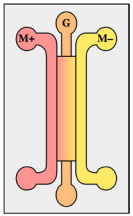
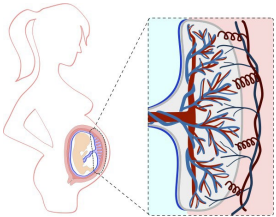
Engineering Human Pregnancy In Vitro and In Silico

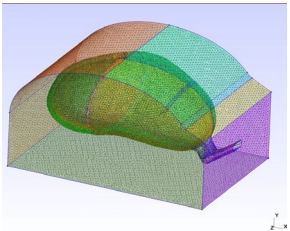
Michelle L. Oyen

Biomedical Engineering, Wayne State University, Detroit

NIH ACRWH October 8, 2024

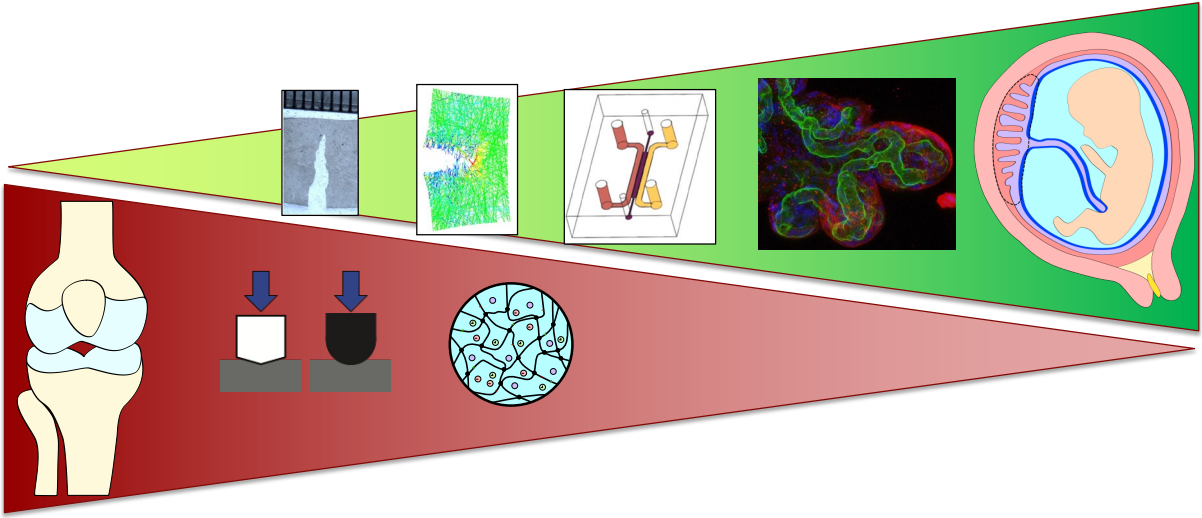






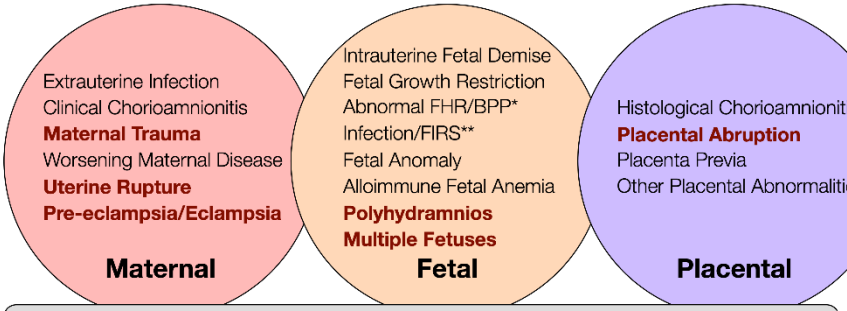
My Research Career Path

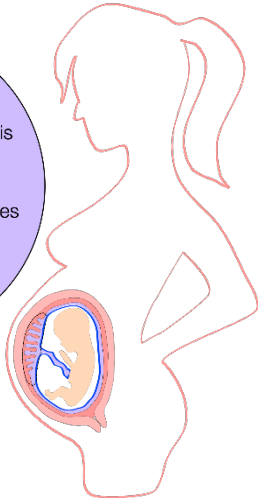
WAYNE STATE UNIVERSITY



Preterm Birth as an Engineering Challenge

WAYNE STATE UNIVERSITY

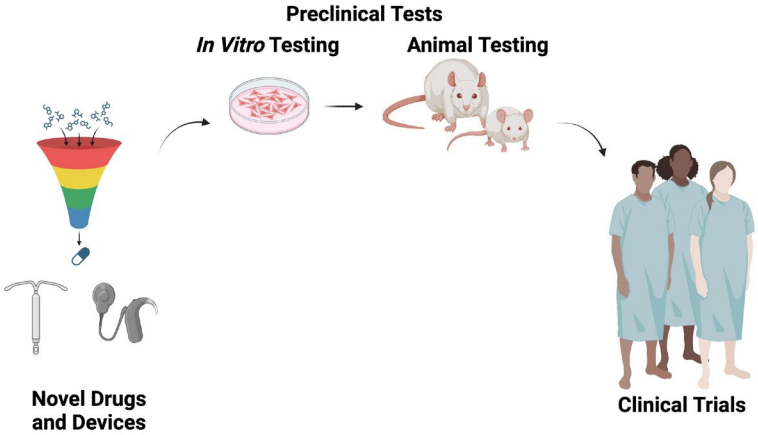




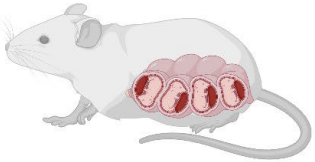
* Fetal Heart Rate/Biophysical Profile; ** Fetal Inflammatory Response Syndrome; ^Preterm Pre-labor Rupture of Membranes

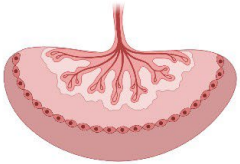
Adapted, by M.L. Oyen, from Villar et al. (2012) *AJOG* doi: 10.1016/j.ajog.2011.10.866

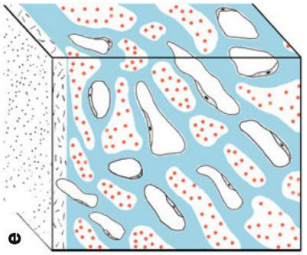
Traditional Route for FDA Drugs and Devices

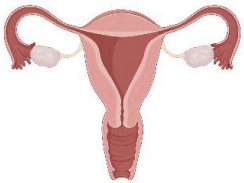


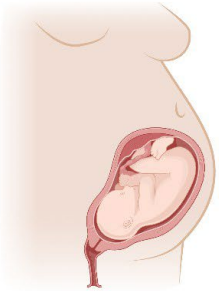
No Mammals Represent *Human* Pregnancy

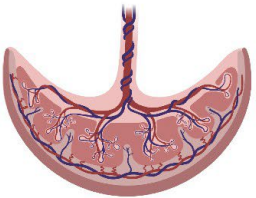


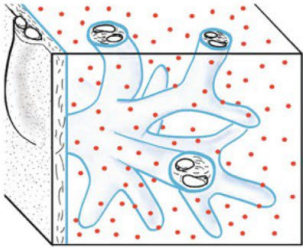






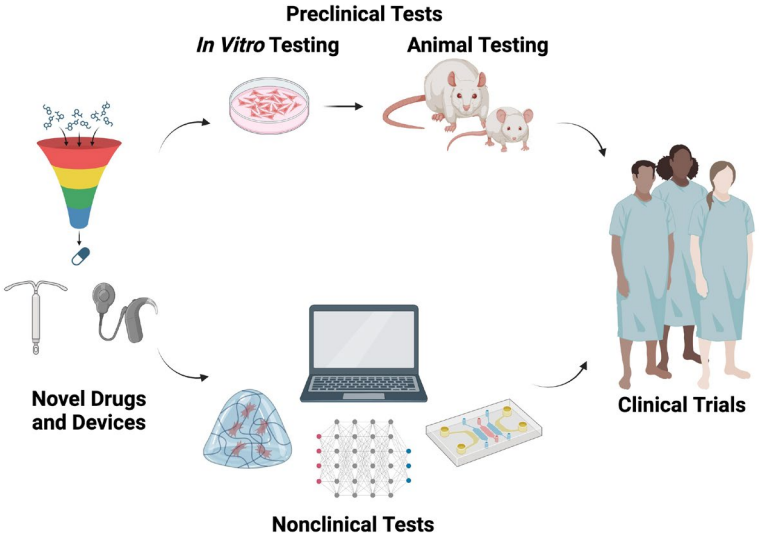




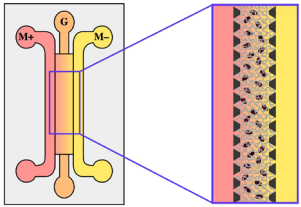


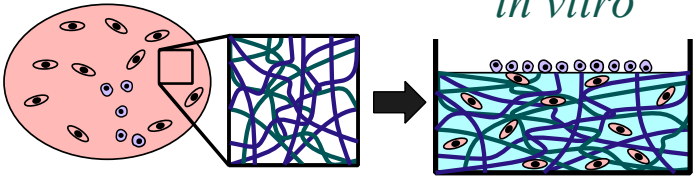
Benirschke's Pathology of the Human Placenta (2022).

FDA Modernization Act 2.0 (Dec. 2022)



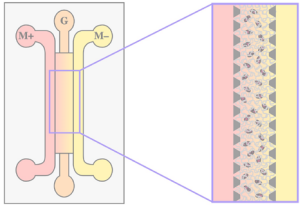
Transform Maternal Health via Engineering

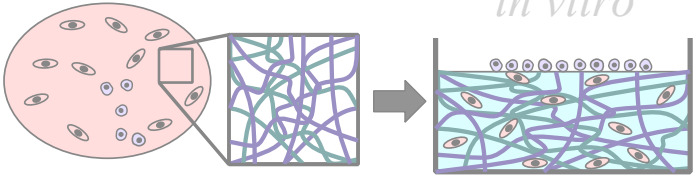




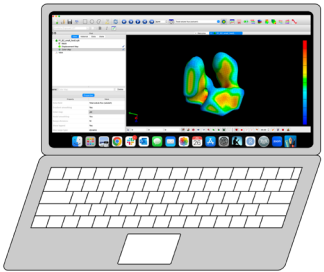
Transform Maternal Health via Engineering

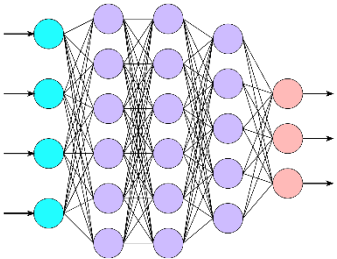
WAYNE STATE UNIVERSITY





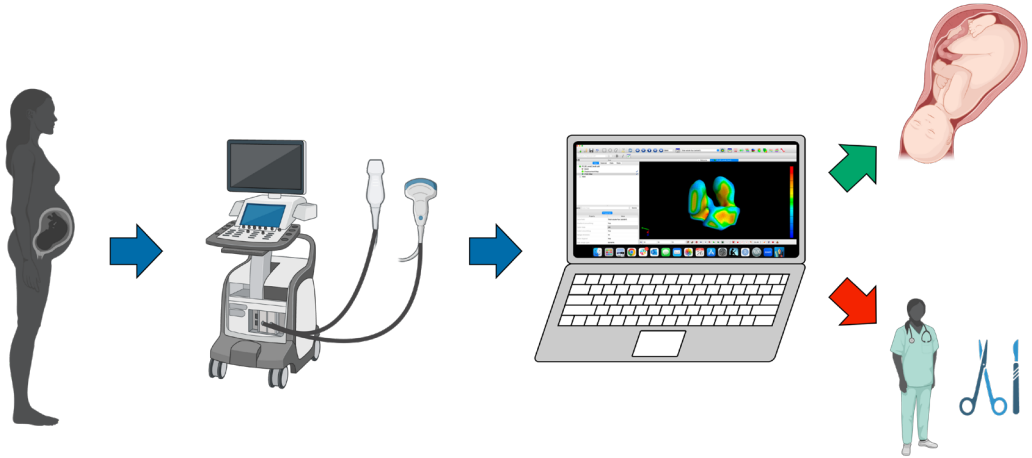
in vitro





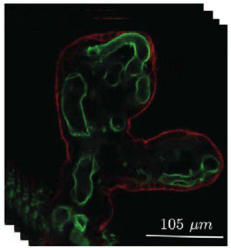
in silico

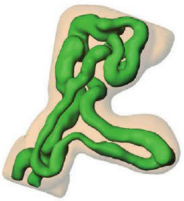
Clinical Engineering Decision Tree

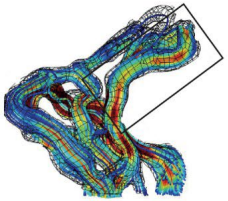


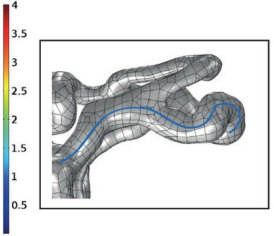
Enabling Technology: Real-Time Models

WAYNE STATE UNIVERSITY

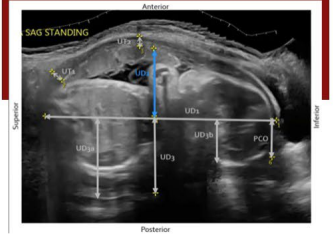




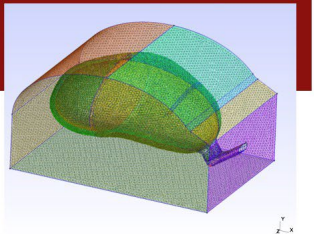




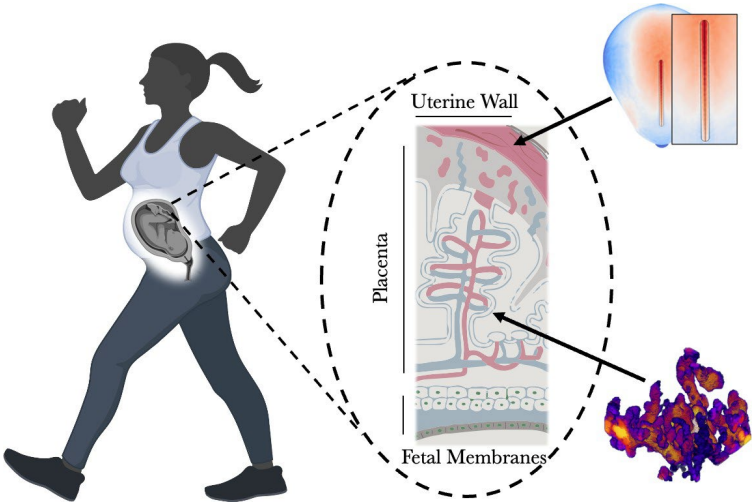
Clinical or Research Image



Patient-Specific Computational Models

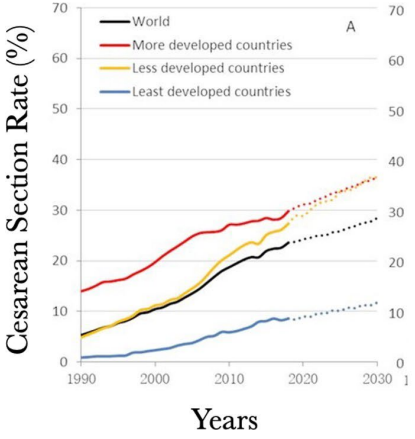


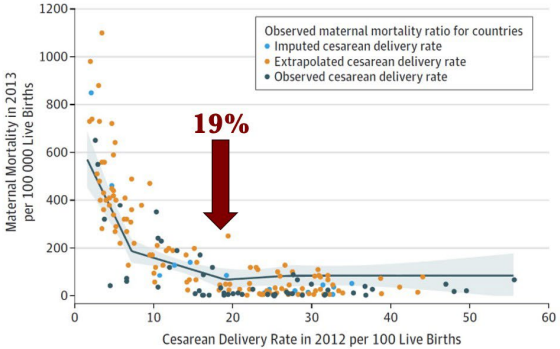
Pregnancy Digital Twin Beginnings



1. C-section scar rupture risk
2. Placenta transport function

Global C-section Rates are Increasing...

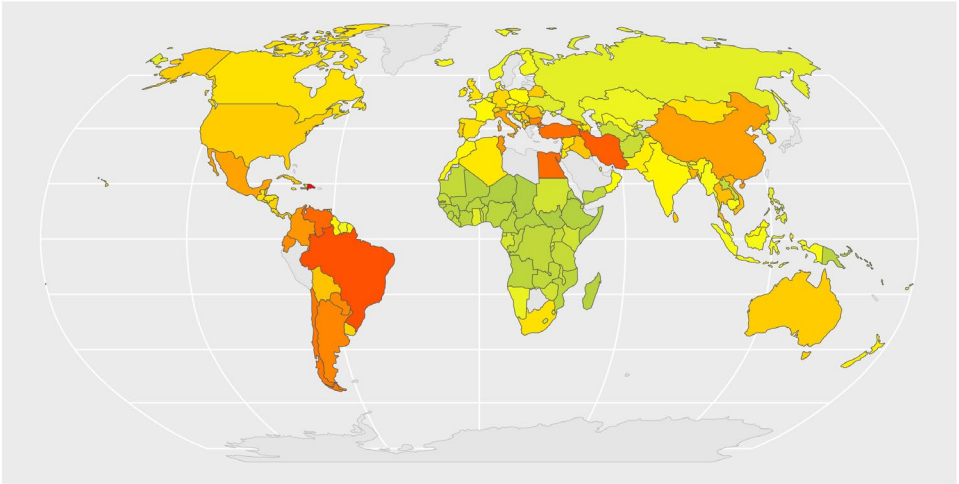




A C-section rate of up to 19 percent improves maternal and neonatal mortality rates, but that benefit plateaus after 19 percent.
JAMA

Betran et al., BMJ Global Health, 2021; Molina et al., JAMA, 2015.

Global C-section Rates are Increasing...



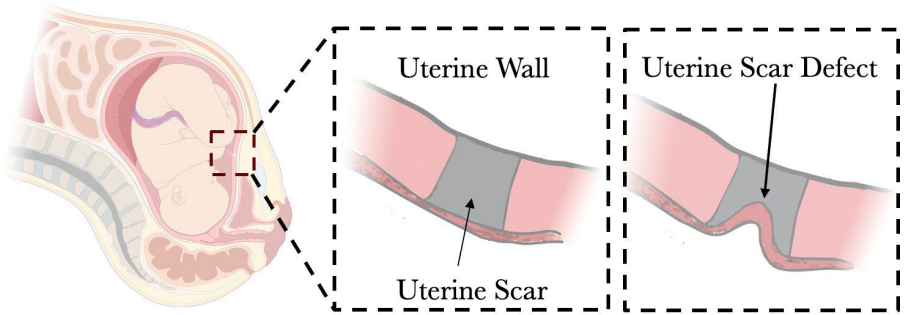
Unicef data, % of births, yellow = 19%

C-sections Have Long-term Consequences

WAYNE STATE UNIVERSITY

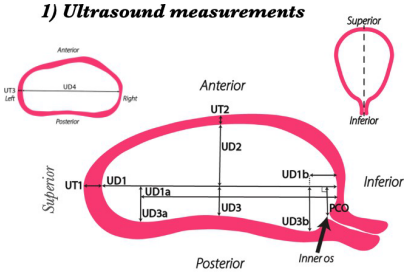
The danger is acute in future pregnancies:

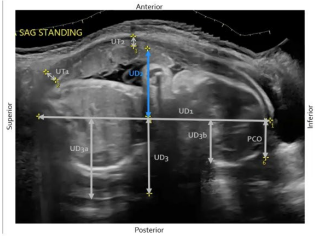
There is both a risk of scar rupture and a risk of implantation at the scar site, leading to ectopic pregnancy or placenta accreta.

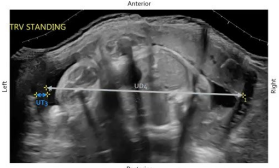


C-section Digital Twin Methods

WAYNE STATE UNIVERSITY







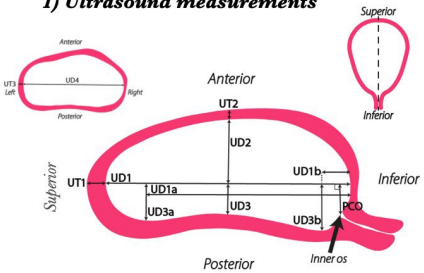
MYERS SOFT TISSUE LAB

Louwagie, E.M. et al., PloS one, 2021

C-section Digital Twin Methods

WAYNE STATE UNIVERSITY

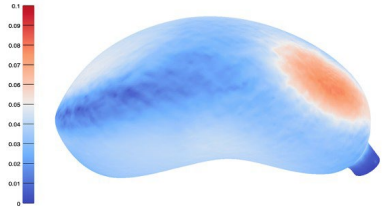
1) Ultrasound measurements



2) 3D Model

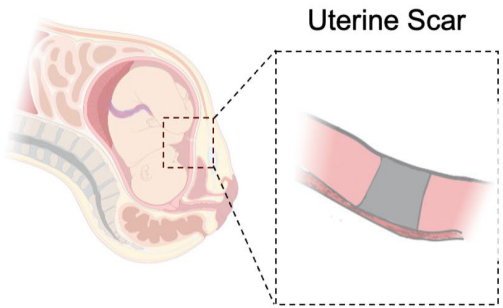
3) Discretize into elements

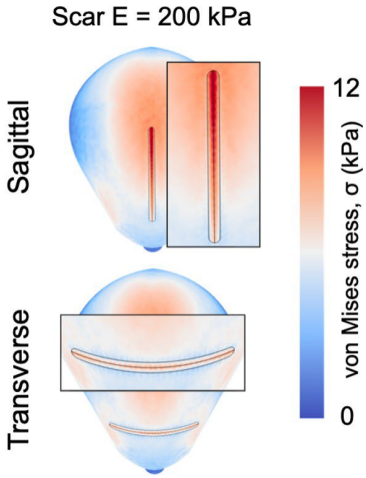
4) Finite Element Model



Louwagie, E.M. et al., PloS one, 2021

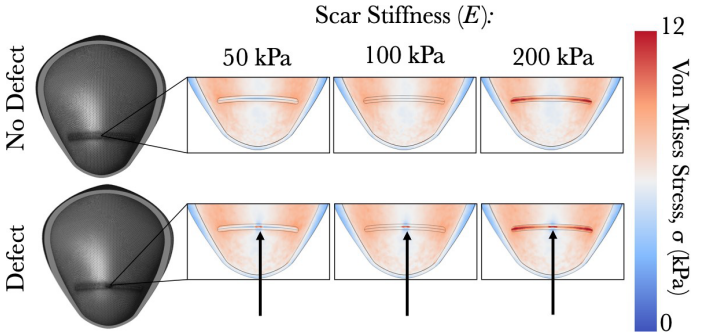
C-section Digital Twin Third Trimester

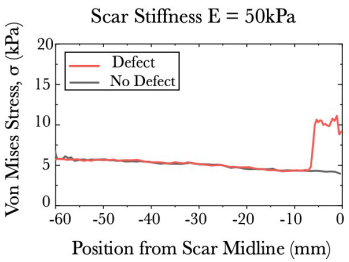




Scott et al. 2024, DOI: 10.1101/2023.11.03.565565

C-section Digital Twin Third Trimester





Scott et al. 2024, *in preparation*

C-section Digital Twin Second Trimester

WAYNE STATE UNIVERSITY

Reproducibility of assessment of full-dilatation Cesarean section scar in women undergoing second-trimester screening for preterm birth

A. BANERJEE[1,2], Z. AL-DABBACH[1], F. E. BREDAKI[1], D. CASAGRANDI[1,2], A. TETTEH[1], N. GREENWOLD[1], M. IVAN[1,2], D. JURKOVIC[2,3], A. L. DAVID[1,2,4] and R. NAPOLITANO[1,2]

[1]*Fetal Medicine Unit, Elizabeth Garrett Anderson Wing, University College London Hospital, London, UK;* [2]*Elizabeth Garrett Anderson Institute for Women's Health, University College London, London, UK;* [3]*Department of Gynaecology, Elizabeth Garrett Anderson Wing, University College London Hospital, London, UK;* [4]*National Institute for Health Research, University College London Hospitals Biomedical Research Centre, London, UK*

Banerjee, A., et al. "Reproducibility of assessment of full-dilatation Cesarean section scar in women undergoing second-trimester screening for preterm birth." *Ultrasound in Obstetrics & Gynecology* 60.3 (2022): 396-403.

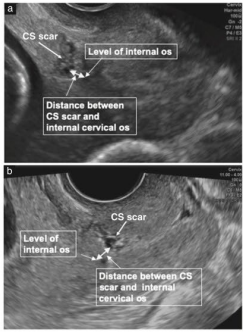


Figure 1 Grayscale ultrasound images showing measurement of the distance from the Cesarean section (CS) scar to the internal cervical os in the sagittal plane in a case with a CS scar above the cervix (a) and a case with a CS scar in the cervix (b). The level of the internal os was determined using color flow mapping of the uterine artery.

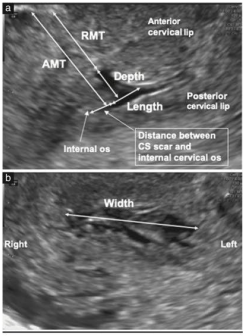
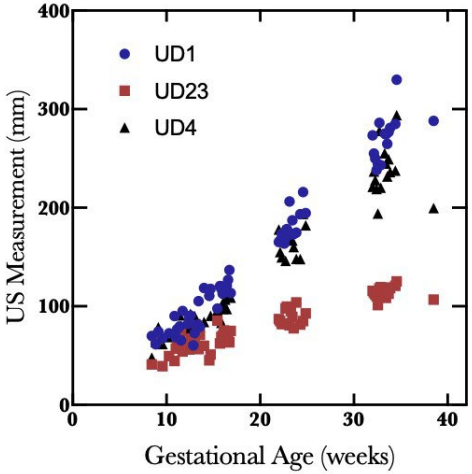
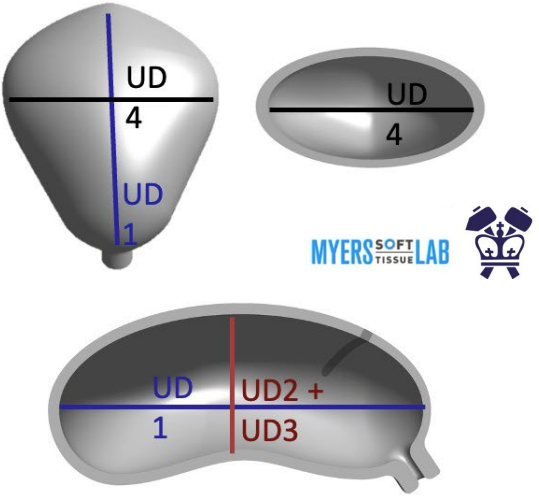


Figure 2 (a) Measurements of Cesarean section (CS) scar niche dimensions in the sagittal plane, including its largest length, largest depth, residual myometrial thickness (RMT) and adjacent myometrial thickness (AMT). (b) Largest width of the CS scar niche measured in the transverse plane.

Banerjee et al., Ultrasound in Obstet. Gynecol (2022)

C-section Digital Twin Second Trimester



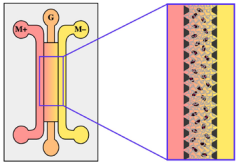


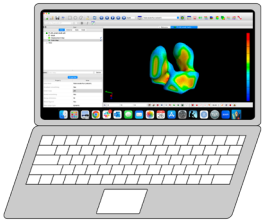
Louwagie et al., PloS one (2021)

Pregnancy and Engineering: Challenges

WAYNE STATE UNIVERSITY

1. ***Interdisciplinary*** collaboration less common in Ob/Gyn than other fields (cancer, orthopedics, cardiovascular).

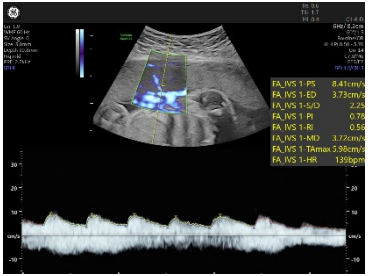


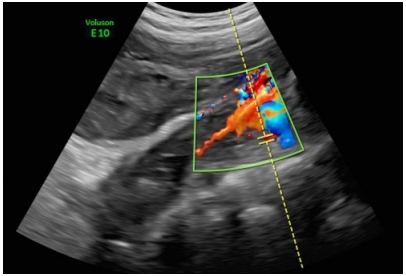


Pregnancy and Engineering: Challenges

WAYNE STATE UNIVERSITY

1. ***Interdisciplinary*** collaboration less common in Ob/Gyn than other fields (cancer, orthopedics, cardiovascular).
2. We need ***training image sets*** for AI/ML.

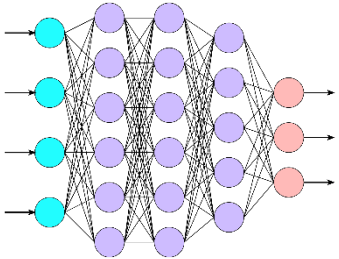




Pregnancy and Engineering: Challenges

WAYNE STATE UNIVERSITY

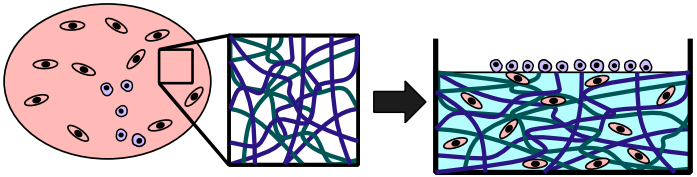
1. ***Interdisciplinary*** collaboration less common in Ob/Gyn than other fields (cancer, orthopedics, cardiovascular).
2. We need ***training image sets*** for AI/ML.
3. We need a mechanism to ethically harness the ***big data*** "natural experiments" in women's health.

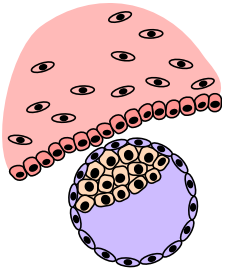


Pregnancy and Engineering: Challenges

WAYNE STATE UNIVERSITY

1. ***Interdisciplinary*** collaboration less common in Ob/Gyn than other fields (cancer, orthopedics, cardiovascular).
2. We need ***training image sets*** for AI/ML.
3. We need a mechanism to ethically harness the ***big data*** "natural experiments" in women's health.
4. We need human cell sources and consistent biomimetic tissue scaffolds for ***in vitro studies***.





Pregnancy and Engineering: Challenges

WAYNE STATE UNIVERSITY

1. ***Interdisciplinary*** collaboration less common in Ob/Gyn than other fields (cancer, orthopedics, cardiovascular).
2. We need ***training image sets*** for AI/ML.
3. We need a mechanism to ethically harness the ***big data*** "natural experiments" in women's health.
4. We need human cell sources and consistent biomimetic tissue scaffolds for ***in vitro studies***.
5. Better diagnosis shifts the need to better intervention and prevention but only with advances in ***mechanistic understanding***.

Acknowledgements

Some figures created in part with BioRender.com

Oyen Lab
Adrienne Scott, PhD
Samantha Zambuto, PhD
Patrick Yang
Samyuktha Kolluru
Amelia Hines
Tari Santosa
Abir Hamdaoui
Sudha Anilkumar
Deadalus Chen

Collaborators
Anthony Odibo, MD
Abigail Arter
Caroline Fosher
Ulugbek Kamilov, PhD

Columbia University:
Kristin M. Myers, Erin M. Louwagie, + team

University College London:
Anna David, MD,
Raffaele Napolitano, MD, + team

Funding: