FINAL SCRIPT: APPROVED FOR FILMING

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Title: A Magnetic Resonance Imaging-Based Computational Protocol for Analysis of Plaque Morphology and Hemodynamics in Patients with Carotid Artery Stenosis

Authors and Affiliations:
Drew J. Braet[1,2], Ismael Z. Assi[2,3], Vivek Dandu[2], Meng Lu[4], Siddhant Ranjane[2], Hsu-Lei Lee[4], Jacob Richardson[5], Yibin Xie[4], C. Alberto Figueroa[1,2]

[1]Department of Surgery, University of Michigan
[2]Department of Biomedical Engineering, University of Michigan
[3]School of Medicine, University of Cincinnati
[4]Department of Biomedical Sciences, Cedars Sinai Medical Center
[5]Department of Radiology, University of Michigan

Corresponding Authors:

Drew J. Braet	djbraet@med.umich.edu

Email Addresses for All Authors:

Drew J. Braet	djbraet@med.umich.edu
Ismael Z. Assi	ismael@umich.edu
Vivek Dandu	vdandu@umich.edu
Meng Lu	meng.lu@csmc.edu
Siddhant Ranjane	sranjane@umich.edu
Hsu-Lei Lee	hsu-lei.lee@cshs.org
Jacob Richardson	ricjacob@med.umich.edu
Yibin Xie	yibin.xie@cshs.org
C. Alberto Figueroa	figueroc@med.umich.edu

Author Questionnaire

1. We have marked your project as author-provided footage, meaning you film the video yourself and provide JoVE with the footage to edit. JoVE will not send the videographer. Please confirm that this is correct.

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2. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

3. Software: Does the part of your protocol being filmed include step-by-step descriptions of software usage? **YES, all done**

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When you are ready to submit your video files, please contact our Content Manager, Utkarsh Khare.

Current Protocol Length

Number of Steps: 19
Number of Shots: 35

Introduction

1.1. **Drew Braet:** Our research assesses physiologically-relevant risk factors for plaque embolism and stroke in patients with carotid artery stenosis. We look at how plaque morphology and its hemodynamic environment differ amongst patients with carotid artery stenoses.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:5.7*

What are the most recent developments in your field of research?

1.2. **Drew Braet:** Recent efforts aim to identify stroke predictors in asymptomatic carotid stenosis, focusing on patient-specific risk factors, imaging characteristics, and hemodynamic parameters linked to increased stroke risk.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:5.4.2*

What technologies are currently used to advance research in your field?

1.3. **Drew Braet :** Computational fluid dynamics enables non-invasive, patient-specific analysis of blood flow and is increasingly used alongside magnetic resonance imaging and photon-counting computed tomography angiography to assess carotid plaque structure and composition.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:2.2*

What are the current experimental challenges?

1.4. **Drew Braet :** Current magnetic resonance imaging is limited by long scan times, complex interpretation, and repositioning errors, while computational fluid dynamics suffers from limited patient-specific data and poor model tuning, reducing accuracy.

1.4.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

What significant findings have you established in your field?

1.5. **Drew Braet :** Our group demonstrated that patients with similar internal carotid artery narrowing exhibit distinct hemodynamic profiles, and that bilateral stenosis severity influences each side’s flow, underscoring complex cerebrovascular-hemodynamic interactions.

1.5.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:5.3*

Ethics Title Card

This research has been approved by the Institutional Review Board at the University of Michigan

Protocol

2. Geometric Modeling for Computational Fluid Dynamics in CRIMSON

Demonstrator: Drew Braet

2.1. To begin, launch the CRIMSON *(crimson)* software on a computer system **[1].** Import de-identified DICOM *(die-com)* image data for patient-specific anatomy into CRIMSON by using the import button in the data manager **[2]**.

2.1.1. WIDE: Talent launching the CRIMSON software on the computer.

2.1.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4 0.00-0.30

2.2. Using the **Geometry Modeling** window, select **Vessel Path Editing** and create a vessel tree containing the common carotid artery, external carotid artery, and internal carotid artery **[1]**. ~~Using the **Vessel Path Editing** window, place centreline points along each vessel of interest **[2]**.~~
NOTE: Shot deleted since it is redundant

2.2.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 0.30-0.50

~~2.2.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 0.30-0.50~~

2.3. Begin the common carotid artery centreline at the level of C5 where the PC-MRI flow waveform was obtained **[1]**. Place the internal carotid artery centreline so it ends one to two centimeters distal to the stenosis, matching the PC-MRI waveform location **[2]**. Then place the external carotid artery centreline endpoint proximal to the first-order branches, matching the PC-MRI waveform acquisition location **[3]**.

2.3.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 0.50-01:18

2.3.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 02.30-02:40, 03:10-03:30

2.3.3. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 01:08-02:20

2.4. Now, use the **Vessel Re-slice** *(Vessel-Re-Slice)* window to visualize the centerline and cross-sectional views perpendicular to the centerline, after adding at least two points along each vessel **[1-TXT]**.

2.4.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4 . 02:20-02:40 and 4.00-4.06
TXT: Vessel centerlines may also be imported in CRIMSON in the VTK file format

2.5. Using the same window, add vessel contours to specify the boundaries of the vessel wall **[1].** The left side of the **Vessel Re-Slice** window displays the original image while the right side displays the image gradient for defining contours **[2].**

2.5.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 4.12-04:45

2.5.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 4.45
Video Editor: Please emphasize the top left blurry panel and the top right clearer panel

2.6. Place contours frequently enough to capture vessel curvature and changing geometry without overfitting **[1]**. After defining all contours, use the **Loft** button in the **Vessel Contour Modeling** window to generate a combined three-dimensional solid model via lofting **[2]**.

2.6.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 6.36-06:58

2.6.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 6.09-6.27

2.7. Then use the **Vessel Blending** window to select the fillet algorithm for blending the vessel model into a single solid geometry **[1-TXT]**.

2.7.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 9.29-09:57
TXT: Fillet size: 0.3 - 1 mm

3. Mesh Configuration and Boundary Condition Setup for Computational Fluid Dynamics in CRIMSON

3.1. Open the **Meshing and Solver Setup** window and click the **meshing** button to view meshing options to configure mesh parameters **[1]**. In the **global options** window, set the **global element size** to an absolute value between 0.5 millimeter and 0.75 millimeter **[2]**.

3.1.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 10.14-10.20

3.1.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 10.20-10.38

3.2. Then set **boundary layer** type to **geometric growth**, the **total number of layers** to **3, the first layer thickness** to 0.2 millimeter, and **total layer thickness** of 1 millimeter **[1]**. Then apply curvature refinement to add mesh elements at high-curvature regions such as the stenosis **[2]**.

3.2.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 11.45-12.11

3.2.2. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 10.45-10:57

3.3. Right-click on the mesh and click on the **Mesh Information** button to review mesh metrics including element count, aspect ratios, and distribution **[1]**.

3.3.1. SCREEN: JoVE-2.1.2.-3.3.1.mp4. 11.26-11.33, and 12.20-12.25

3.4. To specify boundary conditions, click on the **Meshing and Solver Setup** window, select the **Solver Setup** icon, then add a boundary condition set using the **BC** icon **[1].** View the boundary conditions currently available in CRIMSON **[2].**

3.4.1. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 0.00-0.19

3.4.2. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 0.20
AND
TEXT ON PLAIN BACKGROUND:
Inlet: Pressure, Prescribed Velocity (Flow Waveform), custom lumped parameter circuit (any arbitrary combination of resistors, capacitors, inductors, pressure nodes, and custom circuit elements defined via a Python script)

Wall: No slip (refers to a rigid or non-deformable wall), Deformable

Outlet: Pressure, RCR, Prescribed Velocity (Flow Waveform), custom lumped-parameter circuit

Video Editor: Please play both shots side by side

3.5. Click the **BC** icon again, select **No Slip** to implement rigid, non-deformable walls and apply this to all walls using the **Apply to all walls** option **[1].** Then select **Prescribed Velocity**, import the previously defined inflow waveform, and map a parabolic velocity profile to the CCA *(C-C-A)* inlet **[2-TXT]**. Similarly, import the ECA *(E-C-A)* pulsatile outflow waveform, mapping a parabolic velocity profile to the ECA outlet **[3]**.

3.5.1. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 0.20-0.38

3.5.2. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 0.42-01:02, 01:11-1.22
TXT: In CRIMSON, the convention is for inlet flows to be negative and outlet flows to be positive.

3.5.3. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 1.22-1.56

3.6. Now click the **BC** icon, choose **RCR** and populate a three-element Windkessel model consisting of proximal resistance, distal resistance, capacitor **[1].** Map the RCR to the ICA outlet based on patient-specific calculations **[2]**.

3.6.1. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 1.56-02:08, 02:16-02:30

3.6.2. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 02:30-2.42
JoVE-3.6.2-TEXT.mp4 00:43-00:49
Video Editor: Please highlight the table in bold on the right side of the screen for Jove-3.6.3-TEXT.mp4
AND
TEXT ON PLAIN BACKGROUND:
Total arterial resistance : $R_T = P_{mean}/Q_T$
where the mean blood pressure $P_{mean} = 1/3\ P_{systolic} + 2/3\ P_{diastolic}$
Q_T is total cardiac flow entering the model

Total arterial compliance : $C_T = (Q_{T,max}-Q_{T,min})/(P_{systolic}-P_{diastolic})*\Delta t$
where $Q_{T,max}$ and $Q_{T,min}$: maximum and minimum values of CCA inflow

Δt : time lapse between these values
Video Editor: Please play both shots side by side

4. **Solver Configuration and Execution for Hemodynamic Modeling**

4.1. To prepare solver parameters, navigate to the **Meshing and Solver** window, click on the **Solver Setup** icon then choose **Solver Parameters [1].** Set the step size to 0.1 millisecond for four cardiac cycles, requires residual to 10^{-4} , and blood density to 1060 kilogram per cubic meter **[2]**.

4.1.1. SCREEN: JoVE-3.4.1.-4.2.1.mp4 2.48-2.54

4.1.2. SCREEN: JoVE-3.4.1.-4.2.1.mp4 3.00-3.16

4.2. Use **Solver Setup** to generate all simulation input files including the flow data, inlet flow at each time step, the mesh and boundary conditions, face on which each boundary condition is applied, the first time step number of the simulation, 3-element Windkessel data, pressure and velocity at every point in the mesh and the instructions for the flowsolver **[1]**.

4.2.1. SCREEN: JoVE-3.4.1.-4.2.1.mp4. 3.16-3.45

4.3. Add the Carreau-Yasuda model into the solver.inp (*Solver-dot-I-N-P)* and add to the simulation files to allow for blood to be modeled as a Non-Newtonian fluid **[1].**

4.3.1. SCREEN: JoVE-4.3.1-4.6.1.mp4. 0.00-0.23

4.4. Now, run Simulation in the **Study** pane of the **Solver Setup** window to run the CRIMSON Navier-Stokes flowsolver. Specify the number of processors in the command window **[1].** ~~Alternatively, if performing simulations on a HPC cluster, transfer all solver files to the cluster and run using 72 to 108 cores **[3]**.~~

4.4.1. SCREEN: JoVE-4.3.1-4.6.1.mp4. 0.36-0.50

~~4.4.2. SCREEN: JoVE-4.3.1-4.6.1.mp4.~~

~~4.4.3. SCREEN: JoVE-4.3.1-4.6.1.mp4.~~

4.5. When the solver starts running, the output file histor.dat *(His-tor-dot-Dat)* will be printed in the command line and saved in a new directory, "n-procs-case" *(N-Procks-Case)***.** Use the linux prompt "tail -f histor.dat" *(tail-minus-F-His-tor-Dat)* to observe the file in real time **[1].**

4.5.1. SCREEN: JoVE-4.3.1-4.6.1.mp4. 0.54-01.00

4.6. The first column of the file corresponds to time step, the second column is the elapsed time, the third column is the non-linear residual, and the fourth column is the log residual value **[1]**.

4.6.1. SCREEN: JoVE-4.3.1-4.6.1.mp4. 1.00-1.28

Results

5. Results

5.1. A high-quality mesh with low aspect ratio elements was generated to accurately represent the carotid artery bifurcation geometry **[1]**.

5.1.1. LAB MEDIA: Figure 1A. *Video editor: Emphasise the "Mesh" panel*

5.2. A representative velocity profile across the carotid bifurcation and ICA stenosis was simulated **[1],** showing a maximum flow velocity of approximately 275 centimeters per second at peak systole across the stenosis **[2]**.

5.2.1. LAB MEDIA: Figure 2.

5.2.2. LAB MEDIA: Figure 2. *Video editor: Highlight the peak of the velocity curve on the left graph.*

5.3. Pressure mapping showed negligible pressure gradient across the stenosis in one case, with proximal and distal pressures nearly overlapping throughout the cardiac cycle **[1]**. In a contrasting case, pressure proximal to the stenosis was significantly higher than distal pressure, revealing a prominent pressure drop **[2]**.

5.3.1. LAB MEDIA: Figure 3A. *Video editor: Highlight both red and blue pressure curves on the lower graph.*

5.3.2. LAB MEDIA: Figure 3B. *Video editor: Highlight the red and blue curves on the lower graph*

5.4. Wall shear stress was low across the bifurcation in the non-stenotic model, especially in the outer walls of the internal and external carotid arteries **[1]**. In the stenotic model, high wall shear stress was concentrated at the internal carotid artery stenosis **[2]**.

5.4.1. LAB MEDIA: Figure 4A. *Video editor: Highlight the blue-colored regions labeled "Low WSS".*

5.4.2. LAB MEDIA: Figure 4B. *Video editor: Highlight the red-colored region labeled "High WSS".*

5.5. Oscillatory shear index mapping showed lesion-associated OSI *(O-S-I)* values before surgery were lower compared to post-operative values **[1]**.

5.5.1. LAB MEDIA: Figure 5A and B. *Video editor: Highlight red patches both anterior and posterior pre-operative views.*

5.6. qMatch imaging identified intraplaque hemorrhage through hyperintense signal on T1-weighted imaging **[1]** and lowered values on the T1 map **[2]**.

5.6.1. LAB MEDIA: Figure 6B. *Video editor: Highlight the bright region within the* *dashed yellow outline*

5.6.2. LAB MEDIA: Figure 6E. *Video editor: Highlight the dark-colored region within the same outline in the T1 map.*

5.7. Calcified plaque was identified by consistently hypointense signal on dark blood, T1-weighted, and T2-weighted sequences **[1].**

5.7.1. LAB MEDIA: Figure 7A-C. *Video editor: Highlight the dark region within the dashed orange circle in A-C*

Pronunciation Guide:

1. Magnetic resonance imaging
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/magnetic%20resonance%20imaging
- **IPA (American):** /mæɡˈnɛtɪk ˈrɛzənəns ˈɪmɪdʒɪŋ/
- **Phonetic Spelling:** mag-NET-ik REZ-uh-nuhns IM-ij-ing

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2. Hemodynamics
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/hemodynamics
- **IPA (American):** /ˌhiːmoʊdaɪˈnæmɪks/
- **Phonetic Spelling:** hee-moh-dy-NAM-iks

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3. Carotid
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/carotid
- **IPA (American):** /kəˈrɑːtɪd/
- **Phonetic Spelling:** kuh-RAH-tid

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4. Stenosis
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/stenosis
- **IPA (American):** /stəˈnoʊsɪs/
- **Phonetic Spelling:** stuh-NOH-sis

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5. Computational fluid dynamics
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/computational
- **IPA (American):** /ˌkɑːmpjuˈteɪʃənəl ˈfluːɪd daɪˈnæmɪks/
- **Phonetic Spelling:** kom-pyoo-TAY-shuh-nuhl FLOO-id dy-NAM-iks

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6. Anatomy
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/anatomy
- **IPA (American):** /əˈnætəmi/
- **Phonetic Spelling:** uh-NAT-uh-mee

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7. Centreline
- **Pronunciation link:** No confirmed link found
- **IPA (American):** /ˈsɛntərˌlaɪn/
- **Phonetic Spelling:** SEN-ter-lyn

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8. Waveform
- **Pronunciation link:** https://www.merriam-webster.com/dictionary/waveform
- **IPA (American):** /ˈweɪvˌfɔːrm/
- **Phonetic Spelling:** wayv-form

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9. Oscillatory

- **Pronunciation link:** https://www.merriam-webster.com/dictionary/oscillatory
- **IPA (American):** /ˈɑːsəˌleɪtɔːri/ or /ˈɑːsɪləˌtɔːri/
- **Phonetic Spelling:** AH-suh-luh-tor-ee or AH-sil-uh-tor-ee

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10. Windkessel

- **Pronunciation link:** No confirmed link found
- **IPA (American):** /ˈvɪndˌkɛsəl/ (from German origin)
- **Phonetic Spelling:** VIND-kess-uhl