformation gradient $F^{(k)}$, wherein $D^{(k)} = F(S^{(k)})$;
   (d) for each node, calculating a displacement $E^{(k)}$ representing the difference between the pressurised configuration model $D^{(k)}$ and the configuration model S at the each node;
   (e) calculating an updated configuration model $S^{(k+1)} = D^{(k)} - F^{-1(k)} \odot E^{(k)}$, wherein $F^{-1(k)}$ is the inverse of the deformation gradient and $\odot$ is an elementwise product;
   (f) if a maximum value of $E^{(k)}$ is less than a predetermined error threshold, repeat steps (b) to (e), wherein k=k+1; else output $S^{(k)}$ as the unpressurised configuration of the blood vessel.

2. A method according to claim 1, wherein step (f) comprises determining a relative difference between a maximum value of $E^{(k)}$ and a maximum value of $E^{(k-1)}$ and comparing the relative difference to a predetermine relative error threshold.

3. A method according to claim 1 or claim 2, wherein providing a structural model comprises the steps of:
   providing a segmented image of the blood vessel;
   obtaining contour data for the segmented image; and
   using the contour data to generate the structural model.

4. A method according to claim 3, wherein the segmented image is obtained according to an imaging technique.

5. A method according to claim 4, wherein the imaging technique is magnetic resonance imaging (MRI), computed tomography (CT) or ultrasound.

6. A method according to claim 3 or claim 5, wherein, in step (b), pressure p is measured at the time at which the segmented image is provided.

7. A method according to claim 3 or claim 5, wherein, in step (b), pressure p is measured as a systolic or diastolic mean blood pressure.

8. A method according to any preceding claim, wherein the blood vessel is an artery or vein.

9. A system for determining an unpressurised configuration of a blood vessel, the system comprising a processor, the processor being configured to:

(a) provide a configuration model $S^{(k=1)}$ of the blood vessel comprising a mesh of N nodes;
(b) apply a pressure p to the configuration model $S^{(k)}$ to obtain a pressurised configuration model $D^{(k)}$;
(c) determine a deformation gradient $F^{(k)}$, wherein $D^{(k)} = F(S^{(k)})$;
(d) for each node, calculate a displacement $E^{(k)}$ representing the difference between the pressurised configuration model $D^{(k)}$ and the configuration model S at the each node;
(e) calculate an updated configuration model $S^{(k+1)} = D^{(k)} - F^{-1(k)} \odot E^{(k)}$, wherein $F^{-1(k)}$ is the inverse of the deformation gradient and $\odot$ is an elementwise product;
(f) if a maximum value of $E^{(k)}$ is less than a predetermined error threshold, repeat steps (b) to (e), wherein k=k+1; else output $S^{(k)}$ as the unpressurised configuration of the blood vessel.

10. A system according to claim 9, further comprising an imaging module configured to:
provide a segmented image of the blood vessel;
obtain contour data for the segmented image; and

use the contour data to generate the structural model.

11. A system according to claim 10, wherein the imaging module is a magnetic resonance imaging (MRI) module, computed tomography (CT) module or ultrasound module.

12. A system according to claim 10 or claim 11, the system further comprising means to measure the pressure p at the time at which the segmented image is provided.

13. A system according to claim 10 or claim 11, the system further comprising means to measure the pressure p as a systolic or diastolic mean blood pressure.

14. A system according to any of claims 10 to 13, wherein the blood vessel is an artery or vein.

Intellectual Property Office

Application No:	GB1901132.9	**Examiner:**	Mr Iwan Thomas
Claims searched:	1-14	**Date of search:**	3 December 2019

Patents Act 1977: Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
X	1-14	Peirlinck M., "A modular inverse elastostatics approach to resolve the pressure-induced stress state for in vivo imaging based on cardiovascular modeling", 2018, Journal of the Mechanical Behavior of Biomedical Materials, vol 85, pages 124-133 See especially first to thirteenth line of the second full paragraph of page 131
X	1-14	Raghavan M. L., "Non-Invasive Determination of Zero-Pressure Geometry of Arterial Aneurysms", 2006, Annals of Biomedical Engineering, vol. 34, pages 1414-1419 See whole document
X	1-14	Sellier M., "An iterative method for the inverse elasto-static problem", 2011, Journal of Fluids and Structures, vol. 27, pages 1461-1470 See whole document

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
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Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^{X} :

Worldwide search of patent documents classified in the following areas of the IPC

G06T

The following online and other databases have been used in the preparation of this search report

WPI, EPODOC, INSPEC

International Classification:

Subclass	Subgroup	Valid From
G06T	0019/00	01/01/2011