ORIGINAL ARTICLE

Accurate quantifcation of blood fow wall shear stress using simulation‑based imaging: a synthetic, comparative study

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Received: 29 September 2021 / Accepted: 6 June 2022 / Published online: 10 August 2022 © The Author(s) 2022

Abstract

Simulation-based imaging (SBI) is a blood fow imaging technique that optimally fts a computational fuid dynamics (CFD) simulation to low-resolution, noisy magnetic resonance (MR) fow data to produce a high-resolution velocity feld. In this work, we study the efectivity of SBI in predicting wall shear stress (WSS) relative to standard magnetic resonance imaging (MRI) postprocessing techniques using two synthetic numerical experiments: steady fow through an idealized, two-dimensional stenotic vessel and a model of an adult aorta. In particular, we study the sensitivity of these two approaches with respect to the Reynolds number of the underlying fow, the resolution of the MRI data, and the noise in the MRI data. We found that the SBI WSS reconstruction: (1) is insensitive to Reynolds number over the range considered (Re \leq 1000), (2) improves as the amount of MRI data increases and provides accurate reconstructions with as little as three MRI voxels per diameter, and (3) degrades linearly as the noise in the data increases with a slope determined by the resolution of the MRI data. We also consider the sensitivity of SBI to the resolution of the CFD mesh and found there is fexibility in the mesh used for SBI, although the WSS reconstruction becomes more sensitive to other parameters, particularly the resolution of the MRI data, for coarser meshes. This indicates a fundamental trade-off between scan time (i.e., MRI data quality and resolution) and reconstruction time using SBI, which is inherently different than the trade-off between scan time and reconstruction quality observed in standard MRI postprocessing techniques.

Keywords Simulation-based imaging · Magnetic resonance imaging · Wall shear stress · Congenital heart disease

1 Background

Magnetic resonance imaging (MRI) is a powerful method to investigate cardiovascular physiology. High-resolution in vivo images can help understand patient-specifc blood flow and provide important quantitative biomarkers such as wall shear stress (WSS). However, these methods are limited by a fundamental trade-off between scan time, resolution, and noise $[1, 2]$ $[1, 2]$ $[1, 2]$ $[1, 2]$ $[1, 2]$, which limits their utility for applications that demand very high-resolution images, such as infants and children, with congenital heart disease [\[3](#page-15-2)]. This is further complicated when estimates of biomarkers must be extracted from these fow images with poorly resolved features. This motivates the need for imaging methods that can use sparse, noisy data to provide sufficiently high-resolution reconstructions that can be used to accurately compute quantitative biomarkers.

Recent advances in compressed sensing [[4](#page-15-3)–[7\]](#page-15-4) and machine learning $[8, 9]$ $[8, 9]$ $[8, 9]$ $[8, 9]$ have been used to enhance MRIbased flow reconstructions, leading to improved image quality and reduced scan times. Neural networks have proven efective in taking sparse or missing data in k-space and accurately reconstructing them into natural images. Machine learning approaches are valuable, but face drawbacks of high training cost and not being patient-specifc. However, recent work on physics-informed neural networks (PINNs) applied to hemodynamics have shown promise in one-dimensional pulsatile fows [[10\]](#page-15-7) and two- and three-dimensional steady flows [[11](#page-15-8)]. Several simulation-based imaging (SBI) methods [\[12](#page-15-9)[–18](#page-15-10)] exist that match a computational fuid dynamics (CFD) simulation to magnetic resonance (MR) flow data by optimizing free parameters of the CFD simulation (usually

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boundary and initial conditions), use a metric to measure the difference between CFD and MR flow imaging, and update the free parameters to minimize the cost function via their own strategy. The method used in this work [[18\]](#page-15-10) uses a high-order CFD discretization, efficient adjoint-based PDE-constrained optimization, and a novel objective function that mimics the point-spread function of MRI scanners. This method was shown to efectively reconstruct very highresolution velocity felds from limited MRI data and match ground truth values for both a controlled water tank experiment and an in vivo clinical application. However, the quality to which the method predicts quantitative biomarkers has not been considered to date, nor has there been a detailed investigation into the sensitivity of the method to physiological and imaging parameters (e.g., noise, resolution) due to the computational cost of the reconstruction and difficulty of obtaining a reliable reference solution.

In this paper, we study the accuracy to which an SBI approach [[18](#page-15-10)] predicts the WSS distribution relative to standard MRI postprocessing approaches using two synthetic numerical experiments. The two synthetic experiments employ several unrealistic assumptions to simplify the problem (steady, two-dimensional, laminar flow of a Newtonian fuid), assume full knowledge of the vessel geometry, and extract MRI data from a CFD simulation via weighted averaging of the velocity feld over MRI voxels. These simplifcations keep the computational cost of SBI manageable to allow for detailed sensitivity analysis (requiring hundreds of reconstructions), a well-defned reference solution, and a fair side-by-side comparison of SBI and MRI (both of which beneft from these assumptions) with respect to WSS prediction.

We focus on WSS because it is known to correlate to atherosclerosis, the formation and rupture aneurysms, as well as numerous congenital heart diseases [\[19–](#page-15-11)[28\]](#page-15-12). Furthermore, it has proven difficult to estimate directly using standard MRI postprocessing techniques [\[29](#page-15-13)–[31\]](#page-16-0) because WSS requires accurate estimation of the velocity gradient that can be difficult using only piecewise constant voxel data. Current methods for postprocessing MR fow data to obtain quantities of interest, e.g., phase-contrast (PC) MRI velocity mapping, Fourier velocity encoding (FVE), and intravoxel velocity standard deviation mapping [[32–](#page-16-1)[34](#page-16-2)], can be unreliable.

We study the impact of the Reynolds number of the underlying fow and the resolution and noise of the MRI data to understand the sensitivity of each method with respect to these critical parameters. Noise is a critical source of error for in vivo imaging and extraction of biomarkers [[35\]](#page-16-3) and becomes increasingly problematic as the resolution of the MRI grid increases or if faster scans are required, e.g. for sedated children or to reduce costs of health care. On the other hand, the resolution of the MRI data can lead to higher-resolution images and more accurate biomarker computations; however, it is usually accompanied with increased noise and requires longer scans. The Reynolds number is studied because it has been observed that the accuracy of the WSS computed directly from MRI data decreases as the Reynolds number of the flow increases [[33](#page-16-4)]. Furthermore, we study the impact of the resolution of the CFD mesh used in SBI because this determines the overall cost of the reconstruction.

2 Methods

Two synthetic numerical experiments were conducted to compare the accuracy of MRI methods with SBI in measuring wall shear stress. To perform comprehensive studies, SBI was simplifed for use in two-dimensional, time-independent problems, instead of three-dimensional, unsteady problems as in our previous study [\[18](#page-15-10)]. The experiments are synthetic in the sense that no in vivo MRI flow data or geometries were used; synthetic data were constructed to be representative of a realistic situation and consistent with in vivo measurements to the extent possible, e.g., regarding noise levels, MRI resolution, and extraction of MRI data from a velocity feld. The synthetic experiments allow for a highly controlled study with a known reference ("truth") flow so the impact of various parameters, e.g., Reynolds number, noise, MRI grid resolution, on WSS reconstruction accuracy can be isolated and identifed. The remainder of this section will describe the numerical experiments in detail. Section [2.1](#page-1-0) introduces the setup of the synthetic experiments, Sect. [2.2](#page-3-0) details the creation of synthetic phase-contrast MRI data and WSS reconstruction, and Sect. [2.3](#page-6-0) reviews the SBI method and corresponding WSS computation.

2.1 Synthetic experiments

We use two synthetic experiments to investigate the accuracy of WSS measurements from SBI relative to standard MRI methods: 1) flow through an idealized stenotic vessel and 2) flow through an idealized aorta with a coarctation. The geometry of the stenotic vessel with 60% grade is the set $\Omega \subset \mathbb{R}^d$ (*d* = 2 in this work; formulas not pertaining to domain geometries hold for general *d*), defned as

$$
\Omega := \{ (x, \pm y(x)) \mid x \in [0, 6] \}, \quad y: x \mapsto B_0 - \frac{A}{\sqrt{2\pi\sigma^2}} \exp\left(\frac{(x - c)^2}{2\sigma^2}\right) \tag{1}
$$

where $B_0 = 0.3$ cm, $c = 3$ cm, $\sigma = 0.6$ cm, $A = 0.18$ cm² (Fig. [1](#page-2-0)). The geometry of the coarctated aorta (40% grade) is shown in Fig. [1](#page-2-0). In practice, these geometries would be obtained from MRI scans; however, we chose to explicitly defne the geometry to ensure a controlled setting in which to study WSS reconstruction. Most of the studies in this work

Fig. 1 Idealized stenotic vessel with 60% grade (left) and coarctated aorta with 40% grade (right) geometry $Ω$ used for numerical experiments with boundaries: $\partial \Omega_w$ (continuous black line), $\partial \Omega_{in}$ (continuous

are conducted using the vessel due to its simplicity; the aorta is used to confrm our fndings on a more realistic geometry.

The blood flow is modeled as an incompressible, Newtonian fuid governed by the Navier–Stokes equations

$$
\frac{\partial v}{\partial t} + (v \cdot \nabla)v - v \nabla^2 v + \frac{1}{\rho_0} \nabla P = 0, \quad \nabla \cdot v = 0 \quad \text{in } \Omega, \tag{2}
$$

where $\rho_0 \in \mathbb{R}_{>0}$ is the density of the fluid, $v \in \mathbb{R}_{>0}$ is the kinematic viscosity of the fluid, and $v : \Omega \to \mathbb{R}^d$ and *P* : $\Omega \to \mathbb{R}_{>0}$ are the velocity and pressure, respectively, of the fuid implicitly defned as the solution of [\(2\)](#page-2-1). In this work, we assume the fuid is blood and take the material properties to be $\rho_0 = 1060 \text{ kg/m}^3$ [\[36](#page-16-5)] and $v = 2.83 \times 10^{-6}$ m^2 /s [[37\]](#page-16-6) for both test cases. We consider the case where the flow has reached a steady state and the time derivative, $\frac{\partial v}{\partial t}$, vanishes. Boundary conditions for the boundaries identifed in Fig. [1](#page-2-0) are

$$
v = 0
$$
 on $\partial \Omega_w$, $v = v_{in}$ on $\partial \Omega_{in}$, $\sigma \cdot n = 0$ on $\partial \Omega_{out}$
(3)

where v_{in} : $x \mapsto \bar{v}_{\text{in}}(B_0^2 - x_2^2)/B_0^2$ is the parabolic inlet profile with peak value $\bar{v}_{in} \in \mathbb{R}^d$ (for the stenotic vessel) and $n: \partial\Omega \to \mathbb{R}^d$ is the outward unit normal to the boundary of the domain. The rate-of-strain, $\epsilon : \Omega \to \mathbb{R}^{d \times d}$, and stress, σ : $\Omega \rightarrow \mathbb{R}^{d \times d}$, tensors are defined as

blue line), $\partial \Omega_{\text{out}}$ (continuous red line). The MRI scan region for each geometry is indicated with (dashed pink line). Units: cm

$$
\epsilon = \frac{1}{2} (\nabla v + \nabla v^T), \qquad \sigma = 2\mu \epsilon + P I_d,
$$
\n(4)

where $\mu = \rho_0 v$ is the dynamic viscosity and I_d is the $d \times d$ identity matrix. The Reynolds number, $Re \in \mathbb{R}_{>0}$, of the flow is defined based on the full cross-sectional diameter of the geometry, $D \in \mathbb{R}_{>0}$, and the peak inlet velocity as $\text{Re} = \frac{D\|\bar{v}_{in}\|}{v}$. The WSS, σ^{wss} : $\partial\Omega \to \mathbb{R}$, the quantitative biomarker considered in this work, is defned as the magnitude of the tangential component of the surface traction [[38\]](#page-16-7)

$$
t = \sigma \cdot n,
$$
 $\tau = t - (t \cdot n)n,$ $\sigma^{\text{wss}} = ||\tau||,$ (5)

where $t : \partial \Omega \to \mathbb{R}^d$ is the surface traction and $\tau : \partial \Omega \to \mathbb{R}^d$ is its tangential component.

The Navier–Stokes equations are approximated using the fnite element method on an unstructured triangular mesh consisting of $\mathcal{P}^3 - \mathcal{P}^2$ Taylor–Hood elements implemented in an in-house software [\[39](#page-16-8)]. A linear mesh (straight-sided triangles) is generated using DistMesh [[40\]](#page-16-9) and the boundary edges are projected onto the exact geometry (and interior nodes smoothed) for a high-order representation. Let v_h denote the finite element solution of the Navier–Stokes equations. This CFD solution defines our reference or "truth" flow, e.g., corresponding to the in vivo flow, which is not available in practice, but essential to conduct thorough inquiries. The reference or "truth" value for WSS is computed from [\(5\)](#page-2-2) using the finite element solution v_h ;

Fig. 2 Computational mesh (**a**) and corresponding velocity feld (**b**) used to define the true flow (v_h) through the stenotic vessel $(Re = 1000)$. The velocity field is mapped to the MR data space $(\Xi_i(\nu_h))$ to produce the noise-free MRI data (c); the MRI grid contains $N = 9$ VPD. The Gaussian noise model with standard deviation

equal to $\kappa = 20\%$ of the peak velocity is added to the noise-free MRI data to produce the actual MRI data (\bar{v}_i) (**d**). Simulation-based imaging is used to reconstruct the velocity feld from the noisy MRI data, which leads to the field $(v_H(\cdot;\theta^*))$ (**e**) and corresponding representation in the MR data space $(\Xi_i(\nu_H(\cdot;\theta^*))$ (f). Colorbar: $||\nu||$ (cm/s)

the pointwise velocity and necessary derivatives are readily available from the fnite element basis functions. The reference WSS value computed from the reference fnite element solution v_h is denoted σ_h^{wss} . Figures [2](#page-3-1) and [3](#page-4-0) show the computational mesh and corresponding velocity feld $(Re = 1000)$ used to define the true flow for the stenosis and aorta test cases, respectively. The corresponding WSS (σ_h^{wss}) is shown in Fig. [4](#page-5-0) for both test cases. Synthetic MRI data are extracted from the reference solution v_h and perturbed with noise using the approach in [[18\]](#page-15-10) (summarized in Sect. [2.2](#page-3-0)). In Sect. [3](#page-6-1), we will use this synthetic MRI data to reconstruct the WSS using standard MRI techniques (Sect. [2.2](#page-3-0)) and SBI (Sect. [2.3](#page-6-0)) to study the accuracy and sensitivity of each app roach.

2.2 Magnetic resonance imaging

Phase-contrast MRI scans extract velocities averaged over a Cartesian grid of voxels from an in vivo fow. The resolution of the voxel grid determines both the resolution and noise of the velocity data $[1, 2]$ $[1, 2]$ $[1, 2]$. In blood flow imaging, the resolution is reported in millimeters, but an important metric for fow accuracy is the number of voxels per diameter (VPD) [\[41](#page-16-10)], which can range from 5 to 20 VPD for adults [[42\]](#page-16-11) and 3–5 VPD for infants [[43,](#page-16-12) [44\]](#page-16-13). Furthermore, the number of VPD can vary for diferent vascular territories [\[45](#page-16-14)].

In the synthetic setting, we compute synthetic data consistent with the approach in $[18]$ $[18]$ $[18]$, specialized to the case of steady fow, i.e., a weighted integral of the true velocity

feld over a given voxel and its neighbors. For simplicity, we assume the voxel grid is aligned with the coordinate axes. We consider a grid consisting of N_r voxels in the x_1 -direction and *N_y* voxels in the *x*₂-direction and let $\Delta x, \Delta y \in \mathbb{R}_{>0}$ denote the spacing of the voxel grid in the respective direction. We endow the $N = N_x N_y$ voxels with an ordering and let $(X_i, Y_i) \in \mathbb{R}^2$ denote the centroid of the *i*th voxel for *i* = 1, …, *N*. We leverage an abuse of notation to let *N* denote the resolution of the voxel grid, either stated in terms of the total number of voxels (N_rN_v) or the number of VPD, depending on the context. With this notation, the synthetic MR flow velocity data associated with the *i*th voxel, $\bar{v}_i \in \mathbb{R}^2$, is extracted from a CFD simulation as

$$
\bar{\nu}_i := \Xi_i(\nu_h) + \varphi_i,\tag{6}
$$

where φ _{*i*} is a normally distributed random variable with mean 0 and standard deviation proportional to the peak fow velocity, i.e., $\kappa \sup_{x \in \Omega} v_h(x)$ with noise level $\kappa \in \mathbb{R}_{\geq 0}$, and $\varphi_1, \ldots, \varphi_N$ are independent and identically distributed [[46,](#page-16-15) [47](#page-16-16)]. This ensures that the noise is randomly sampled and is relative to the peak velocity of the true fow to model the efect of the velocity encoding parameter (VENC) used in 4D fow acquisition. The velocity standard deviation due to noise is proportional to VENC [[48](#page-16-17)], and the VENC is commonly set to be slightly larger than the highest velocity encountered in the region of interest to avoid aliasing (phase wrap-around). Following the approach in $[18]$, the pointspread function maps a continuous velocity feld to the MR

Fig. 3 Computational mesh (**a**) and corresponding velocity feld (**b**) used to defne the true flow (v_h) through the aorta $(Re = 1000)$. The velocity field is mapped to the MR data space $(\Xi_i(\nu_h))$ to produce the noisefree MRI data (**c**); the MRI grid contains $N = 10$ VPD. The Gaussian noise model with standard deviation equal to $\kappa = 20\%$ of the peak velocity is added to the noise-free MRI data to produce the actual MRI data (\bar{v}_i) (**d**). Simulation-based imaging is used to reconstruct the velocity feld from the noisy MRI data, which leads to the field $(v_H(\cdot;\theta^{\star}))$ (**e**) and corresponding representation in the MR data space $(\Xi_i(\nu_H(\cdot;\theta^{\star})))$ (**f**). Colorbar: ‖*v*‖ (cm/s)

data space through a weighted average of the velocity feld over a given voxel as

$$
\Xi_i: u \mapsto \int_{\Omega} w_i u \, \mathrm{d}v \tag{7}
$$

for $i = 1, \ldots, N$. The weighting function for the *i*th voxel, $w_i : \Omega \to \mathbb{R}$, is the normalized tensor product of a sinc function with a smoothed box centered at (X_i, Y_i) , i.e.,

$$
w_i: x \mapsto \bar{w}_i(x) \bigg(\int_{\Omega} \bar{w}_i \, d\nu \bigg)^{-1},
$$

\n
$$
\bar{w}_i: x \mapsto \Psi(x_1, X_i, \Delta x) \Psi(x_2, Y_i, \Delta y),
$$
\n(8)

where the component-wise, non-normalized weighting function, $\Psi : \mathbb{R} \times \mathbb{R} \times \mathbb{R}_{>0} \to \mathbb{R}$, is defined as

$$
\Psi : (s, c, \Delta s) \mapsto \text{sinc}\left(\frac{s-c}{\Delta s}\right) \chi(s, c, 4\Delta s). \tag{9}
$$

The sinc function is included to mimic the point-spread function of MRI scanners that use a Fourier transform to map raw MRI data into flow velocities $[18, 49]$ $[18, 49]$ $[18, 49]$ $[18, 49]$. The onedimensional smoothed box function, $\chi : \mathbb{R} \times \mathbb{R} \times \mathbb{R}_{>0} \to \mathbb{R}$, is defned as

$$
\chi: (s, s_0, \omega) \mapsto \frac{1}{1 + \exp(-(s - (s_0 - \omega/2))/\gamma)}
$$

-
$$
\frac{1}{1 + \exp(-(s - (s_0 + \omega/2))/\gamma)}
$$
(10)

with center s_0 , width ω , and smoothness parameter γ . The smoothed box function localizes the integrand in ([7](#page-4-1)) to the center of a particular voxel, allowing for some overlap between voxels, and ensures the integrand is sufficiently smooth for the integral to be well-approximated using numerical quadrature. Following the work in [\[18](#page-15-10)], we take the smoothness parameter to be proportional to the voxel spacing, $\gamma = 0.1 \min{\{\Delta x, \Delta y\}}$. In this work, ([6\)](#page-3-2) is used to

Fig. 4 True wall shear stress distribution σ_h^{wss} (continuous black line) and its reconstruction using simulation-based imaging $\sigma_H^{wss}(\cdot, \theta^{\star})$ from MRI grids ($N = 9$ VPD for stenosis, $N = 10$ VPD for aorta)

defne the synthetic MRI data and defne the SBI cost function (Sect. [2.3\)](#page-6-0); a complete description of the approach can be found in [[18](#page-15-10)]. Figures [2](#page-3-1) and [3](#page-4-0) show the synthetic MRI data ($N = 9$ VPD for stenosis, $N = 10$ VPD for aorta) extracted from the true flow with $(k = 20\%)$ and without noise for the stenosis and aorta test cases, respectively.

We use standard methods from the MRI literature to compute the WSS directly from the MRI data, $\sigma_N^{\text{wss}}(x)$, at any point $x \in \partial \Omega_w$ [\[33,](#page-16-4) [50\]](#page-16-19). First, we use the raw voxel velocity data v_h to compute a bilinear flow field reconstruction; we call this bilinear flow field v_N . Then, assuming no flow penetration through the walls, the tangential component of the surface traction in (5) (5) can be written as

$$
\tau = \mu(BB^T)\nabla v \cdot n,\tag{11}
$$

where the columns of $B(x) \in \mathbb{R}^{d \times (d-1)}$ form a basis of the tangent space at $x \in \Omega_w$ (orthogonal complement of $n(x)$); see derivation in Appendix [1](#page-14-0). The normal gradient is computed using an approach similar to that in [\[33](#page-16-4), [50](#page-16-19)], i.e., construct a quadratic approximation of the velocity feld in the normal direction from the bilinear fow feld and assume the velocity is zero at *x*, because it performed favorably relative to several alternatives in a comparative study [[33](#page-16-4)]. The quadratic velocity along the outward normal *n* originating at the point *x* takes the form

$$
\tilde{v}_N(\cdot; x, n): \mathbb{R} \to \mathbb{R}^d,
$$

\n
$$
\tilde{v}_N(\cdot; x, n): r \mapsto v_N(x - \delta n)\psi_1(r) + v_N(x - 2\delta n)\psi_2(r)
$$
\n(12)

with a noise level of $\kappa = 20\%$ (dashed red line) along the intersection of the top wall of stenotic vessel (left) and bottom wall of the aorta (right) with the MRI domain, both at $Re = 1000$

where $\{\psi_0, \psi_1, \psi_2\}$ are one-dimensional quadratic Lagrangian polynomials associated with the nodes $\{0, \delta, 2\delta\}$, and $\delta \in \mathbb{R}_{>0}$ is the increment used to determine the points along the normal at which to fit the quadratic function to the bilinear flow field [[31\]](#page-16-0). In this work, we choose the increment to be proportional to the voxel spacing, $\delta = 1.2 \min\{\Delta x, \Delta y, 0.06\}$ (cm) to ensure the step is large enough to avoid sampling from MRI voxels that intersect the wall (to avoid corruption from the partial volume effect), if possible, and small enough for the quadratic reconstruction to be accurate. Finally, the gradient of the velocity in the normal direction is approximated as $\tilde{v}'_N(0)$ and the tangential component of the surface traction (τ_N) and wall shear stress (σ_N^{wss}) at $x \in \Omega$ are computed as

$$
\tau_N(x) = \mu(B(x)B(x)^T)\tilde{v}_N'(0;x,n(x)), \qquad \sigma_N^{\text{wss}}(x) = ||\tau_N(x)||. \tag{13}
$$

This approach makes two unrealistic assumptions, namely, that the point on the boundary *x* and corresponding normal $n(x)$ are known exactly. In practice, these geometric properties must be approximated from scanned images, which introduces additional error that was quantifed in [[33\]](#page-16-4). Since the position on the wall and the corresponding normal are known in the SBI setting, we use this information to maintain fairness in the comparison between MRI postprocessing and SBI.

2.3 Simulation‑based imaging

Simulation-based imaging aims to reconstruct a high-fdelity in vivo flow image from a CFD simulation that has been certifed with MRI fow measurements. It optimally fts a CFD simulation to MRI fow data that can be noisy, sparse, and low-resolution by modifying the boundary conditions, material properties, and the initial condition. In this work, we adjust the infow boundary conditions to ft the CFD simulation to the MRI data. That is, we consider the Navier–Stokes equation in [\(2](#page-2-1)) subject to the following boundary conditions

$$
v = 0 \text{ on } \partial \Omega_{\text{w}}, \quad v = \hat{v}(\cdot;\theta)
$$

on $\partial \Omega_{\text{in}}, \quad \sigma \cdot n = 0 \text{ on } \partial \Omega_{\text{out}}$ (14)

where \hat{v} : $\mathbb{R}^d \times \mathcal{D} \rightarrow \mathbb{R}^d$ is the parametrized inflow function, $\theta \in \mathcal{D}$ is a vector of parameters, and $\mathcal{D} \subset \mathbb{R}^d$ is the admissible parameter space. In this work, we take the infow velocity to be parallel to the normal of the infow boundary surface following $[18]$ $[18]$, which leads to

$$
\hat{v} : (x; \theta) \mapsto \frac{(B_0 - x_2)(B_0 + x_2)}{B_0^2}(\theta, 0)
$$
\n(15)

for the vessel case study, i.e., a parabolic profile for the x_1 velocity that is zero at the wall $(x_2 = \pm B_0)$ with θ defining the peak of the parabola. A similar parabolic parametrization of the normal-directed infow velocity is used for the aorta.

Remark 1 In practice, a zero traction outlet boundary condition does not necessarily lead to a physically relevant CFD model due to the potential for the actual blood flow to split between major branches of the aorta. For such cases, the outfow velocities and pressure can be treated as unknowns and determined using the SBI framework. This was shown to be an effective approach in $[18]$ $[18]$ $[18]$. In this work, we use the zero-traction outfow because it is a reasonable assumption for the problems considered.

The CFD simulation underlying SBI discretizes the Navier–Stokes equation in [\(2](#page-2-1)) with the parametrized boundary conditions in [\(14\)](#page-6-2) using the fnite element method as described in Sect. [2.1](#page-1-0); the corresponding velocity feld is denoted $v_H(x;\theta)$. In the in vivo setting, the geometry of the fow domain is obtained by segmenting an angiogram scan from which a mesh is generated using standard tools [[51–](#page-16-20)[53\]](#page-16-21). In this study, we directly generate a high-order mesh of the two geometries considered (Sect. [2.1](#page-1-0)).

The parameterized infow boundary conditions are determined by optimally ftting the parameterized CFD solution to the MRI data

$$
\theta^{\star} = \operatorname{argmin}_{\theta \in \mathcal{D}} I(\theta), \qquad I : \theta \mapsto \sum_{i=1}^{N} \frac{\alpha_{i}}{2} \|\Xi_{i}(v_{H}(\cdot;\theta)) - \bar{v}_{i}\|_{2}^{2},
$$
\n(16)

where $\alpha_i = 1$ if the *i*th voxel is entirely within the domain and zero otherwise (to avoid corruption from the partial volume effect) and $I: \mathcal{D} \to \mathbb{R}$ is the cost function that measures the misft between the MRI data and its prediction from the CFD simulation. The optimization problem in [\(16](#page-6-3)) is solved using a quasi-Newton method globalized with a line search [[54\]](#page-16-22) and gradients of the objective function are computed efficiently using the adjoint method. From the solution of the SBI optimization problem (θ^*) , the reconstructed flow field is the CFD simulation at the optimal parameter configuration, i.e., $v_H(\cdot;\theta^{\star})$. From the SBI reconstructed flow, we calculate the corresponding WSS, denoted $\sigma_H^{\text{wss}}(\cdot;\theta^{\star})$, using [\(5](#page-2-2)) with the SBI state $v_H(\cdot;\theta^*)$. The necessary derivatives of the flow solution required in (5) (5) are readily available from the fnite element basis functions.

Figures [2](#page-3-1) and [3](#page-4-0) show the SBI reconstruction of the flow feld and its representation in the MR data space for the stenosis and aorta test cases, respectively. Additionally, Fig. [4](#page-5-0) shows the WSS reconstruction using SBI for both test cases.

The same point-spread function (Ξ) used to defne the MRI data is used to sample the CFD solution for matching to the MR fow data in the objective function. This assumes the numerical point-spread function [\(6](#page-3-2)) will exactly reproduce the point-spread function of the MRI scanner, which is not true in practice, which may introduce additional modeling error. However, in this work, we do not consider the sensitivity of SBI to the point-spread function, instead we focus on its performance with respect to Reynolds number, MRI resolution, and noise. Another unrealistic assumption is the domain (Ω) and its boundary are known with certainty, whereas there would be errors in the vessel geometry that is segmented from angiogram scans, which will introduce errors into the SBI reconstruction and WSS computation. The sensitivity of SBI to the geometry was considered in [[55\]](#page-16-23).

3 Results

In this section, we study the performance of MRI- and SBI-based wall shear stress reconstructions as a function of MRI noise level, resolution of the MRI voxel grid, Reynolds number, and resolution of the CFD mesh used for SBI reconstruction. Comprehensive studies for the ideal stenosis geometry are used to draw conclusions regarding the performance of MRI and SBI wall shear stress reconstruction;

Fig. 5 Meshes (left) of stenotic vessel used to study the sensitivity of SBI to resolution of the CFD mesh and the corresponding velocity feld (right). Number of elements in mesh: $N_e = 368$ (top row), $N_e = 766$ (middle row), and $N_e = 1590$ (bottom row). Colorbar in Fig. [2](#page-3-1)

these conclusions are then verifed for the more complex setting of fow through an idealized aorta using targeted studies.

In each of these studies, we will quantitatively compare the WSS distributions, i.e., $\sigma_H^{\text{wss}}(\cdot;\theta^{\star})$ (SBI) and σ_N^{wss} (MRI) to σ_h^{wss} (true WSS), along the curve $\Gamma \subset \partial \Omega_w$, where Γ is the intersection of the top (bottom) wall of the vessel (aorta) with the limits of the MRI domain (which does not span the entire domain for the stenotic vessel case). The error will be quantified using the relative L^2 norm, reported as percentages,

$$
e_{\text{SBI}} = \frac{\sqrt{\int_{\Gamma} |\sigma_h^{\text{wss}}(x) - \sigma_H^{\text{wss}}(x;\theta^*)|^2 dS}}{\sqrt{\int_{\Gamma} |\sigma_h^{\text{wss}}(x)|^2 dS}},
$$

$$
e_{\text{MRI}} = \frac{\sqrt{\int_{\Gamma} |\sigma_h^{\text{wss}}(x) - \sigma_N^{\text{wss}}(x)|^2 dS}}{\sqrt{\int_{\Gamma} |\sigma_h^{\text{wss}}(x)|^2 dS}},
$$
(17)

where $e_{SBI}, e_{MRI} \in \mathbb{R}_{\geq 0}$ are the SBI and MRI WSS distribution errors, respectively, and the integrals are computed using Gaussian quadrature.

3.1 Impact of the CFD resolution

The CFD mesh resolution used for SBI impacts the computational cost of the method so we study the sensitivity of the SBI wall shear stress reconstruction to the resolution of the mesh. For this study, we vary the noise $\kappa \in \{0, 5, 10, 15, 20\}$ (%), Reynolds number Re ∈ {100, 500, 1000}, MRI grid resolution $N \in \{3, 9, 15, 28\}$ (VPD), and consider the three meshes of increasing resolution shown in Fig. $5 (N_e = 368,$ $5 (N_e = 368,$ 766, 1590 elements, respectively). The finest mesh $(N_e = 1590)$ is used to compute the reference ("true") flow and smoothly resolves all fow features, whereas the two coarser meshes (N_e = 368 and N_e = 766) lead to numerical artifacts in the stenosis, but contain two and four times fewer elements, respectively, and the corresponding CFD simulations require a fraction of the compute time.

Remark 2 The mesh used for the reference solution was determined through a careful refnement study. We considered a sequence of meshes with increasing refnement and selected the reference mesh once the relative error in the WSS distribution between successive refnement levels dropped below 0.1%. Because the discretization uses a cubic approximation of the velocity feld within each element, a relatively coarse mesh (compared to the refnement required by conventional second-order methods) is sufficient to reach high accuracy.

First, we observe that the WSS reconstruction error using SBI decreases as the CFD mesh is refned (Fig. [6](#page-8-0)), which holds for almost all Reynolds numbers, noise levels, and MRI voxel grids considered. The noise in the MRI data tends to degrade the accuracy of the WSS reconstruction; however, its infuence diminishes as the MRI voxel grid is refined, i.e., there is very little difference in the $\kappa = 0\%$ and $\kappa = 20\%$ WSS reconstruction with $N = 28$ VPD MRI grid, whereas there is a substantial difference with $N = 3$ VPD. We note that for the finest mesh ($N_e = 1590$), the WSS reconstruction has a relatively weak dependence on the Reynolds number of the fow, whereas there is a signifcant dependence on Reynolds number for the coarser meshes, e.g., for the coarse mesh with $N = 3$ VPD and $\kappa = 10\%$, the WSS error is around 5% for Re = 100 and close to 15% for $Re = 1000$. Even in the cases with large error, the optimization problem underlying SBI drives the CFD simulation to a confguration that agrees reasonably well with the true WSS distribution given the limitations of the discretization (Fig. [7\)](#page-9-0).

Together these observations imply that an underresolved mesh can be used for the SBI reconstruction at the cost of increasing the sensitivity of the WSS reconstruction to Reynolds number and the MRI voxel grid. This is signifcant because it means the high computational cost of SBI can be reduced using a coarse mesh without signifcant loss in WSS reconstruction accuracy, provided a sufficiently high-resolution MRI data set is used. Alternatively, it implies that a limited amount of MRI data can

Fig. 6 WSS reconstruction error using SBI as a function of CFD mesh resolution for various MRI grids (columns) and noise levels (lines) at Reynolds number 100 (top row), 500 (middle row), and 1000 (bottom row) for the stenotic vessel test case. Legend: $\kappa = 0\%$ (continuous black line with centered black circle), $\kappa = 5\%$ (continu-

ous blue line with centered blue square), $\kappa = 10\%$ (continuous red line with centered red triangle), $\kappa = 15\%$ (continuous pink line with centered pink diamond), $\kappa = 20\%$ (continuous green line with centered green pentagon)

be used (e.g., from fast patient scans) provided the CFD mesh used for SBI reconstruction is relatively fne, which indicates an inherent trade-off between scan and reconstruction time when using SBI. In the remainder, we will fix the CFD mesh resolution at $N_e = 1590$ and focus on the impact of the remaining parameters (noise, Reynolds number, MRI resolution).

3.2 Impact of noise, Reynolds number, and MRI resolution

In this section, we study the coupled effect that noise, Reynolds number, and the MRI voxel grid resolution have on the accuracy to which WSS is reconstructed using SBI (Sect. [2.3\)](#page-6-0) and standard MRI reconstruction (Sect. [2.2](#page-3-0)). We vary the Reynolds number $\text{Re} \in \{100, 500, 1000\}$ because it is known to strongly impact the accuracy of WSS reconstructions based solely on MRI [[33](#page-16-4)]. We vary the noise $\kappa \in \{0, 5, 10, 15, 20\}$ (%) and MRI voxel grid $N \in \{3, 9, 15, 28\}$ (VPD) because these incorporate extreme

(best-case and worst-case) scenarios seen in practice; usually, for infant patients, noise levels are 3–10% and MRI resolution is 3–5 VPD [\[43](#page-16-12), [44](#page-16-13)]. We use the CFD mesh with $N_e = 1590$ elements for SBI reconstruction.

Remark 3 In practice, it is rarely, if ever, practical to achieve an MRI resolution of 28 VPD; however, we include it in the study to gain insight into each method in the limit of extreme resolution. Similarly, Reynolds numbers in practical blood flows are usually well above 100; $Re = 100$ was included in the study to provide a well-defned controlled condition on which to base further investigations. We then increased the Reynolds number to obtain measurements at higher flow rates, but limited this to $Re = 1000$ to ensure that flow is kept steady and laminar.

First, we focus on the relationship between the WSS reconstruction error and resolution of the MRI voxel grid for various noise levels and Reynolds numbers (Fig. [8\)](#page-9-1). The error in the WSS reconstruction from MRI trends toward

Fig. 7 Wall shear stress distribution over intersection of top wall of stenotic vessel with MRI domain (Γ) using SBI with diferent mesh resolutions at Reynolds number $Re = 1000$, noise $\kappa = 20\%$, and MRI resolution $N = 9$ VPD (scenario in Fig. [2\)](#page-3-1). Legend: WSS distribution from true fow (continuous black line) and SBI WSS distribution using the mesh with $N_e = 368$ elements (dashed red line), $N_e = 766$ elements (dotted blue line), and $N_e = 1590$ elements (dadhdotted pink line); see Fig. [5](#page-7-0) for meshes

zero, albeit slowly, as the voxel grid is refned, which confrms the MRI WSS approach and implementation. Moreover, in the low noise setting, the WSS reconstruction error decreases toward a minimum (non-zero) value as the voxel grid is refned. However, for higher noise levels, additional

MRI voxels can degrade the WSS reconstruction accuracy because it operates directly on the noisy MRI data and the length scale over which the noise (fixed magnitude of κ) varies decreases as the grid is refned, i.e., the noise varies more rapidly in the spatial domain. On the other hand, the WSS reconstruction from SBI is nearly exact in the nonoise setting and the error decreases monotonically as the voxel grid is refned for all Reynolds numbers and noise levels. While the overall error in the WSS reconstruction using SBI does increase with noise, additional MRI voxels do not limit or degrade the approximation as seen in the MRI-based reconstruction. This can be attributed to the fact that the WSS reconstruction using SBI does not directly operate on the noisy data; rather, the noisy data is used to reconstruct a noise-free CFD velocity feld, which is used to compute the WSS. Therefore, the noise-sensitive operations, e.g., diferentiation, are only applied to the noise-free SBI fow feld, which leads to an approximation that is robust to noise in the MRI data. Finally, we observe that in the $3 - 5$ VPD regime, the resolution commonly available for infant patients, the WSS reconstruction using SBI is signifcantly more accurate than using MRI alone. Even in the highest noise scenario ($\kappa = 20\%$), the SBI WSS reconstruction error is less than 10%, whereas the MRI WSS reconstruction error is about 50%.

Next, we investigate the relationship between the WSS reconstruction error and Reynolds number for various noise levels and MRI voxel grids (Fig. [9\)](#page-10-0). The accuracy of the WSS reconstruction directly from the MRI degrades as the Reynolds number increases, which agrees with other studies

Fig. 8 WSS reconstruction error using SBI (top row) and MRI (bottom row) as a function of MRI grid resolution for various noise levels (columns) and Reynolds numbers (lines) for the stenotic vessel test

case. Legend: $Re = 100$ (continuous black line with centered black circle), $Re = 500$ (continuous blue line with centered blue square), $Re = 1000$ (continuous red line with centered red triangle)

Fig. 9 WSS reconstruction error using SBI (top row) and MRI (bottom row) as a function of Reynolds number for various MRI grid resolutions (columns) and noise levels (lines) for the stenotic vessel test case. Legend: $\kappa = 0\%$ (continuous black line with centered black

[\[33\]](#page-16-4). The main exceptions come from configurations with high noise and many voxels per diameter where the error is already quite large (above 40%); in these cases, the WSS reconstruction error can decrease somewhat with increasing Reynolds number. On the other hand, WSS reconstruction from SBI is insensitive to Reynolds number, i.e., the range in the WSS reconstruction error is less than 1% from Re = 100 to $Re = 1000$ for all noise levels and decreases as the MRI grid is refned.

Next, we investigate the relationship between the WSS reconstruction error and noise level for various Reynolds numbers and MRI voxel grids (Fig. [10\)](#page-11-0). For the MRI-based WSS reconstruction, the error increases with noise except for the coarsest voxel grid $(N = 3 \text{ VPD})$ where the error can slightly decrease as noise increases for higher Reynolds numbers (situations where the error is already quite large, at least 50%). As the MRI grid is refned, the rate at which the WSS error increases with respect to noise accelerates due to the decreasing length scale over which the noise varies. The error in the WSS reconstruction using SBI increases linearly with the noise level with a decreasing slope as the MRI resolution increases (opposite of the trend observed with MRIonly WSS reconstruction). These observations hold across all Reynolds numbers considered Re $\in \{100, 500, 1000\}$.

To this point, we have aggregated the entire WSS distribution into a scalar to compare MRI- and SBI-based WSS reconstruction across numerous scenarios. We take a closer look at the entire WSS distribution as a scatter plot, whereby the actual value of WSS is plotted against the reconstructed

circle), $\kappa = 5\%$ (continuous blue line with centered blue square), $\kappa = 10\%$ (continuous red line with centered red triangle), $\kappa = 15\%$ (continuous pink line with centered pink diamond), $\kappa = 20\%$ (continuous green line with centered green pentagon)

WSS for a number of points along the wall $x \in \Gamma$ (Fig. [11](#page-12-0)); tight clustering around the line of identity implies the reconstruction is accurate and reliable. Because of the relatively weak dependence on Reynolds number (Fig. [9](#page-10-0)), we fix Re = 1000 and vary the noise $\kappa \in \{5\%, 10\%, 15\% \}$ and MRI resolution $N \in \{9, 15, 28\}$ VPD. The SBI-based WSS reconstruction lies tightly clustered near the line of identity, whereas the MRI-based WSS reconstruction varies signifcantly from the line, particularly in the high-noise confgurations.

3.3 Verifcation with aorta geometry

A fnal set of numerical experiments was conducted using the coarctated aorta to demonstrate the key fndings from the previous sections generalize to the more complex test case. To limit the parameter space to explore, we do not study the impact of mesh resolution on the SBI reconstruction. Furthermore, given the relative insensitivity of SBI to Reynolds number, we only consider a limited sampling of Reynolds numbers, i.e., $\text{Re} \in \{100, 1000\}$. We vary the noise κ ∈ {0, 5, 10, 20} and MRI voxel grid $N \in \{3, 5, 10\}$ VPD; the finest MRI grid is restricted to $N = 10$ VPD (corresponds to 60×90 voxel grid) because the MRI domain covers a larger region compared to the stenotic vessel.

The relationship between the WSS reconstruction error and resolution of the MRI voxel grid for various noise levels and Reynolds numbers (Fig. [12\)](#page-13-0) is consistent with fndings

Fig. 10 WSS reconstruction error using SBI (top row) and MRI (bottom row) as a function of noise level for various Reynolds numbers (columns) and MRI grid resolutions (lines) for the stenotic vessel test case. Legend: $N = 3$ VPD (continuous black line with centered black

circle), $N = 9$ VPD (continuous red line with centered red triangle), $N = 15$ VPD (continuous pink line with centered pink diamond), $N = 28$ VPD (continuous green line with centered green pentagon)

for the stenotic vessel. That is, the accuracy of the WSS reconstruction from MRI improves as the MRI voxel grid is refned for the low-noise settings, whereas it degrades in the higher noise settings. On the other hand, the WSS reconstruction error from SBI decreases as the MRI voxel grid is refned for all noise levels considered.

Similarly, the relationship between the WSS reconstruction error and noise for various Reynolds numbers and MRI voxel grids (Fig. [13](#page-13-1)) is consistent with fndings for the stenotic vessel. For MRI, the WSS reconstruction error increases rapidly when the noise exceeds $\kappa = 5\%$ and increases most rapidly for the fnest MRI voxel grid. For SBI, the WSS reconstruction error increases linearly with the noise level with a slope that decreases as the MRI voxel grid is refned.

Overall, the results from the aorta test case agree with those from the vessel, particularly the trends with respect to variations in the MRI grid resolution and noise.

4 Discussion

4.1 Discussion of results

The wall shear stress reconstruction directly from MRI data showed sensitivity to the Reynolds number of the flow, the resolution of the MRI grid, and the noise in the MRI data.

Without noise, the reconstructed WSS converged to the true WSS distribution as the MRI grid is refned; however, for higher noise levels the accuracy degrades as the MRI grid is refned. This can be attributed to the noise in the domain varying more rapidly, i.e., over a smaller length scale given by the MRI voxel spacing. Because the MRI WSS reconstruction fits a quadratic function to this noisy data, it is inherently sensitive to the length scale over which the noise varies. We also observed the accuracy of the WSS reconstruction directly from the MRI data degrades as the Reynolds number of the fow increases for most voxel grids and noise levels considered. Lastly, we found the error of the WSS reconstruction increases as the noise in the MRI data increases and grows faster as the MRI grid is refned. These findings are consistent with studies in the literature $[29-31,$ $[29-31,$ [33](#page-16-4), [35\]](#page-16-3), which show that the accuracy of WSS computations directly from MRI data are limited by a fundamental tradeoff between noise and resolution and become less reliable as the Reynolds number of the fow increases.

On the other hand, WSS reconstruction from SBI is relatively insensitive to the Reynolds number of the fow, the resolution of the MRI grid, and the noise in the MRI data. For all Reynolds numbers and noise levels considered, the WSS reconstruction accuracy improves as the MRI grid is refned. Furthermore, the reconstruction is reliable for all MRI grids considered, i.e., the largest WSS reconstruction

Fig. 11 Scatter plot of the true WSS vs. the reconstructed WSS using SBI (red circle) and MRI (blue plus) for 200 points along the upper wall intersected with the MRI domain (Γ) for the stenotic vessel. The rows correspond to noise levels $\kappa = 5\%, 10\%, 15\%$ and the columns

correspond to MRI resolutions $N = 9, 15, 28$ VPD. Tight clustering around the line of identity (continuous black line) indicates accurate WSS reconstruction along Γ

error for the coarctated aorta test case was $e_{SBI} = 6\%,$ which occurred at Reynolds number $Re = 1000$ with only $N = 3$ VPD and $\kappa = 20\%$ noise level. The accurate WSS reconstruction in the small data and high noise regime is attributed to the signifcant amount of a priori information leveraged by SBI including the geometry of the domain and governing equations (with unknown infow boundary conditions) that are not exploited when reconstructing WSS from MRI data alone. Next, we observed that WSS reconstruction from SBI showed relatively little sensitivity to the Reynolds number of the fow over the limited range considered in this work. We expect these results to generalize throughout the laminar regime, but break down as the transitional and turbulent regimes are approached. Lastly, for all Reynolds numbers and MRI grids considered, the error in the WSS reconstruction using SBI increased linearly with noise; the maximum error observed is 10% for the stenotic vessel and 6% for the coarctated aorta which occur at a larger noise than usually observed in practice ($\kappa = 20\%$). This relatively minor sensitivity to noise is attributed to the fact that SBI does not directly compute WSS from a noisy feld; rather, the noisy MRI data is used to reconstruct a noise-free CFD velocity feld, which is then used to compute WSS. Because the velocity feld reconstruction is reliable in the presence of zero-mean noise, the overall WSS reconstruction is reliable.

The SBI framework was shown to be moderately sensitive to the resolution of the mesh used for the SBI reconstruction. That is, a coarser mesh can be used for the SBI

Fig. 12 WSS reconstruction error using SBI (top row) and MRI (bottom row) as a function of MRI grid resolution for various noise levels (columns) and Reynolds numbers (lines) for coarctated aorta test

case. Legend: $Re = 100$ (continuous black line with centered black circle), Re = 1000 (continuous red line with centered red triangle)

Fig. 13 WSS reconstruction error using SBI (top row) and MRI (bottom row) as a function of noise level for various Reynolds numbers (columns) and MRI grid resolutions (lines) for the coarctated aorta test case. Legend: $N = 3$ VPD (continuous black line with centered black circle), $N = 5$ VPD (continuous blue line with centered blue square), $N = 10$ VPD (continuous red line with centered red triangle)

reconstruction than used to simulate the true flow; however, the sensitivity of the WSS reconstruction with respect to MRI resolution and Reynolds number increases. This provides an opportunity to reduce the computational cost of SBI for in vivo applications as it suggests there is some fexibility

in designing the mesh used for SBI provided care is taken to ensure underresolution of the CFD velocity feld is compensated with additional MRI resolution. Multi-fdelity optimization approaches that progressively refne inexpensive models, e.g., simulations on coarser meshes [[56\]](#page-16-24) or reducedorder models [\[57](#page-16-25)] [[58\]](#page-16-26), to accelerate convergence could be used to further reduce the cost of SBI. Alternatively, this observation implies that a limited amount of MRI data can be used (e.g., from fast patient scans) provided the CFD mesh used for SBI reconstruction is relatively fne due to the insensitivity of SBI to the quality/resolution of the MRI data in this scenario. This leads to an inherent trade-off between scan and reconstruction time when using SBI, which is fundamentally different and preferred than the trade-off between scan time and reconstruction quality attributed to traditional MRI postprocessing techniques.

4.2 Summary

This paper details a simulation-based imaging framework for blood fow imaging and WSS reconstruction based on using numerical optimization to ft a CFD simulation to MRI fow velocity data. The primary contribution of the paper are two synthetic test cases—fow through a stenotic vessel and coarctated aorta—that directly compare WSS reconstruction accuracy using SBI and standard MRI postprocessing techniques. We found the SBI method can accurately reconstruct WSS and is relatively insensitive to the resolution of the MRI data and Reynolds number of the fow. The WSS reconstruction error of SBI increases only linearly with noise in the MRI data with a slope that is inversely proportional to the resolution of the MRI data. Furthermore, coarser CFD grids can be used for the SBI reconstruction than used for the reference fow at the cost of increased sensitivity to the resolution of the MRI data and Reynolds number of the fow. On the other hand, WSS reconstruction from MRI data is less accurate than SBI and more sensitive to noise, resolution of the MRI data, and the Reynolds number of the fow.

4.3 Limitations and future work

While this study resulted in a number observations regarding the strengths and weaknesses of using SBI to reconstruct WSS, there are a number of limitations that offer promising paths for future research. First, the synthetic experiments employ several unrealistic assumptions to simplify the problem: steady, two-dimensional, laminar flow of a Newtonian fuid and full knowledge of the geometry. While these were important for an extensive, controlled, and fair comparison^{[1](#page-14-1)} between SBI and MRI with respect to WSS prediction in this simplifed setting, they limit the clinical generalizability of the observations and should only be considered a lower bound on the errors that would be observed in more practical settings.

Because most clinically relevant fows are three-dimensional and unsteady, the two-dimensional steady flow assumptions are the most severe, although the SBI approach has been shown to successfully reconstruct in vivo flows for three-dimensional, pulsatile, laminar fows [\[18\]](#page-15-10). The assumption that the geometry is known with certainty is also not practical and would introduce potentially large errors in both the SBI and MRI WSS prediction [[33\]](#page-16-4), which can only be mitigated via detailed uncertainty quantifcation to establish the sensitivity of the WSS reconstruction to variations in the geometry, or higher resolution angiogram scans to extract the vessel wall geometry. The relatively low Reynolds numbers considered ensure the fow is laminar, which is another fundamental limitation of the study. Additional research is needed to determine if SBI will be feasible for turbulent blood fows (e.g., behind a stenosis with small grade) where the inherent chaos of the system can lead to ill-posed optimization problems [[59\]](#page-16-27). Finally, while blood flow does exhibit non-Newtonian behavior in some regimes (low inlet velocities and shears) $[60]$ $[60]$, our Newtonian blood flow model only introduces secondary errors relative to the other assumptions [\[61\]](#page-16-29). Future work should consider the generalizability of these results to three-dimensional, pulsatile fows at higher Reynolds numbers with uncertainty in the vessel

geometry that lead to higher peak WSS and more complex distributions. Even though extensive sensitivity analysis is not necessarily practical in the generalized setting, the studies can be guided by the observations of this work.

Furthermore, a study of the impact of varying the pointspread function used in the SBI reconstruction from that used to compute the true fow would provide insight into the sensitivity of SBI for in vivo applications because the point-spread function of MRI scanners is not known with certainty, but can be modeled and estimated depending on the MRI protocol. Also, it would be interesting to include additional parameters to optimize in the SBI reconstruction, e.g., material properties of blood (with Newtonian or non-Newtonian fuid models) and outfow conditions, to further understand the ability of SBI to reconstruct a fully patientspecific flow.

Appendix

Simplifcation of tangential component of wall traction

To derive the simplifed expression for the tangential component of the wall traction in (11) (11) (11) , we consider a point $x \in \partial \Omega_{w}$. All spatially varying quantities will be evaluated at this point; however, for brevity, the explicit dependence on *x* will be dropped. Let T denote the $(d-1)$ -dimensional tangent space of the wall $\partial \Omega_w$ at *x*, i.e., T is a linear space such that for any $\xi \in T$, $\xi \cdot n = 0$. In addition, let the columns of the matrix $B \in \mathbb{R}^{d \times (d-1)}$ be an orthogonal basis of $\mathcal T$, which implies

$$
B^T n = 0, \t B^T B = I_{d-1}.
$$
\t(18)

From the no-slip condition ($v = 0$ on $\partial \Omega_w$), we have that for any $\xi \in \mathcal{T}, \nabla v \cdot \xi = 0$, which implies

$$
\nabla v \cdot B = 0. \tag{19}
$$

Next, we observe that the columns of $\begin{bmatrix} B & n \end{bmatrix}$ form a basis of \mathbb{R}^d and expand the traction vector at *x* in this basis

$$
t = Bt_s + nt_n,\tag{20}
$$

where $t_s \in \mathbb{R}^{d-1}$ and $t_n \in \mathbb{R}$ are the coefficients of the traction vector expansion. From this expansion, the tangential component of the traction vector reduces to

$$
\tau = (I - nn^T)t = Bt_s,\tag{21}
$$

where we used ([18](#page-14-2)) and unity of the normal vector *n*. Fur-thermore, by multiplying ([20\)](#page-14-3) by B^T and using [\(18](#page-14-2)), we have

$$
t_s = B^T t. \tag{22}
$$

¹ Fairness in the sense that both SBI and MRI WSS reconstruction beneft from these assumptions.

Next, we substitute the expression for the traction in (5) (5) into the above equation to yield

$$
t_s = B^T \left[\mu (\nabla v + \nabla v^T) n + P n \right] = \mu B^T (\nabla v \cdot n), \tag{23}
$$

where we used (18) and (19) (19) . Finally, we combine (21) (21) and ([23\)](#page-15-14) to yield the simplifed expression for the tangential component of the wall traction in ([11\)](#page-5-1).

Acknowledgements The authors would like to thank Fritiof Hegardt for providing the aorta mesh and simulation. This material is based upon work supported by the Air Force Office of Scientific Research (AFOSR) under award number FA9550-20-1-0236 and the Swedish Research Council grant 2018-03721, the Crafoord Foundation, the Swedish strategic e-science research program eSSENCE, and the Swedish Society of Medicine. The content of this publication does not necessarily refect the position or policy of any of these supporters, and no official endorsement should be inferred.

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