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Establishing a massively parallel, patient-specific model of cardiovascular diseases

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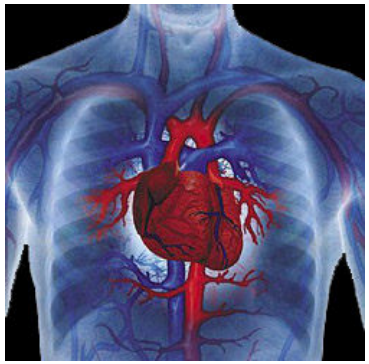
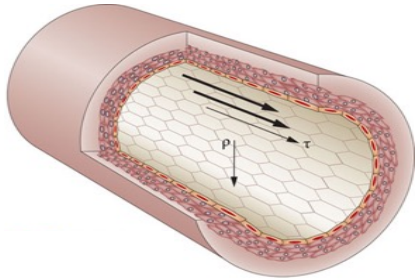
SC20 Doctoral Showcase

Hemodynamics disruption is tied to cardiovascular disease progression

CVDs share highest burden of heart diseases with 17 million death per year



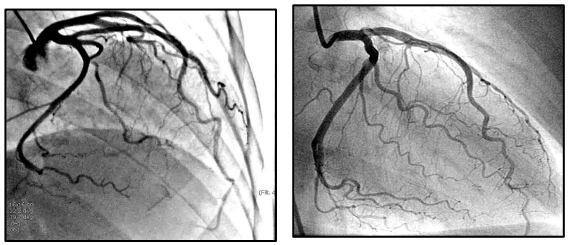
- Altered blood flow
- Modified hemodynamic forces
- **Coronary artery disease**



Modified hemodynamic forces can lead to atherosclerosis and increase stenting complications.[1,2,3,4,5] Currently, a way to assess the hemodynamic forces is using personalized CFD models.[6,7]

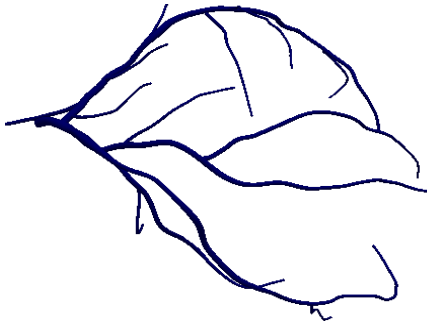
1. Buchanan Jr et al. Atherosclerosis (1999)
2. LaDisa et al, Am J Physiol (2005)
3. Patel et al. Nature Reviews Nephrology (2010)
4. Chatzizisis et al. Circulation (2010)
5. Stone et al JACC Card Int (2018)
6. Fearon et al Circ (2019)
7. Patel et al JACC CI (2020)

Personalized blood flow models: imaging modality and computational model



Medical Imaging Data

Image segmentation, 3D reconstruction

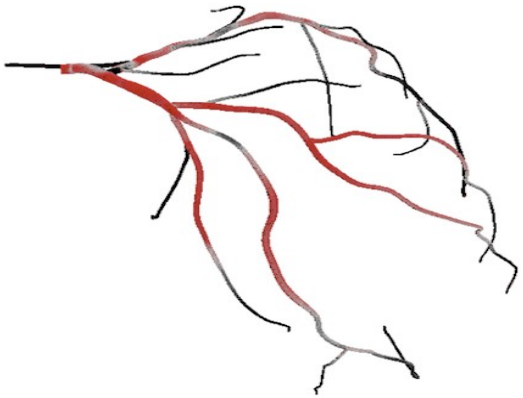


Patient-specific 3D geometries

Modeling based on clinical data

Massively Parallel CFD simulations

Derive hemodynamic risk factors



Patient-specific flow models

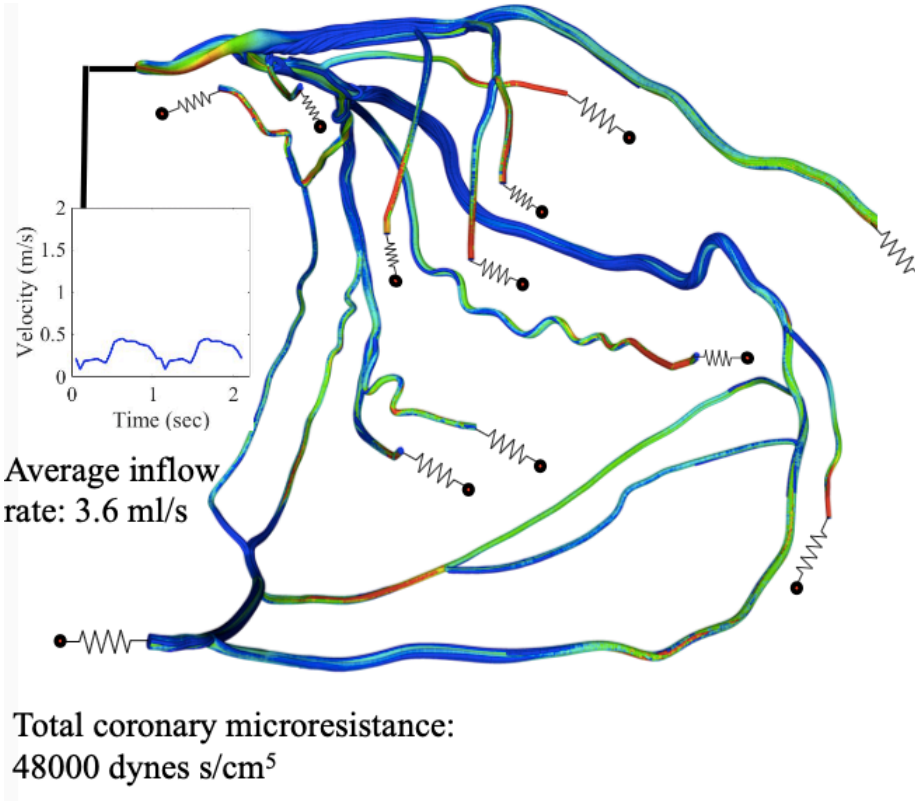
Key challenges to widely adopt CFD models in CADs

Recent years have witnessed a dramatic increase in CFD simulations for diagnosing CADs, however, current frameworks face three key technical challenges:

Challenge 1:	Challenge 2:	Challenge 3:
• 3D CFD simulations are compute intensive with long time-to-solutions	• Need for validation against *in vivo* clinical data using robust personalized flow models	• Lack of suitable visualization methods for clinicians to intuitively interact with CFD data

Challenge 1: Simulations are memory intensive with long time-to-solutions

- Physiological simulations need to be run at 10-20 μm (~250 TB) and are limited by the memory that can fit on the system[1,2]
- We need faster algorithms that can solve bigger problem sizes



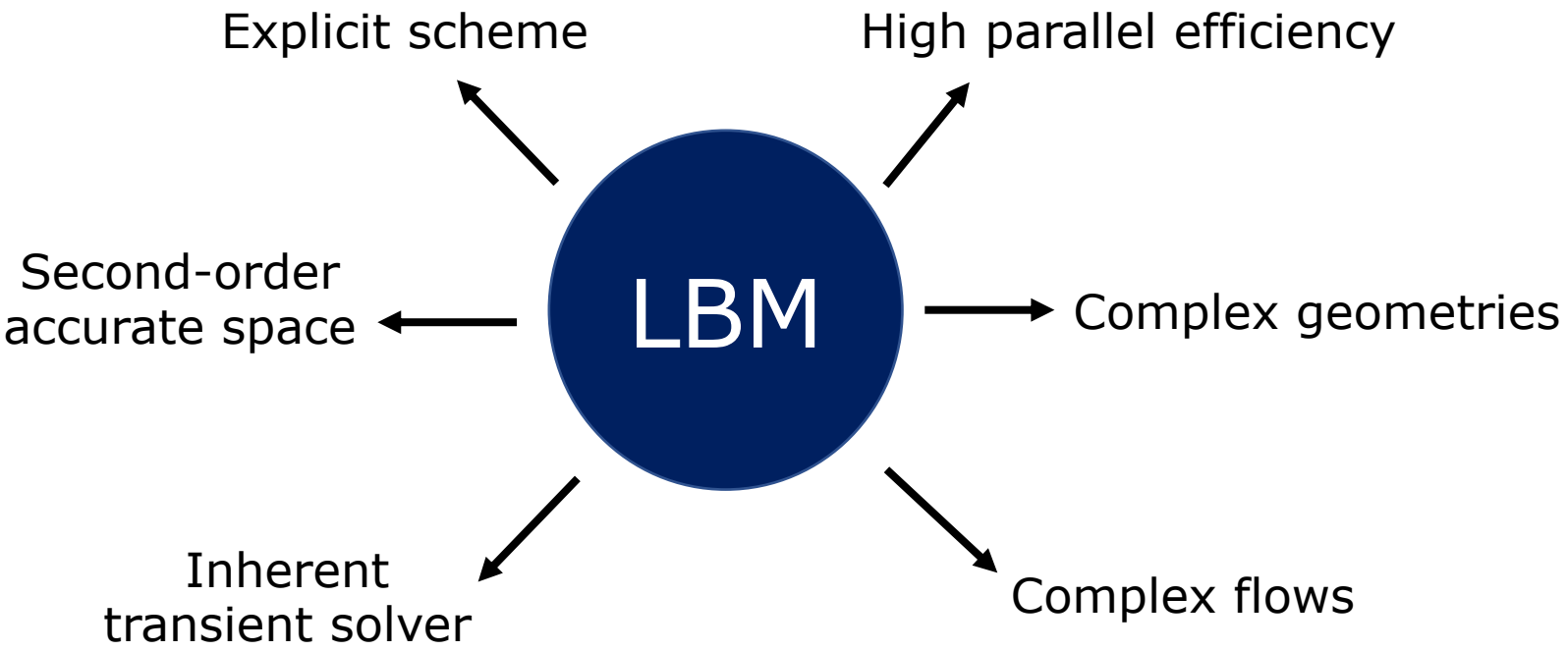
Phase 1: Build a memory-light algorithmic representation that 1) reduces the memory requirements and 2) maintains excellent parallel scalability

1. Bernaschi et al. Supercomputing (2011).
2. Randles et al Supercomputing (2015).

The lattice Boltzmann method (LBM) is a common CFD solver

HARVEY[1]

- A fluid dynamic solver to study blood flow properties in patient-specific vascular geometries[1]
- C/C++ and OpenMP and MPI for parallelization
- Relies on an implementation of the lattice Boltzmann method



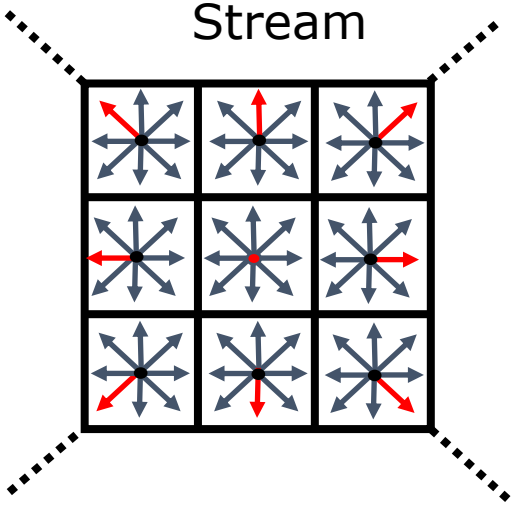
Randles et al. IPDPS 2013

LBM is memory expensive

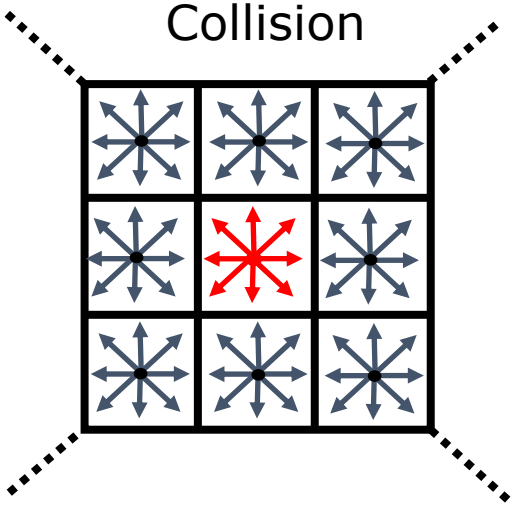
The central quantity in the LBM is the particle distribution function $f_i(x,t)$, evolution of which is given by:

$$f_i(x + c_i, t + 1) = f_i(x,t) + \Omega_i \left(f_i(x,t) - f_i^{eq}(x,t) \right)$$

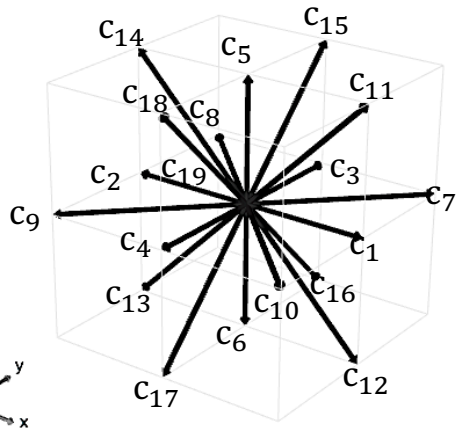
Stream



Collision



D3Q19 lattice

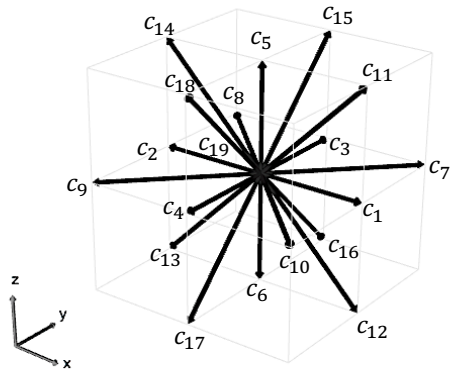


Common LBM implementation requires **38 doubles per lattice site**

Less memory on the supercomputer allows scaling to higher resolution and more complex geometries

STORING MICROSCOPIC VARIABLES → STORING MACROSCOPIC VARIABLES

38 doubles



Discretized velocity distribution

Regularization[1]

10 doubles

Moment data
- Density
- Momentum
- Stress tensor

1. Latt and Chopard, Math and Comp in Simulations, 2006

Moment Representation of the regularized LBM (MR-LBM)

Zeroth and first order moments

$$\rho = \sum_{i=1}^{19} f_i(x,t) \qquad \rho u_\alpha = \sum_{i=1}^{19} c_{i\alpha} f_i(x,t) \qquad \text{Eq 1}$$

Second order moments

$$\Pi_{\alpha\beta} = \sum_{i=1}^{19} Q_{i\alpha\beta} f_i(x,t) \qquad \text{Eq 2}$$

Maxwell-Boltzmann equilibrium distribution function

$$f_i^{eq}(\rho, u_\alpha) = \omega_i \rho \left(1 + \frac{c_{i\alpha} u_\alpha}{c_s^2} + \frac{Q_{i\alpha\beta} u_\alpha u_\beta}{2c_s^4}\right), \mathrm{Q_{i\alpha\beta}} = \mathrm{c_{i\alpha} c_{i\beta}} - \mathrm{c_s^2}\delta_{\alpha\beta} \qquad \text{Eq 3}$$

Regularized distribution function

$$\hat{f} = f^{eq}(\rho, u_\alpha) + \frac{\omega_i}{2c_s^4} Q_{i\alpha\beta} \left(\Pi_{\alpha\beta} - \Pi_{\alpha\beta}^{eq}\right) \qquad \text{Eq 4}$$

MR-LBM can represent the entire simulation state using only moment data – Implemented in HARVEY

$for\ x \coloneqq 1\ to\ N\ do$

$Read\ moments\ \rho(x,t), \boldsymbol{u}(x,t), \boldsymbol{\Pi}(x,t)$

$Compute\ equilibrium\ moments\ \boldsymbol{\Pi^{eq}}(\rho,u)$

$Collision\ \boldsymbol{\Pi}^* = \left(1 - \frac{1}{\tau}\right)\boldsymbol{\Pi} + \frac{1}{\tau}\boldsymbol{\Pi^{eq}}$

$for\ i \coloneqq 1\ to\ 19\ do$

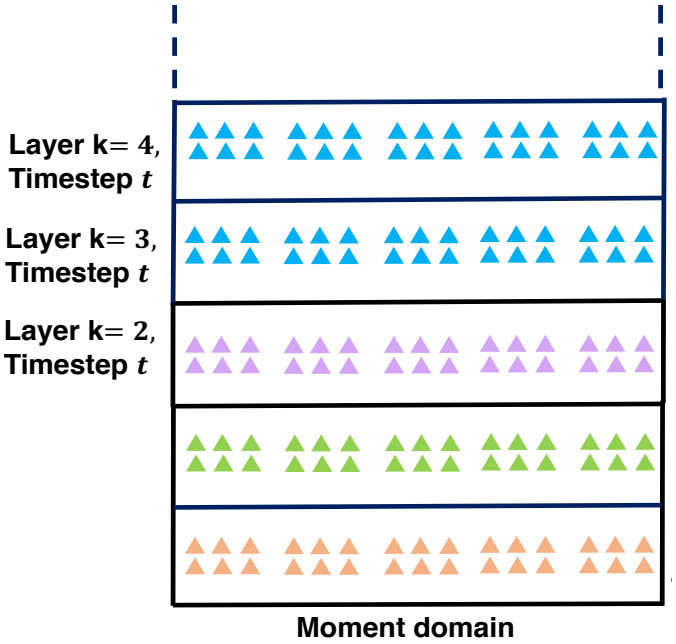
$Compute\ distribution\ f_i^* = \omega_i \rho(1 + c_s^2(\boldsymbol{c_i}.\boldsymbol{u}) + c_s^4 \boldsymbol{Q_i} : \boldsymbol{\Pi})$

$Streaming\ f_i(\boldsymbol{x} + \boldsymbol{c_i}, t+1) = f_i^*$

$Compute\ zeroth, first\ and\ second\ order\ moments$

Vardhan et al. Supercomputing 2019

Layer-based moment representation (MR) method



Simulation state

MR-LBM can represent the entire simulation state using only moment data – Implemented in HARVEY

$for\ x \coloneqq 1\ to\ N\ do$

$Read\ moments\ \rho(x,t), \boldsymbol{u}(x,t), \boldsymbol{\Pi}(x,t)$

$Compute\ equilibrium\ moments\ \boldsymbol{\Pi^{eq}}(\rho,u)$

$Collision\ \boldsymbol{\Pi}^* = \left(1 - \frac{1}{\tau}\right)\boldsymbol{\Pi} + \frac{1}{\tau}\boldsymbol{\Pi^{eq}}$

$for\ i \coloneqq 1\ to\ 19\ do$

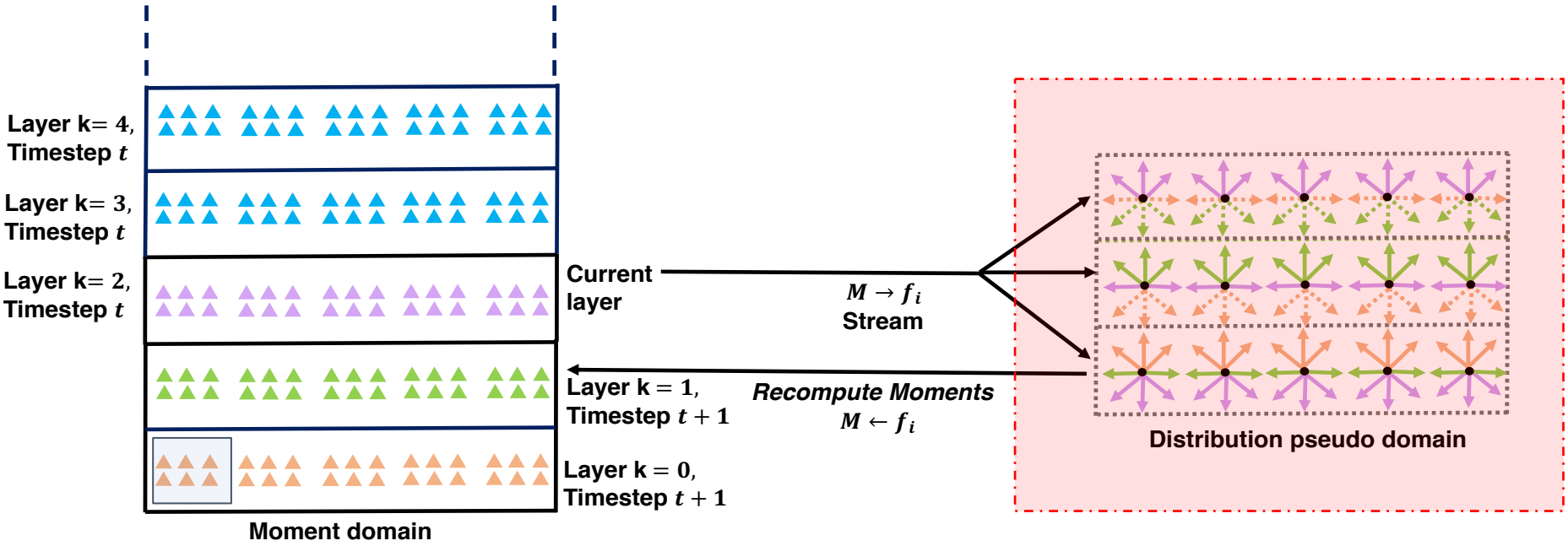
$Compute\ distribution\ f_i^* = \omega_i \rho(1 + c_s^2(\boldsymbol{c_i}.\boldsymbol{u}) + c_s^4 \boldsymbol{Q_i} : \boldsymbol{\Pi})$

$Streaming\ f_i(\boldsymbol{x} + \boldsymbol{c_i}, t+1) = f_i^*$

$Compute\ zeroth, first\ and\ second\ order\ moments$

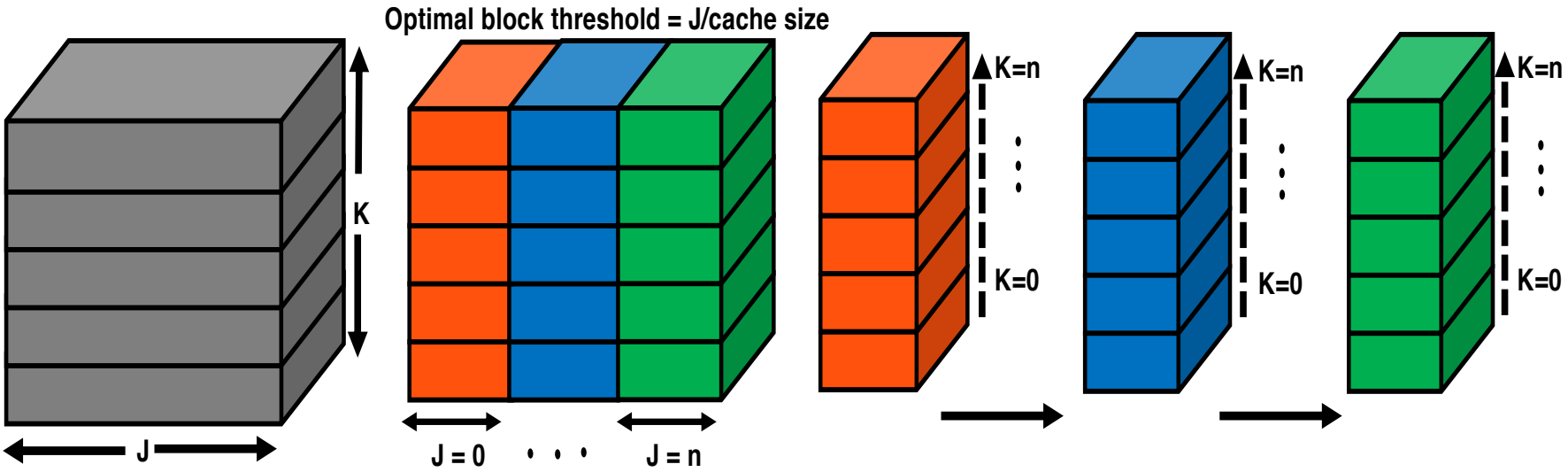
Vardhan et al. Supercomputing 2019

MR-LBM can represent the entire simulation state using only moment data – Implemented in HARVEY

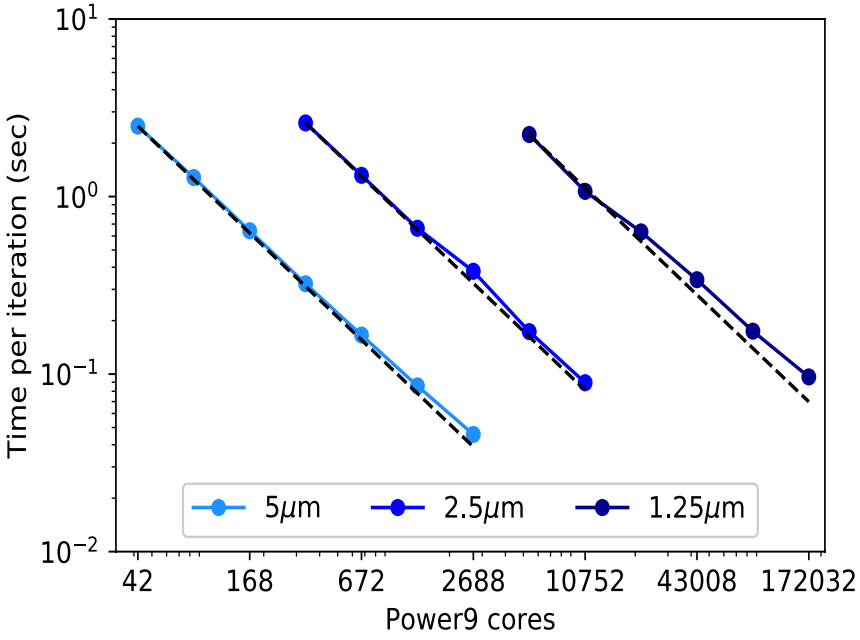


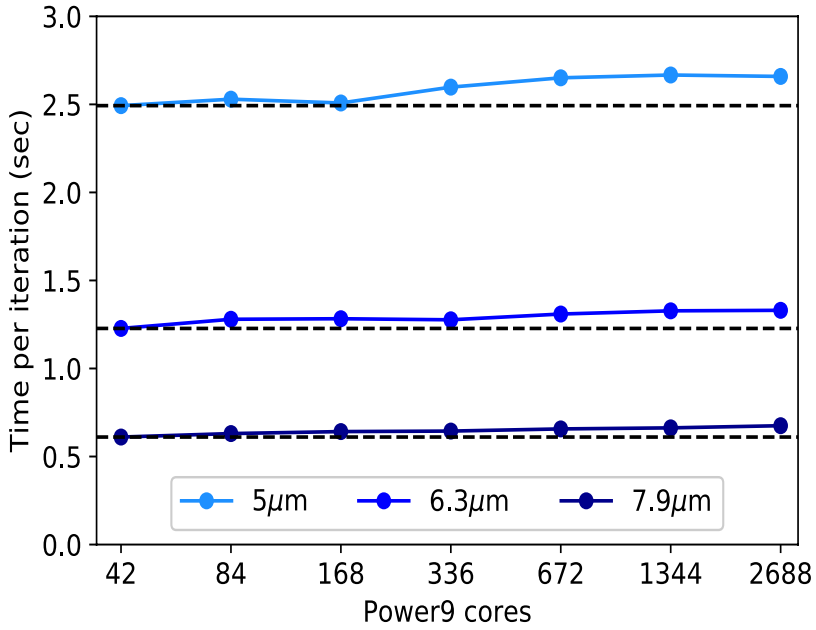
Simulation state

We ensure data-locality and reuse by proposing a cache aware layer scheme (MR-cache-opt)



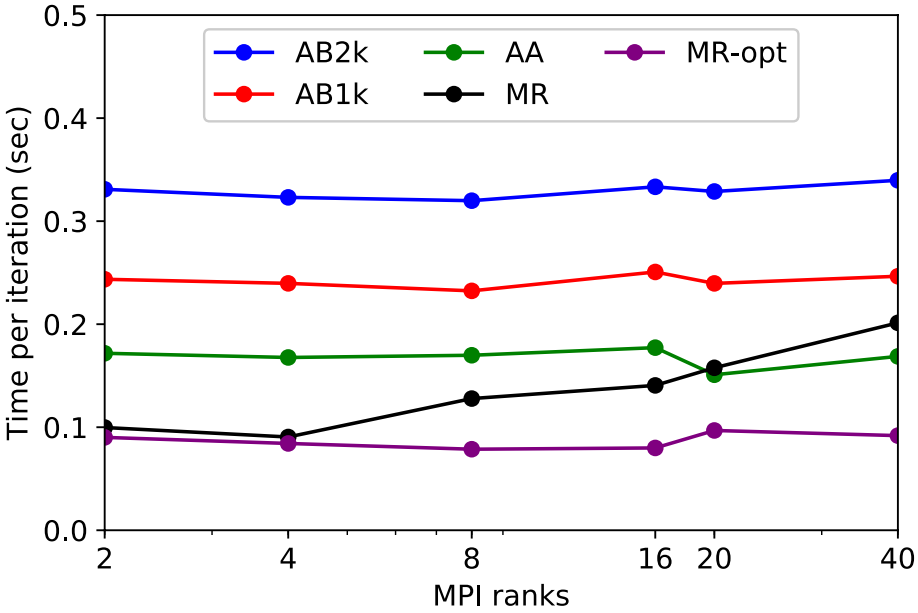
With 74% memory reduction, MR-LBM demonstrates efficient strong and weak scaling analysis on Summit supercomputer



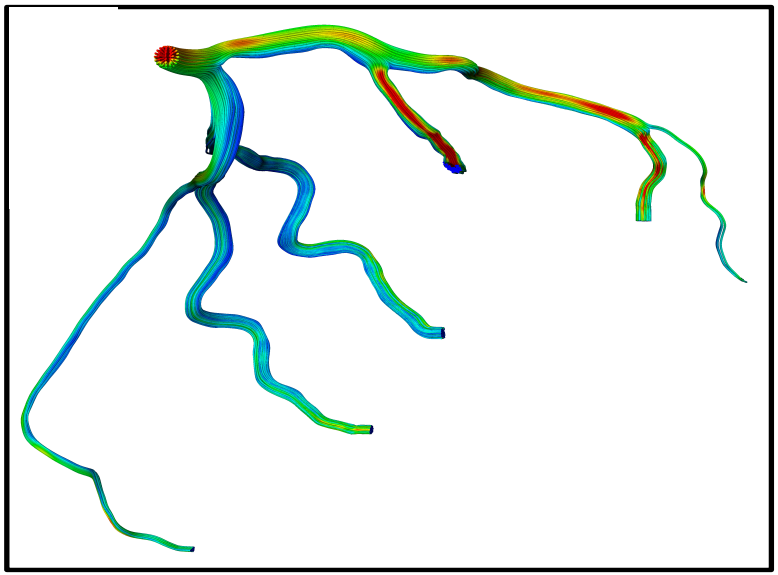


Vardhan et al. Supercomputing 2019

Performance of MR-cache-opt outperforms other distribution patterns and can simulate a complex arterial geometry



MPI + OpenMP configuration on single Broadwell node with 80 hardware threads split evenly among the given number of MPI threads



Velocity streamlines using the layer-based MR algorithm for a complex left coronary arterial geometry

AB2k < AB1k < AA < MR < MR-cache-opt

Phase 1: Impact and Outlook

- The entire simulation state can be represented using only moment data to retrieve second order accurate Navier-Stokes equation, thus accuracy and computations are similar to traditional LBM approach
- This work presents a new scheme for improving both time to solution and the scale of the problem that can fit in memory
- Looking forward to GPUs, this scheme holds immense potential as available memory continues to be a limitation on GPUs

Challenge 2: Need for validation against in vivo clinical measurements

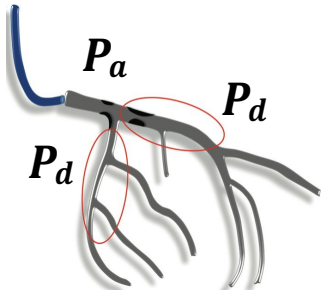
Landmark Clinical Studies: COURAGE NEJM 2007, DEFER Study JACC 2007, FAME NEJM 2009, FAME II NEJM 2012, FAME III AHJ 2015, Clinical outcomes FAME II, Circ. 2019 have led to FFR being the current gold standard for the assessment of coronary artery disease, but remains underused due to procedural cost and time.

Pressure guide-wire

+

Hyperemic drug

=



$$Invasive\ FFR = \frac{P_d}{P_a}$$

Phase 2: Validate our CFD framework through a multicenter, clinical study comparing invasive pressure measurements to calculated values for 200 patients

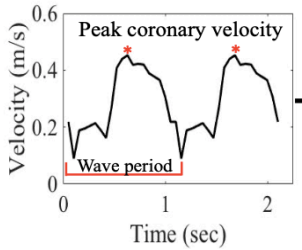
Computing Computational Fluid Dynamics using Coronary Angiography Imaging Data (CFD-CA) FFR

Determine unique coronary pulsatile waveform at hyperemia

Compute hyperemic resistance: SBP, DBP, CO, HR and outlet radii[1-3]

Patient-specific blood flow simulation: hyperemic resistance, velocity waveform, HCT

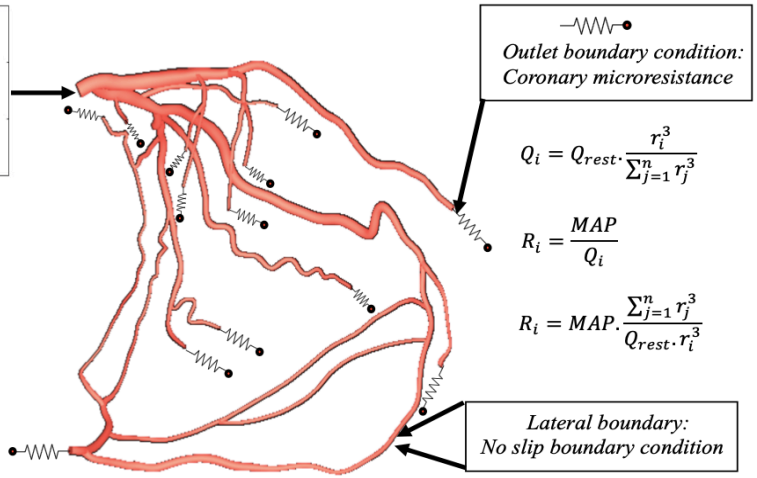
Compute FFR = Pd/Pa

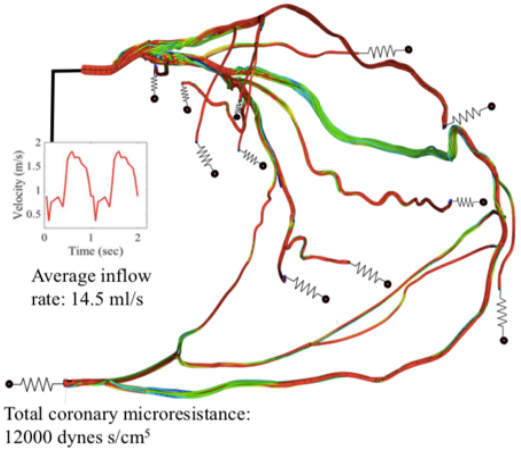


Inlet Boundary Condition: Coronary velocity waveform

$$Average\ coronary\ velocity = \frac{Coronary\ fraction\ .\ CO}{Ostium\ area}$$

$$Wave\ period = BPM/60$$





1. Taylor et al JACC 2013
2. Siasos et al JACC 2018
3. Pirola et al J.Biomech 2017

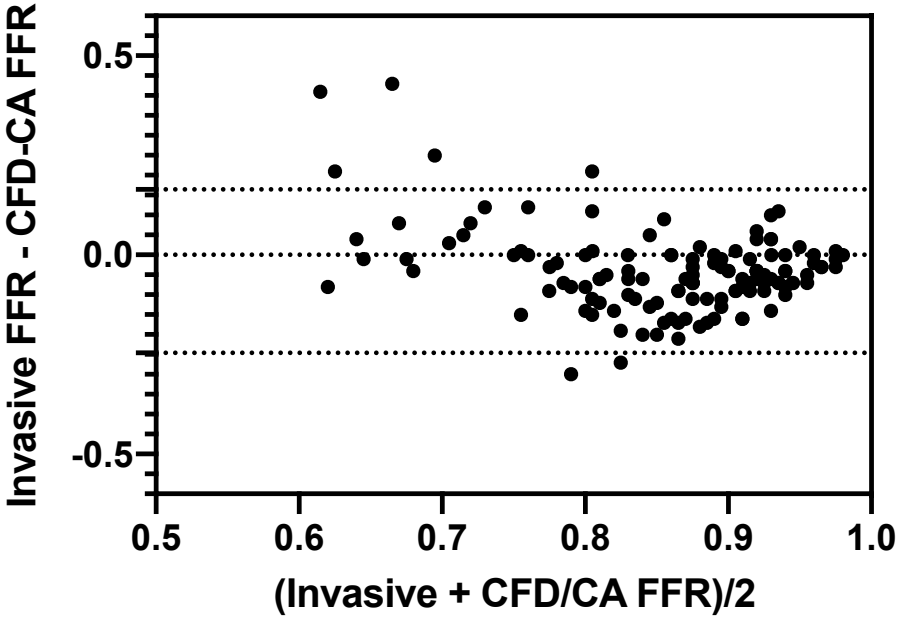
Study design: Multicenter clinical trial

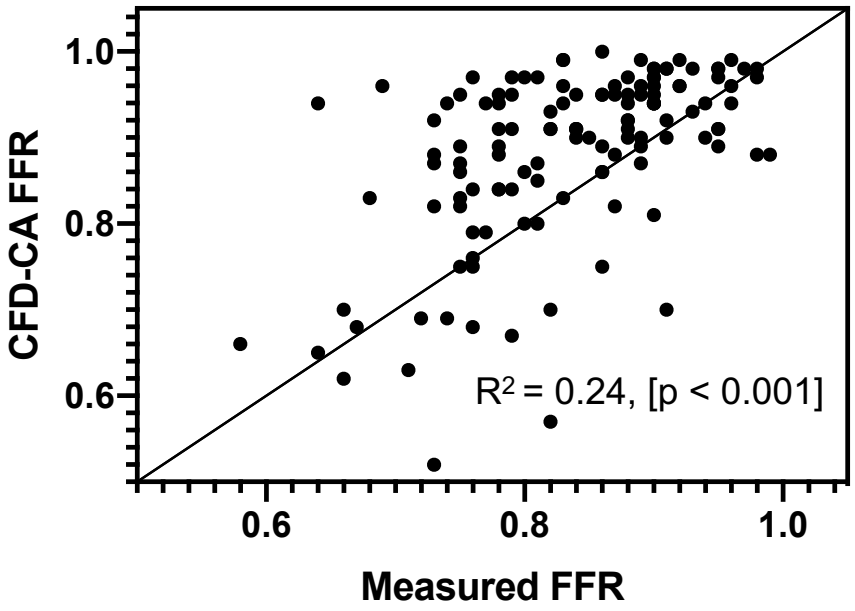
- Clinical trial: Duke Hospital (n=125) and Brigham and Women's Hospital (n=75)

- Methods:
  - Collected 200 patient datasets
  - Reconstructed 194 arterial geometries – validation and modification
  - Completed 180 CFD simulations without incidence

- Results:
  - Compare CFD-CA FFR with invasive FFR
  - Compute hemodynamic quantities
  - Devise novel biomarkers

Preliminary Data: For 130/180 patients, we note encouraging results with good accuracy and moderate correlation





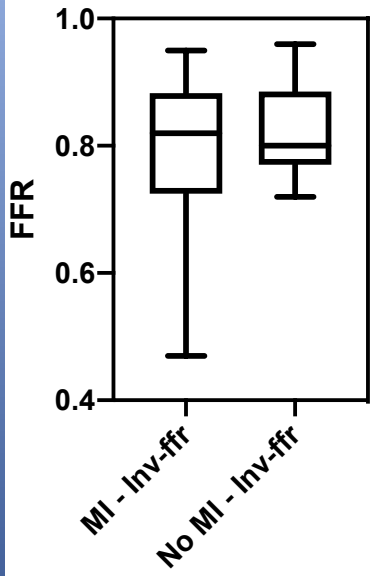
Bias	-0.041
95% Limits of Agreement	0.25 – 0.16

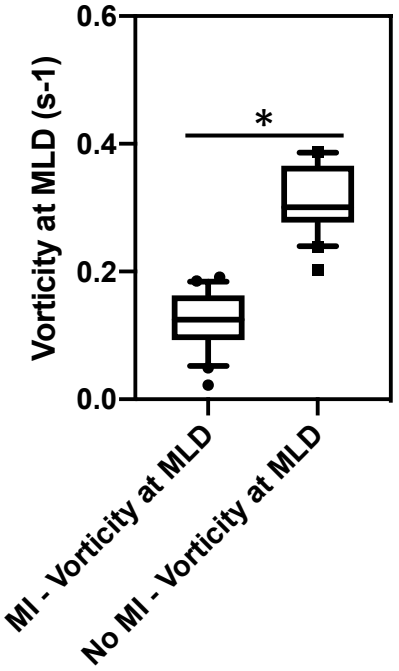
n = 130 BWH = 50/75
Duke = 81/110

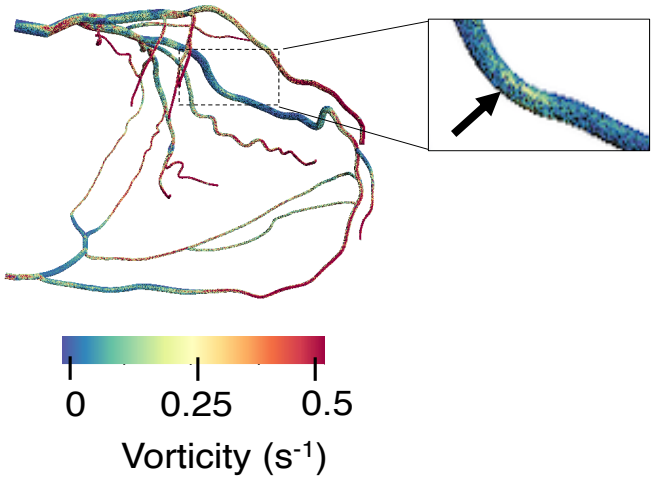
Preliminary Data: Meets expected FDA requirements with improved diagnostic accuracy compared to FFR_{CT}

Statistic	Value	95% CI
Error	10%	
Accuracy	83.08%	75.51% to 89.08%
Sensitivity	83.84%	75.09% to 90.47%
Specificity	80.65%	62.53% to 92.55%
Positive Predictive Value	93.26%	87.03% to 96.61%
Negative Predictive Value	60.98%	49.14% to 71.65%

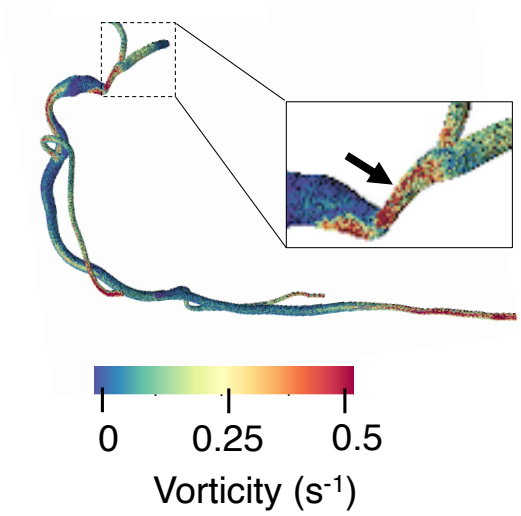
Preliminary Data: Vorticity correlates with FFR and differs between patients with prior myocardial infarction (MI)







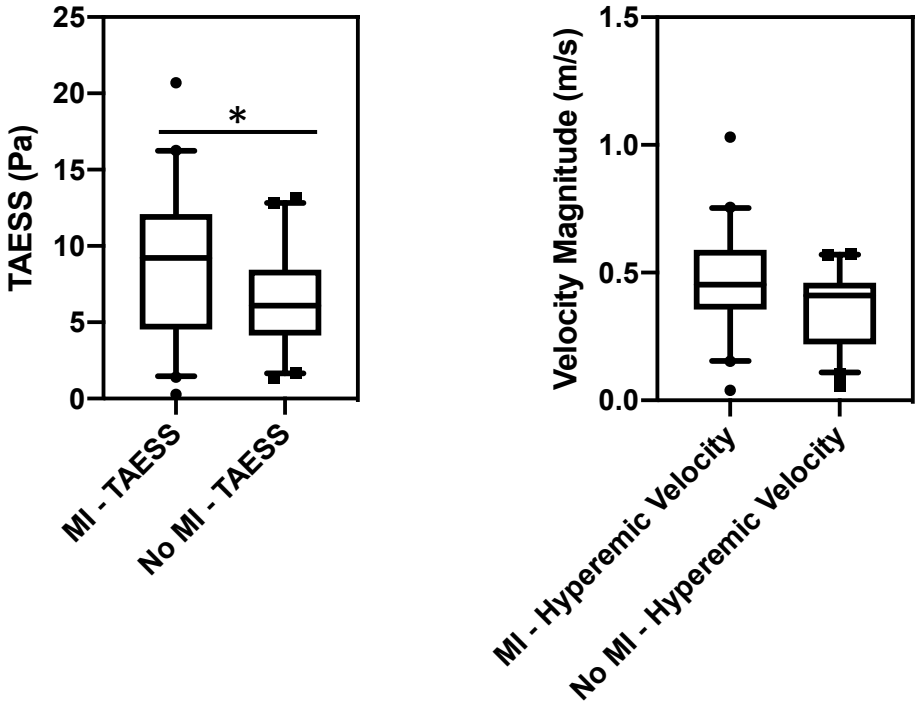
$$\vec{\omega} = \frac{\partial v_z}{\partial y} - \frac{\partial v_y}{\partial z} \quad \frac{\partial v_x}{\partial z} - \frac{\partial v_z}{\partial x} \quad \frac{\partial v_y}{\partial x} - \frac{\partial v_x}{\partial y}$$



N=20 (MI), 20 (No MI)
MI – myocardial infarction
MLD – minimal luminal diameter

Chu et al Atherosclerosis 2018

Preliminary Data: Other intra-arterial hemodynamic metrics differ between MI patients, but do not correlate with FFR



	Vorticity at MLD	TAESS	Hyperemic Velocity
Spearman r	-0.35	-0.008	-0.002
95% confidence interval	-0.61 to -0.032	-0.33 to 0.31	-0.32 to 0.32
P (two-tailed)	0.02*	0.96	0.99

N=20 (MI), 20 (No MI)
MI – myocardial infarction
MLD – minimal luminal diameter

Phase 2: Impact and Outlook

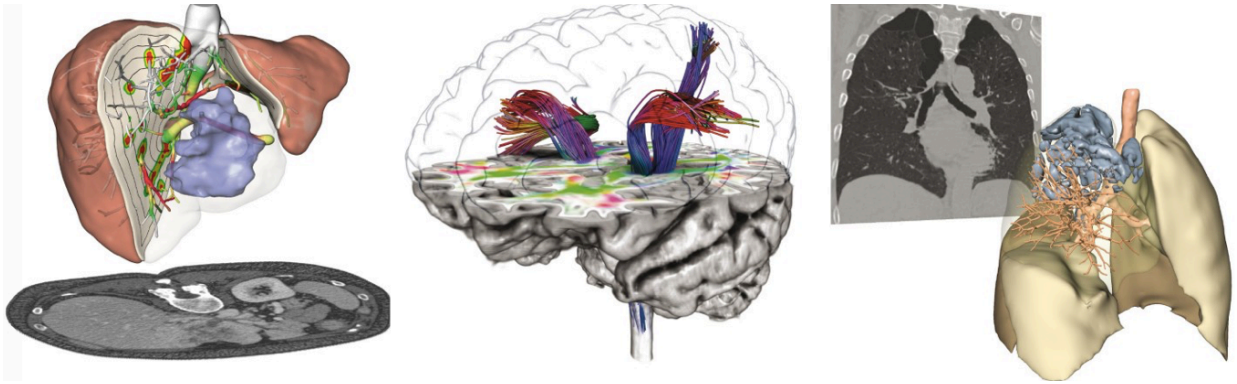
- Completion of this clinical study required millions of compute hours on state-of-art HPC systems. This work establishes the critical step for translating the use of massively parallel simulation-driven diagnostics and treatment planning to the clinic

- CFD vs invasive measurements resulted in 10% average error, 93% positive predictive value and 81% accuracy and successfully meets the current FDA standard for the clinical deployment of CFD-based method to diagnose patients

Challenge 3: Lack of suitable visualization methods for clinicians to intuitively interact with simulation results

Need for VR and simulation-based medical planning system:

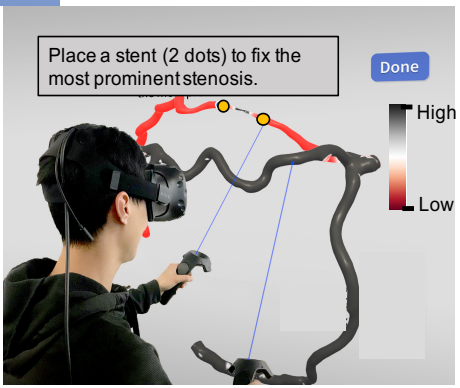
- VR allows 3D viewing and direct interaction with medical imaging data[1-4]
- Clinical decision-making require physiological assessment[5,6]



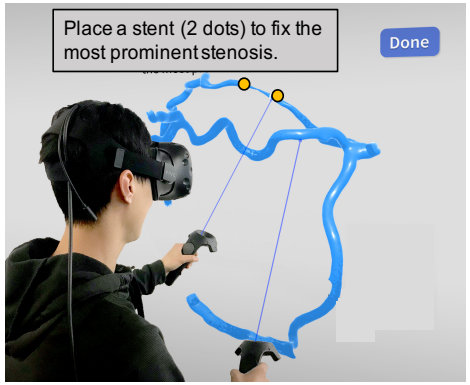
PHASE 3: Assess how physicians interact with large-scale CFD simulation data and present a virtual reality platform for scientific visualization to aid treatment planning

1. Sadeghi et al EurInt 2020
2. Hamacher et al. International neurourology journal (2016)
3. Gosling et al. JACC: Cardiovascular Imaging (2018)
4. Hajek et al. International Conference on Medical Image Computing and Computer-Assisted Intervention. (2018)
5. Patel et al. JACC CI (2020)
6. Fearon et al. Circulation (2018)

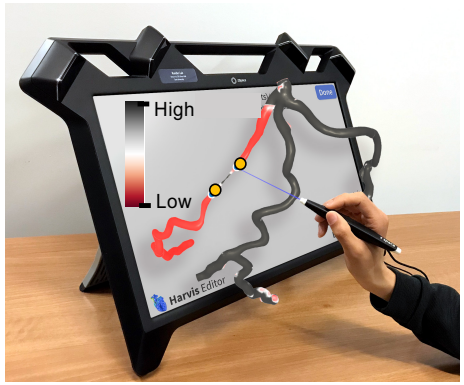
VR-CFD platform for identifying location of stent implantation



Fully Immersive
With WSS



Fully Immersive
No WSS



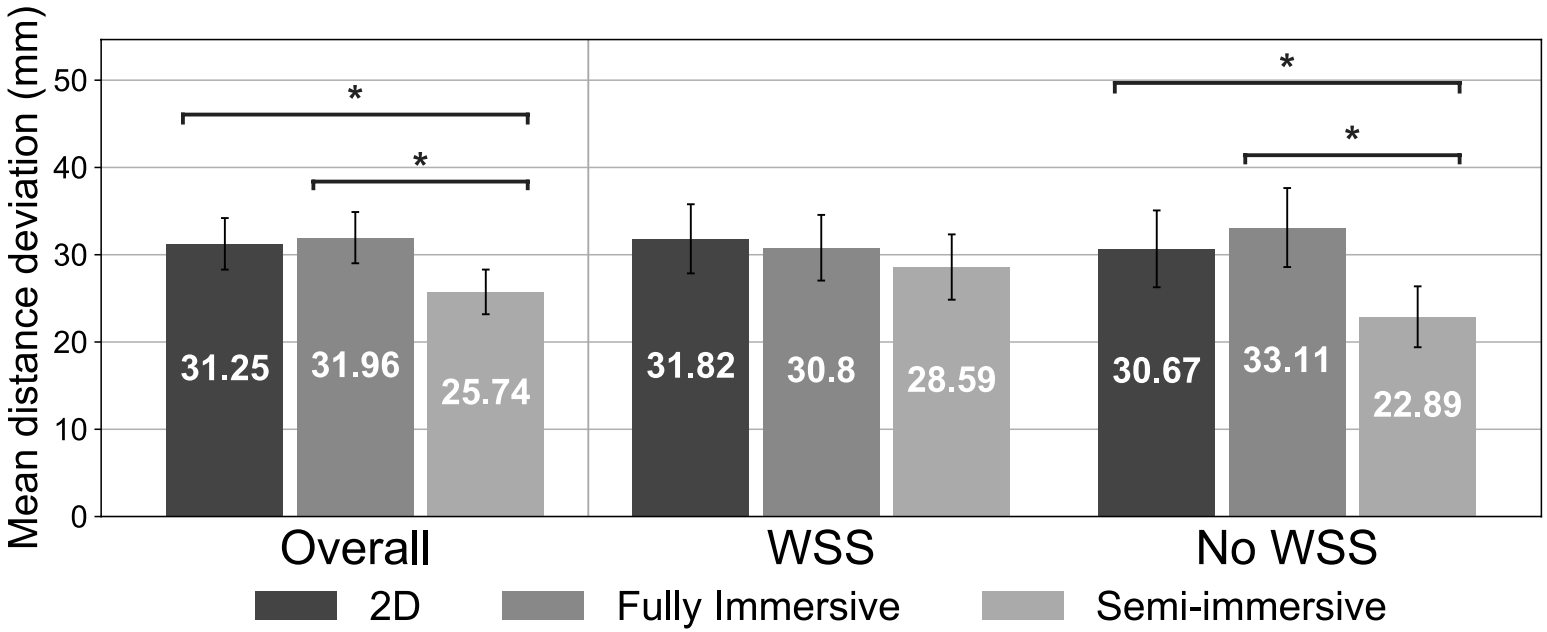
Semi Immersive
With WSS

Semi Immersive
No WSS

- 3 devices: 2D desktop, FI, SI
- VR rendering of 3D arterial geometries (w/ and w/o) CFD with 31 participants, resulting in 558 total trials

Vardhan et al MICCAI 2019

Determining the VR Display Methodology



Overall mean distance deviation for 2D desktop, fully immersive, and semi-immersive devices. Brackets=$p<0.05$. Error bars=SE.

- The lower the distance deviation, the higher the accuracy of stent placement with FI < SI
- Participants use WSS for marking stent location independent of VR device platform

Vardhan et al MICCAI 2019

Phase 3: Impact and Outlook

- In this work, we evaluated the effect of using different VR devices upon treatment planning when viewing both anatomic and CFD simulation data
- Findings demonstrate CFD simulations can guide physicians in treatment planning procedures
- We believe a unified CFD-VR based rehearsal training platform could diminish subjectivity arising from differences in procedural skill sets

Acknowledgements

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