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A NUMERICAL AND 3D PRINTING FRAMEWORK FOR THE IN VIVO MECHANICAL ASSESSMENT OF PATIENT-SPECIFIC CARDIOVASCULAR STRUCTURES

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Abstract. Computational simulations represent a powerful tool for the pre-procedural clinical assessment of minimally invasive cardiovascular interventions. Patient-specific simulations rely on the accurate numerical implementation of both geometrical and mechanical features. While current imaging techniques are able to depict accurately patient-specific anatomies, at date, a similar image-based tool capable to retrieve subject-specific material properties is missing. The scope of this study is to present a framework, involving *in silico* tools and 3D printing, for the refinement of an image-based technique capable to retrieve *in vivo* patient-specific mechanical information from functional and morphological magnetic resonance imaging (MRI) data. The workflow consists in different steps: (i) selection and mechanical testing of 3D commercially available deformable 3D printed materials; (ii) fluid-structure interaction (FSI) simulation of a vessel model under pulsatile regime; (iii) elaboration of *in silico* results and calibration of the image-based method; (iv) 3D printing of the model and experimental replica in MRI environment; (v) finally, the image-based technique is applied to MRI data (iv) to retrieve material information to compare to reference (i). The described workflow strategy was successfully implemented by our group. The deformable material TangBlackPlus FLX980 (TangoPlus) was selected and mechanically tested, resulting in an elastic module (E) of 0.50$\pm$0.02 MPa (n = 5). FSI simulations of a simplified vessel were carried out with different E values (from 0.5 to 32 MPa). *In silico*, the indirect material evaluation resulted, after the calibration, in a good

matching between inputted E values and estimated ones, leading to a percentage difference of $7.8 \pm 4.1\%$ ($n = 12$). The simulated vessel was 3D printed with TangoPlus and acquired in terms of MRI data. The application of the proposed image-based method resulted in a E value of the phantom of $E = 0.54$ MPa, very close to the one directly assessed via tensile tests (0.5 MPa). Although very good results were achieved in this study, other deformable materials and shapes will be investigated by using the described framework. With further refinements, this strategy would lead to an indirect and image-based tool for the *in vivo* assessment of patient-specific material properties, thus enhancing the confidence of patient-specific computational models.

1 INTRODUCTION

Patient-specific computational modeling represent a powerful and promising tool for the simulation of minimally invasive cardiovascular procedures in a clinical pre-planning scenario [1]. However, the use of computational methods in clinics is still scarce and limited [2]. The challenges consist in a faithful adaptation of computational models into the patient-specific clinical conditions [3].

Simulation of such interventions requires specific information on both the patient's implantation site and the device. While this latter is fully known, both for geometrical and mechanical features, accurate data of patient are available only for the anatomy, easily retrievable from current imaging techniques. In fact, actual limitation of cardiovascular computational modeling is represented by the patient-specific material properties which are lacking. This lack of information introduce approximations of the mechanical modelling [4] of patients cardiovascular structures. Enhanced material information, which include patient-specific information, would certainly improve the accuracy of the numerical results, thus favoring the use of computational tools in the daily clinical practice.

In this study we tested a framework involving 3D printing facilities and *in silico* tests for the calibration of a novel technique for the image-based extraction of mechanical information of compliant materials. The feasibility of the presented framework was proven on one material, showing excellent agreement between direct and indirect mechanical assessment. With further refinement, including the testing on different materials and more complex geometries, the proposed method could be applied on *in vivo* imaging data for the assessment of patient-specific material information.

2 MATERIAL AND METHODS

The framework we described in this section aims to predict the elastic modulus of materials based on an indirect and non-invasive method.

The entire workflow of this research consists in the following steps:

1. Selection of a compliant material available on the market of additive manufacturing and its mechanical testing.

2. Fluid-structure interaction (FSI) simulations of a vessel-shaped model subjected to pul-

satile conditions. A wide range of elastic moduli was used as input (E_{INP}) for the mechanical description of the vessel's wall.

3. Post-processing results of the simulations are used to calibrate the QA-based formulation for inferring the E values used in the simulations (E_{OUT}).

4. 3D printing of the vessel model with the selected material and an *in vitro* replica of the simulation; this step includes a phase contrast magnetic resonance imaging (PC MRI) acquisition of the phantom.

5. Segmentation of the PC MRI dataset and application of the proposed image-based method to infer the E value of the material, which is compared to the one directly assessed in step (1) with mechanical tests.

In this work we demonstrated the feasibility of the described framework for one material and shape. A scheme of the described workflow is shown in Fig. 1.

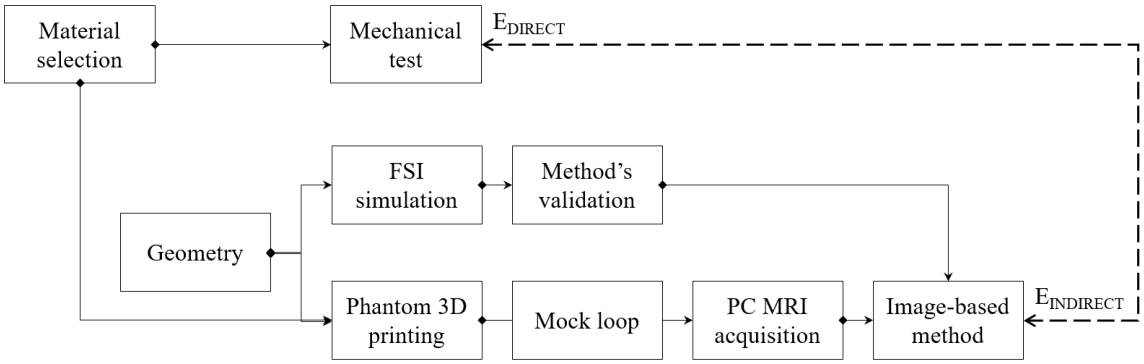

Figure 1: Representative scheme of the described workflow.

2.1 QA-based method

The formulation we propose in this work is based on the flow-area (QA) method and on equations available in literature. The QA method is an image-based technique, first used on MRI data [5] and then on ultrasound images [6], for the assessment of the pulse wave velocity (PWV), which is considered a good surrogate of the arterial stiffness [7, 8]. According to this method, the relationship during the early systolic period between the cross-sectional area of a blood vessel and the passing flow can be approximated as a first-order linear equation. The PWV can be defined as the slope of such linear portion:

$$PWV = \frac{dQ}{dA} \tag{1}$$

where dQ is the incremental variation of the passing flow and dA is the incremental variation of the cross-sectional area of the vessel.

Laurent et al. [9] proposed a formulation for the estimation of the E value of the vessel's wall based on the distensibility compliance (DC) and some geometrical parameters:

$$E_{DC} = \frac{3\left(1+\frac{A_0}{WCSA}\right)}{DC} \tag{2}$$

where A_0 is the cross-sectional area of the vessel, $WCSA$ is the wall cross-sectional area, both evaluated at diastole. Usually the DC value is evaluated by coupling area and pressure information at diastole and systole.

To overcome the use of pressure, which is an invasive measure and moreover not available for all the patients, we considered the inverted Bramwell-Hill equation [10] for the definition of the DC value:

$$DC = \frac{1}{\rho\, PWV^2} \tag{3}$$

where the density of the fluid flowing through the section is ρ.

In our study we defined the following PWV-based equation for the estimation of E value (E_{OUT}):

$$E_{OUT} = k\left(3\,\rho\, PWV^2\left(1+\frac{A_0}{WCSA}\right)\right) \tag{4}$$

Eq. 4 derives by combining Eq. 2 and 3 and it allows the estimation of the E value of a vessel's wall based on the PWV, which can be easily calculated by means of the QA method. The k parameter is a correction factor introduced for a more reliable estimation of the E values.

2.2 Material selection and mechanical testing

For this feasibility study, we selected one deformable material available in the market of additive manufacturing. The chosen material was TangoBlackPlus FLX980 (TangoPlus) which was tested via uniaxial tensile tests. Five dogbone-shaped specimens were 3D printed with an Object500 Connex machine (Stratasys, Minnesota, USA). The samples were mechanically tested with a custom-made tensile machine [11] to retrieve the E value of the 3D printed TangoPlus material. The E value obtained from tensile tests (E_{tt}) was considered as ground of truth and compared to the E value estimated from the MRI experiment (E_{MRI}).

2.3 *In silico* campaign

A vessel model under cardiac-like pulsatile conditions was implemented by using the software LS-DYNA R.10 (LSTC, Livermore, USA). For this study of feasibility, the geometry of the vessel was drawn as cylindrical, with a length of 150 mm, an in internal diameter of 12.7 mm and a thickness of 2 mm. The wall was modelled as isotropic and linear elastic. A total of twelve simulations were carried out with different E_{INP} values for the vessel's wall, ranging from 0.50 MPa to 32 MPa, with an oversampling in the region close to 1 MPa (Fig. 2). The fluid domain was modelled as an incompressible and non-Newtonian fluid with a density of 998

kg/m^3 and a dynamic viscosity of 0.001 kg m^{-1} s^{-1}. Periodic boundary conditions were set up to impose velocity at the inlet and pressure at the outlet. Four cardiac cycles were simulated. A time step of 0.01 s was used.

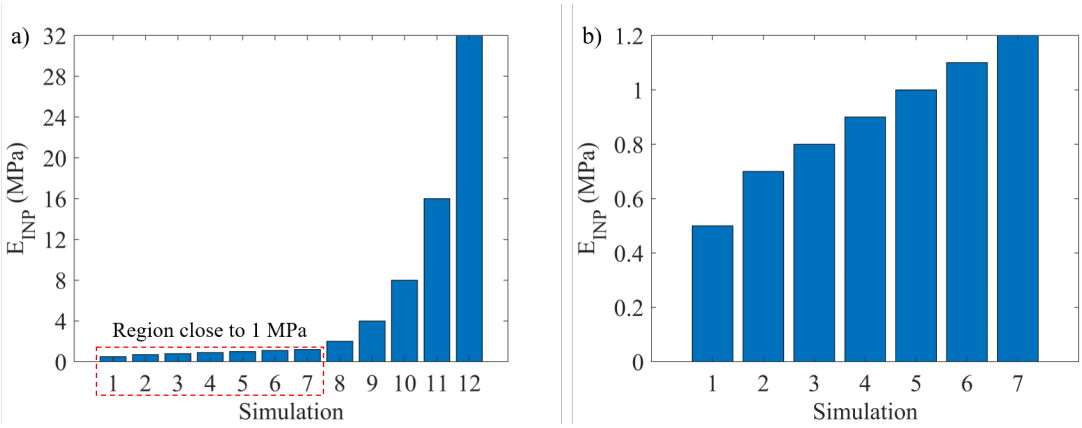

Figure 2: (a) E_{INP} values used in the simulations; (b) zoom of the E_{INP} in the region of 1 MPa.

The twelve simulations were elaborated with the proposed QA-based technique. The last cardiac cycle was considered for analysis. Flow and area information along time were extracted in the middle cross-section of the numerical models using ParaView (https://www.paraview.org/). At this stage, the k parameter was determined with an iterative process until (E_{OUT}) matched (E_{INP}).

2.4 MRI experiment

The simulation was replicated *in vitro*. The vessel model was 3D printed with TangoPlus and inserted in an ad-hoc mock circulation circuit providing a pultatile regime (Fig. 3). Cardiac-like conditions were provided by a Harvard apparatus pulsatile blood pump (Harvard apparatus, Massachussets, USA). Similar flow and pressure conditions were imposed by tuning the action of the pump and adjusting the passive elements of the system in terms or compliance (C) and resistance (R).

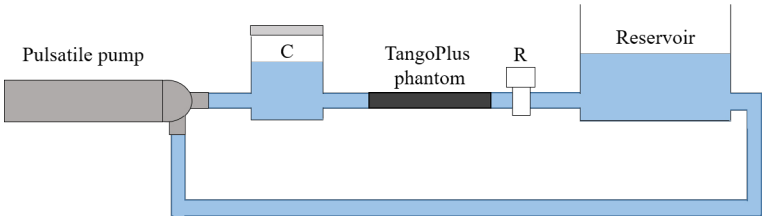

Figure 3: Scheme of the mock loop built for the MRI experiment.

Finally, the circuit was positioned in MRI environment to acquire PC images of the phantom in the middle cross-section. The acquisition resulted in 40 frames along the cardiac cycle.

Images were segmented using Segment v2.0 (http://segment.heiberg.se) [12] to obtain area and flow values for all the frames. The proposed QA-based method was applied and the E_{MRI} value of the phantom was calculated by using Eq. (5) with the k value obtained from the *in silico* analysis.

3 RESULTS

3.1 Tensile tests

Uniaxial tensile tests were successful for all the specimens. The mechanical tests were conducted until the rupture of the sample. The stress-strain curves obtained from the tests were linearly fitted (Fig. 4) to get the E_{tt} value, which resulted to be 0.50±0.02 MPa (n = 5).

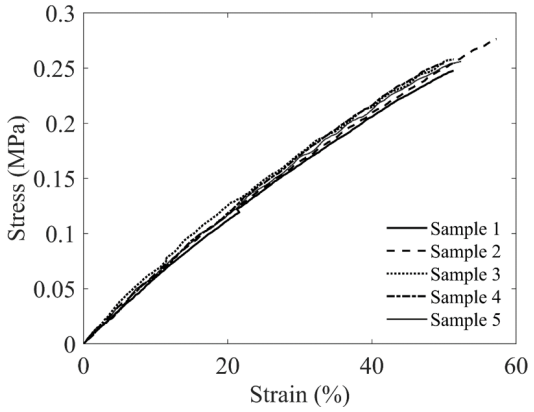

Figure 4: Stress-strain curves from uniaxial tensile tests of the five 3D printed TangoPlus specimens.

3.2 *In silico* outcomes

The twelve FSI simulations with different E_{INP} values reached successfully the convergence. The iterative tuning of the k parameter led to the following definition:

$$k = c\,RAC \tag{5}$$

where RAC is the relative area change expressed as:

$$RAC = \frac{A_{max} - A_0}{A_0} \tag{6}$$

and c is a constant parameter which was defined for each simulation as:

$$c = \frac{E_{INP}}{RAC\,E_{PWV}} \tag{7}$$

The c value, as obtained from Eq. 7 resulted equal to 12.6949±1.1210 (n = 12). The mean value of c ($\bar{c}$ = 12.6949) was used in Eq. 4 to obtain the estimation (E_{OUT}) of the E_{INP} values used in the simulations. The E_{OUT} values well replicated the E_{INP} values, with a mean error of 7.8±4.1% (n = 12). Fig. 5 shows how the inclusion of the $\bar{c}\,RAC$ factor hugely reduces the non-linearity between E_{OUT} and the E_{INP} values in respect to using k = 1.

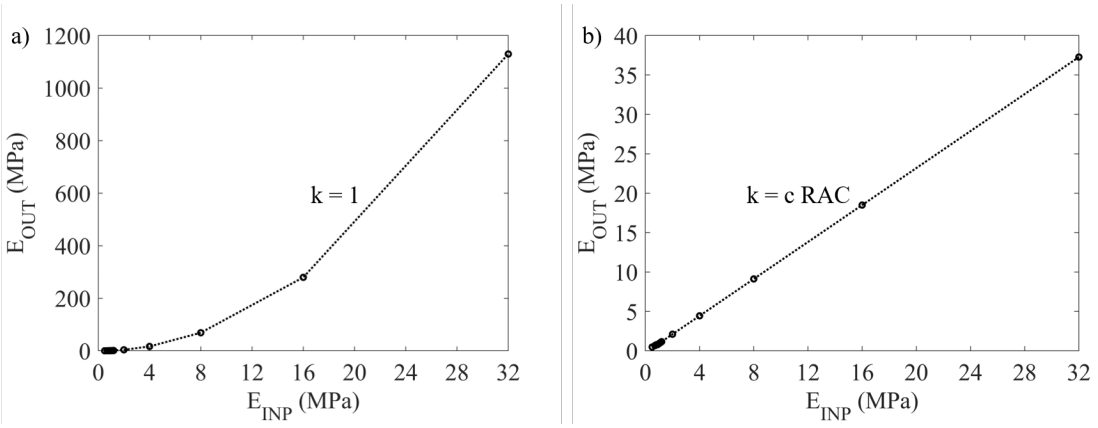

Figure 5: Relationship between E_{OUT} and E_{INP} with k = 1 (a) and k = *c RAC* (b).

3.3 Experimental results

The application of the presented QA-based method was feasible on the acquired PC images. The *PWV*, calculated as stated in Eq. 1, was found to be 5.57 m s^{-1}. Calculation of the E_{OUT} with k = 1 resulted in 0.21 MPa, which, accordingly to the equivalent *in silico* case, underestimates the real E value of the material (E_{tt} = 0.50 MPa). While the application of the found k factor (Eq. 5) led to an E_{MRI} value of 0.54 MPa, with a percentage difference of 8% in respect to the direct estimation.

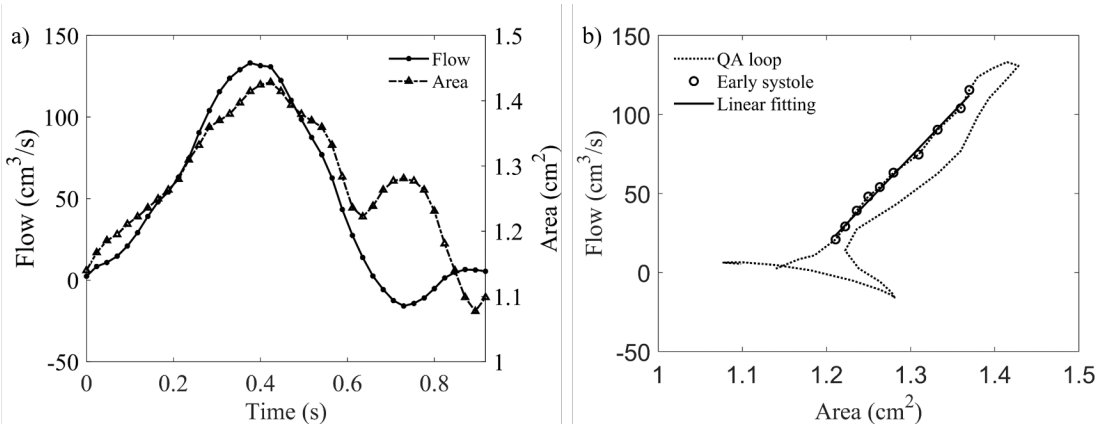

Figure 6: Segmentation results of PC MRI dataset (left) and resulted QA loop (right).

4 DISCUSSION

In this work we presented a proof of concept of a framework able to infer the E value of materials based on PC MRI data. The framework relies on a empirically modified equation based on the QA method. We first tested the proposed formulation in a controlled *in silico* environment taking advantage of the knowing of the E values implemented in the simulations.

This allowed the determination of the c value present in the definition of the k factor (Eq. 5). In fact, while the *RAC* parameter seems to have the role of adjusting the linearity between the inferred E and the reference (Fig. 5), a constant value (i.e. the c value), which may be considered the same for all the stiffnesses, is necessary for a correct matching of the E values. However, the predictive capability of the presented technique was confirmed *in vitro*, where a very good matching between the real E value of the 3D printed material and the image-based one was found (8%).

Although very promising results were achieved, this work represents a study of feasibility of a framework which was experimentally tested just for one material and one geometry. Future works will surely include the analysis of other 3D printed materials, such as Agilus30 (Stratasys, Minnesota, USA) and Elastic and Flexible resins (Formlabs, Massachusetts, USA), as well as different and more complex geometries, starting from different sized pipes to patient-specific anatomies. In fact, with further refinements, this technique would be able to assess an estimation of the patient-specific implantation site material properties, useful for a more reliable implementation of the mechanical response of the vessel's wall against the expansion of a device.

5 CONCLUSIONS

In this study, we demonstrated the feasibility of a framework involving additive manufacturing and *in silico* simulations for the non-invasive assessment of the E value of deformable materials. While computational modeling allowed us to refine the methodology in a controlled space, with 3D printing we were able to test the developed formulation with a ad-hoc MRI experiment and to compare the outcomes against the results from tensile tests, which are for obvious reasons impracticable for *in vivo* tissues. The proposed image-based method showed promising results. Future works will focus on the exploration of other *in silico* and *in vitro* scenarios with the main aim to apply this technique on *in vivo* patient-specific imaging data. This would reduce the gap between numerical and clinical world, thus enhancing the efficacy of the intervention procedures and the healthcare of patients.

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