Artificial Intelligence in Bioelectronic Medicine and Point-of-Care Clinical Applications

Theo Zanos, Ph.D.
Associate Professor
Head, Division of Health AI @ Northwell
Head, Neural & Data Science Lab
Institute of Health System Science
Institute of Bioelectronic Medicine

Feinstein Institutes for Medical Research
Northwell Health®

Neuraldatascience.org

Neural & Data Science Lab

Lab Members

Todd Levy, MS
Shubham Debnath, PhD
Avantika Vardhan, PhD
Michael Scheid, PhD
Hardik Patel, MD
Fylaktis Fylaktou
Lucas Cang
Rebecca Steinberg
Viktor Toth, MS
Ioannis Koulas, MD

National Institutes of Health — Turning Discovery Into Health

National Institute of Nursing Research

SPARC

isansys

TIVIC HEALTH

Collaborators

Stavros Zanos, MD PhD
Kevin Tracey, MD
Jamie Hirsch, MD
Alex Makhnevic, MD
Douglas Barnaby, MD
Stuart Cohen, MD
Paul Chung, MD
Beth Friedmann, RN
Marc Paradis, MS
Matt Barish, MD
Lawrence Lau, MD
Ciaran Friel, PhD
Lance Becker, MD
Tom McGinn, MD
Karina Davidson, PhD

Neuraldatascience.org
mlmd.org

Why Health AI?

nature medicine
REVIEW ARTICLE
https://doi.org/10.1038/s41591-022-01981-2
Check for updates

Multimodal biomedical AI

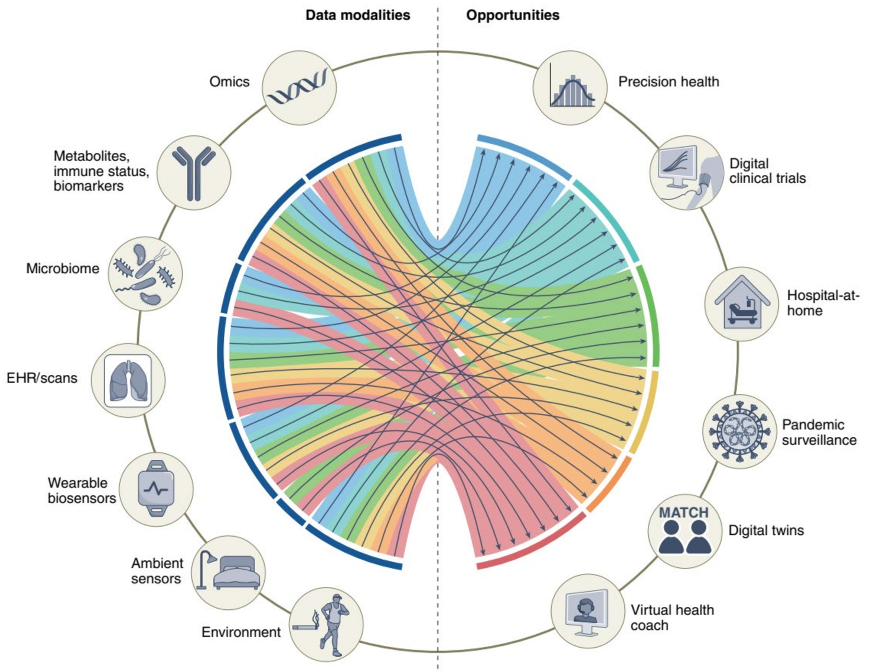
Julián N. Acosta[1], Guido J. Falcone[1], Pranav Rajpurkar[2,4] and Eric J. Topol[3,4]

"The **promise** of artificial intelligence in medicine is to provide composite, panoramic views of individuals' medical data; to improve decision making; to avoid errors such as misdiagnosis and unnecessary procedures; to help in the ordering and interpretation of appropriate tests; and to recommend treatment."
- Eric Topol, MD

"While AI in medicine will not come all at once, early adopters of AI in their practices will be ready to be future leaders in health care."
- Bibb Allen, MD

FDA has now cleared more than 500 healthcare AI algorithms

Dave Fornell | *February 06, 2023* | *Artificial Intelligence*



"AI won't replace doctors, doctors that use AI will replace those that don't."

Feinstein Institutes for Medical Research
Northwell Health

Setting expectations

State of AI in Healthcare

- Thousands of startups
- Tens of thousands of publications
- Billions invested
- But only <u>few hundred</u> RCTs to date

But…

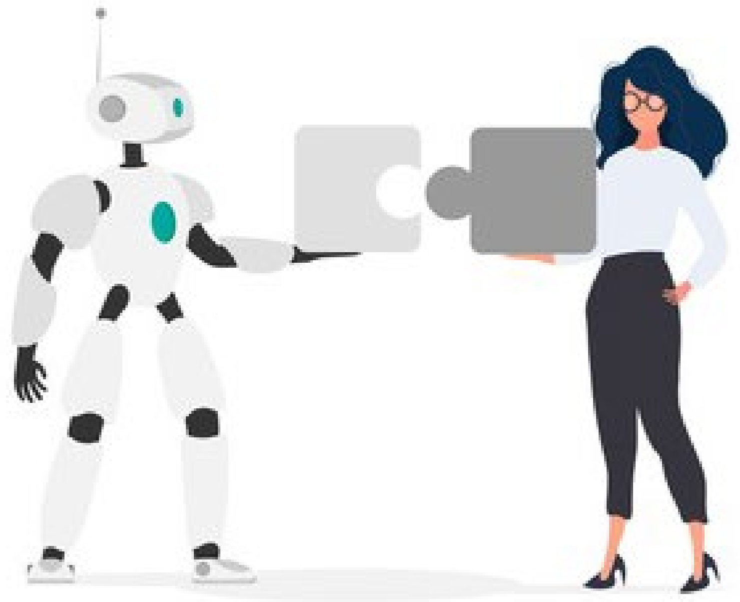
- Current DL/AI models relatively new (~10 years), with healthcare AI models trailing uptake of other industries
- ~87% of developed AI/ML models in any industry never make it into production

JAMA Network | Open

Original Investigation | Health Informatics

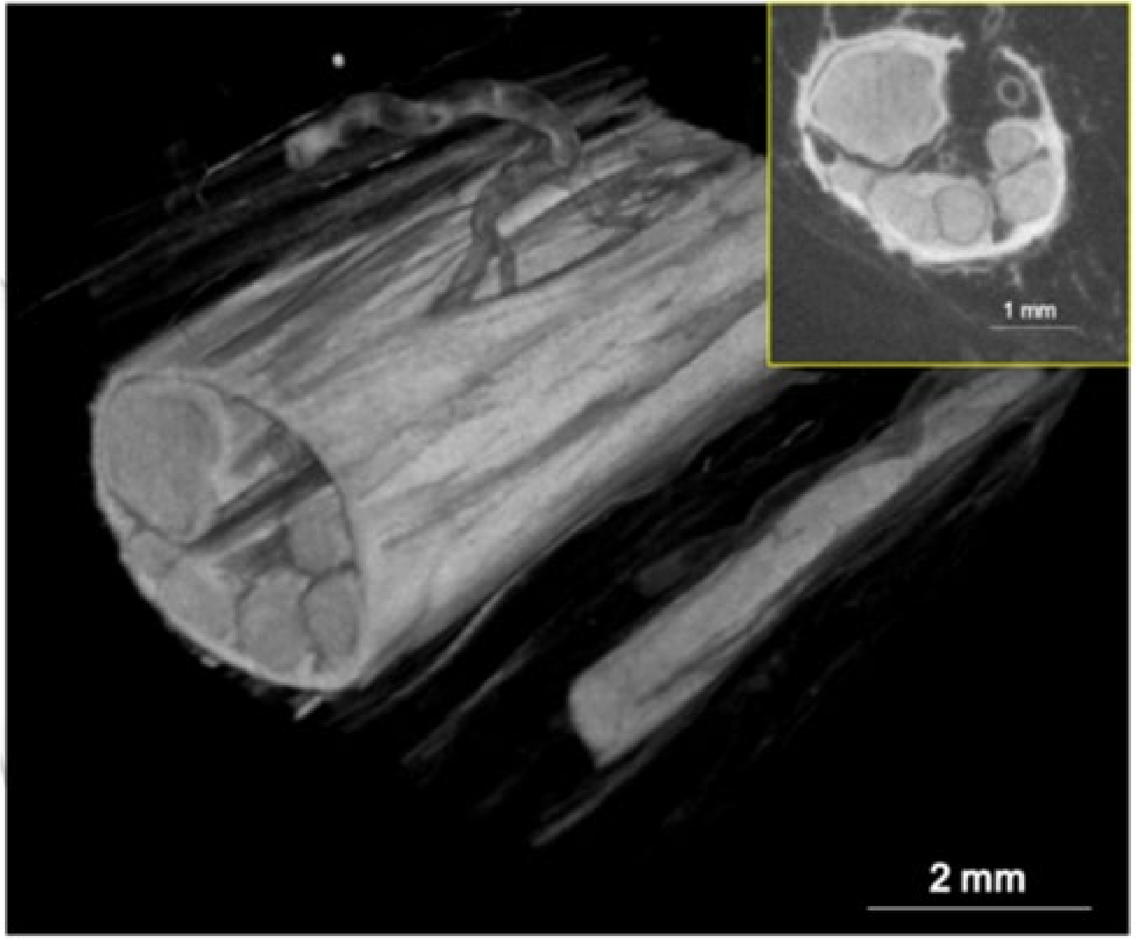
Randomized Clinical Trials of Machine Learning Interventions in Health Care
A Systematic Review

Deborah Plana, BS; Dennis L. Shung, MD, PhD; Alyssa A. Grimshaw, MSLIS; Anurag Saraf, MD; Joseph J. Y. Sung, MBBS, PhD; Benjamin H. Kann, MD



Focus on importance of question, tool usability, deployment details, trustworthiness, performance drifts
Rather than incremental performance improvements, methodological innovation

Bioelectronic Medicine applications



Reconstructing Vagal Anatomy

- Vagal fibers travel inside fascicles form branches to innervate organs and regulate/monitor organ functions
- Existing Vagus Nerve Stimulation (VNS) therapies stimulate the nerve non-selectively
  - Reduced efficacy
  - Side-effects from non-targeted organs/systems
- Spatial arrangement of fascicles/fibers in the human vagal trunk is unknown
  - Essential to build selective VNS therapies

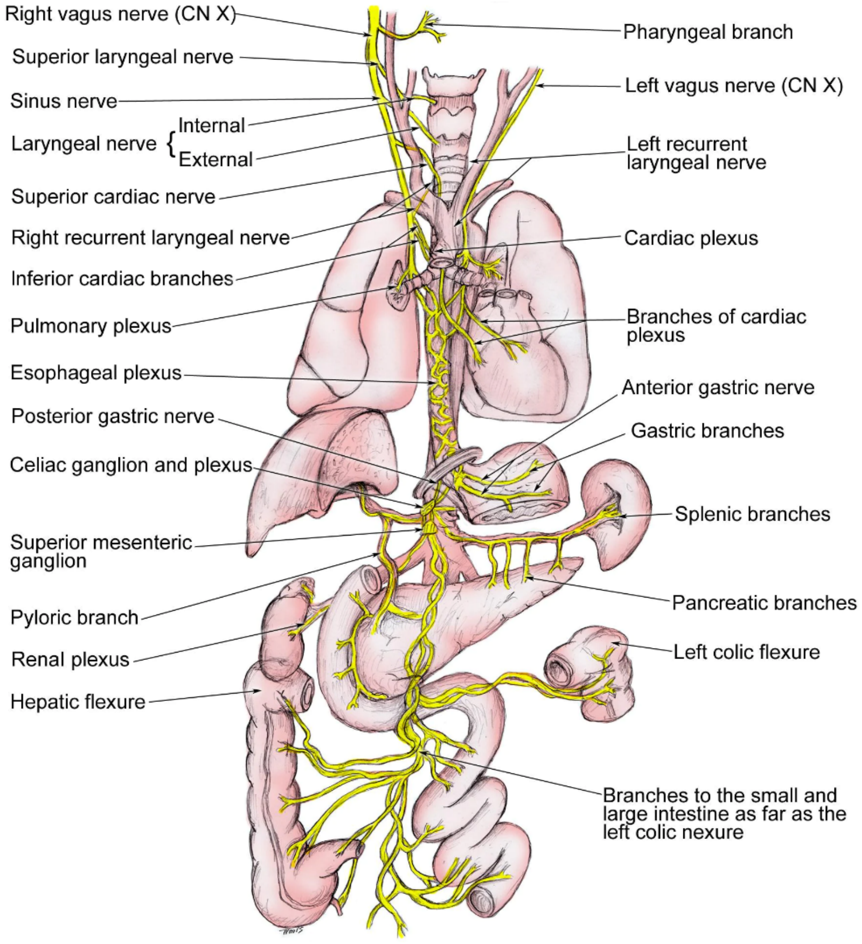
Jayaprakash et al, 2022 Brain Stim

National Institutes of Health
Turning Discovery Into Health

SPARC

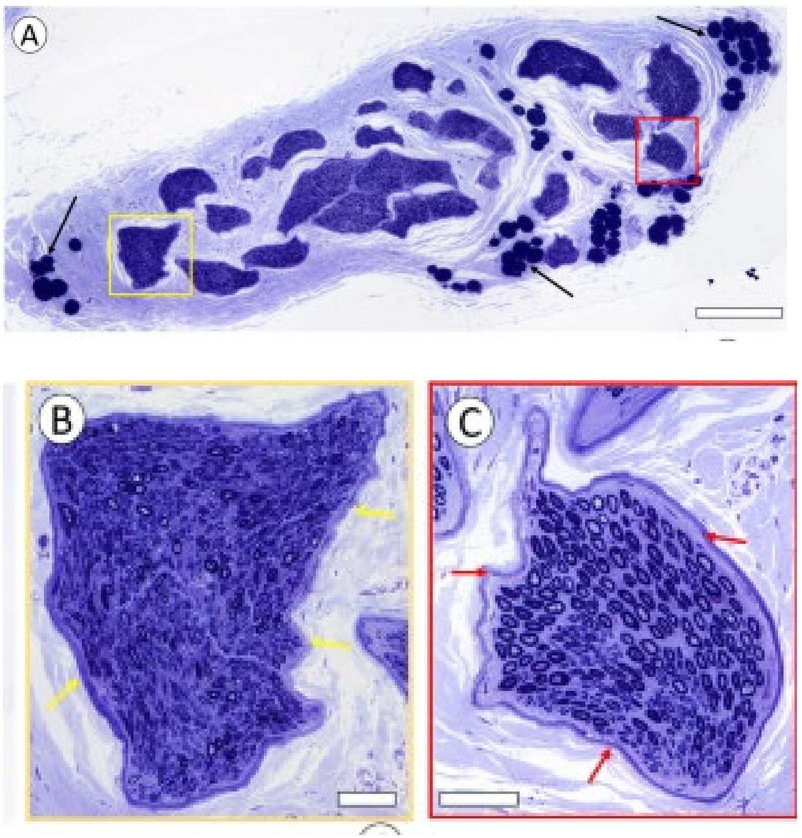
3-year, $6.7M grant

Branches emerging from trunk



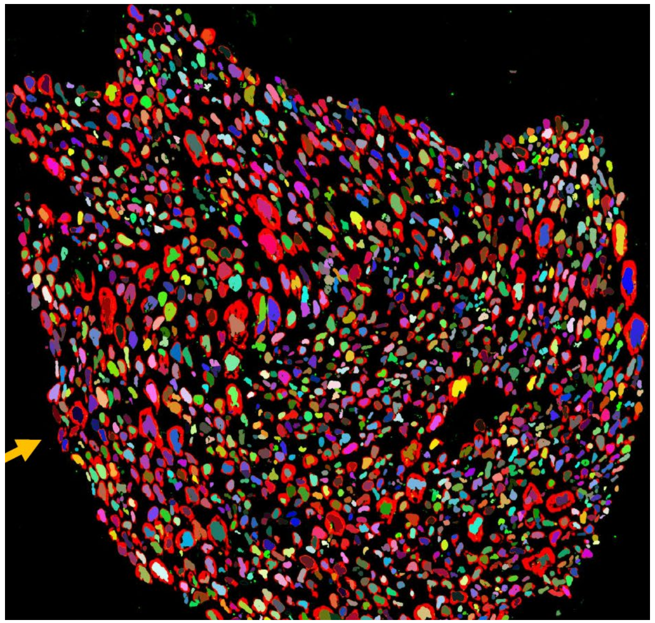
Medscape.com

Fascicles in trunk



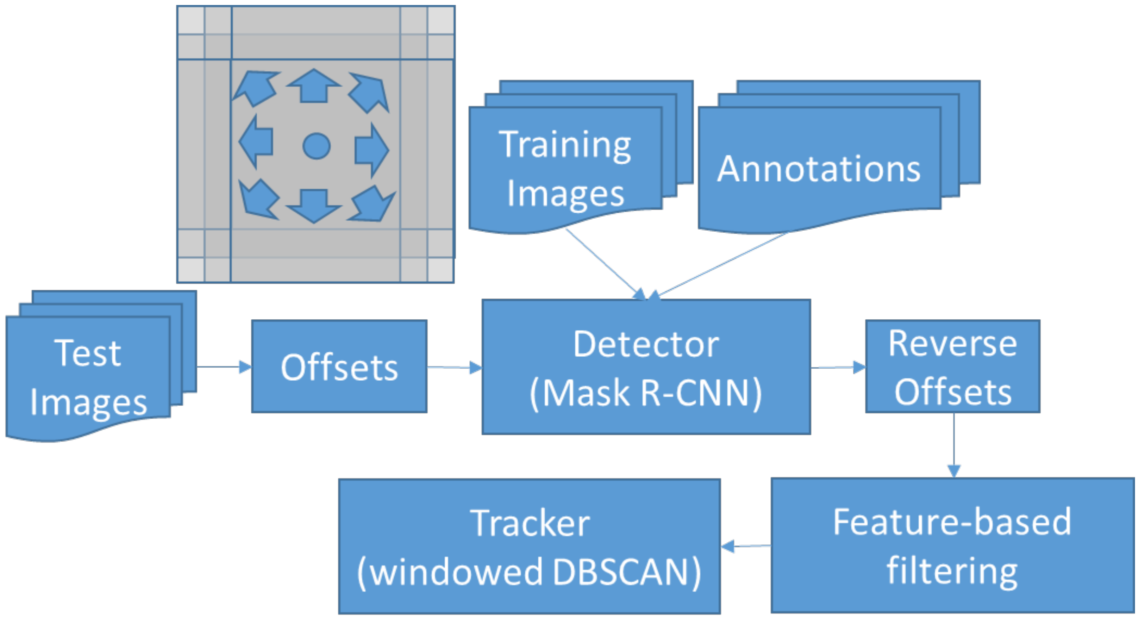
Havton et al, 2021

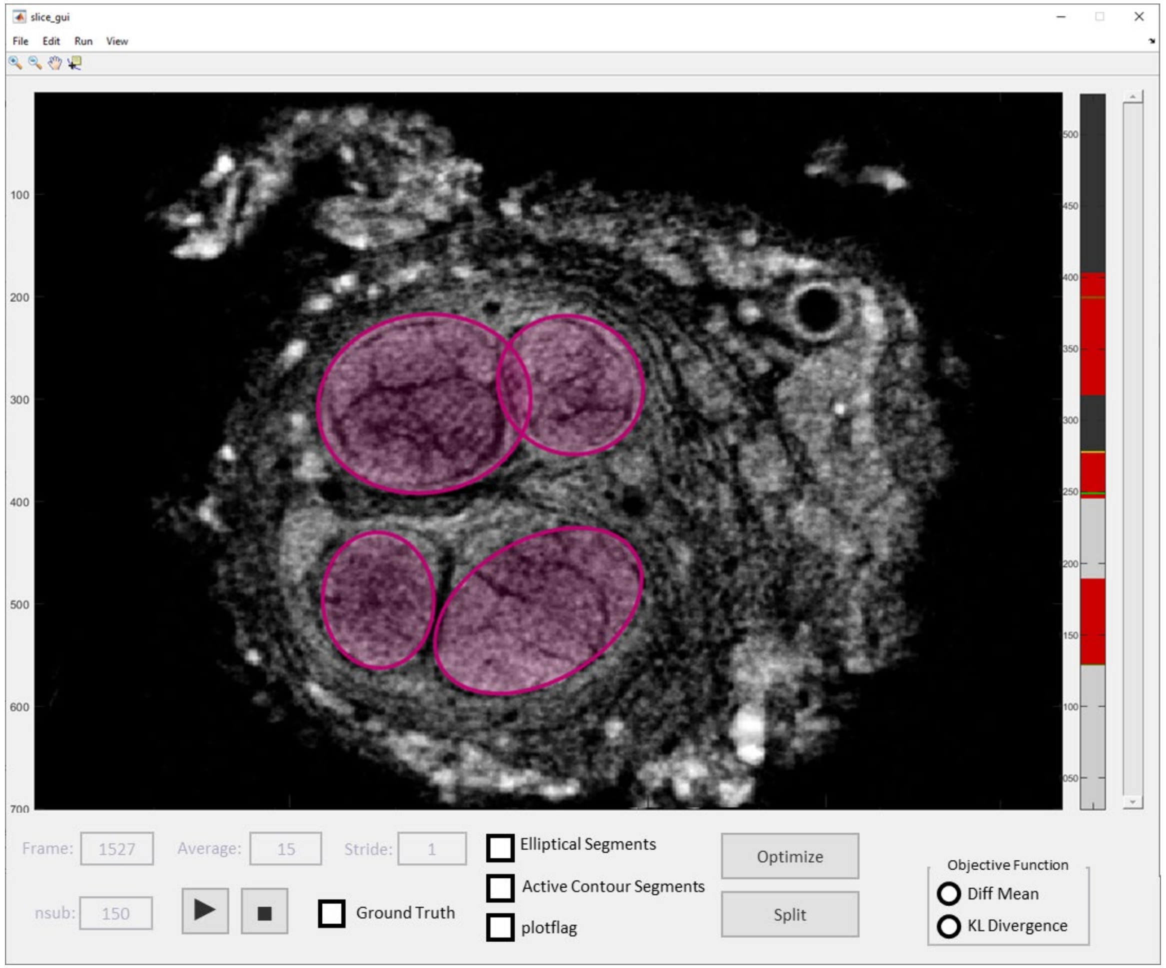
Fibers in fascicles



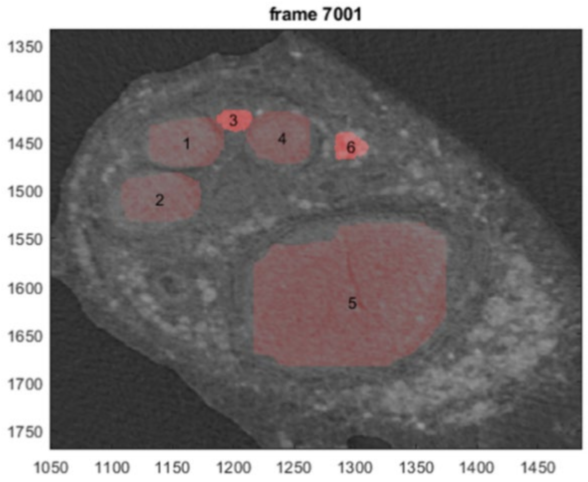
Toth et al, 2020 IEEE EMBC

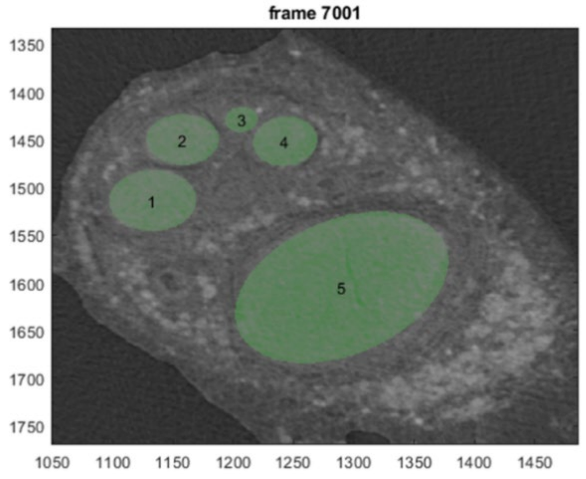
Deep Learning for micro-CT imaging data

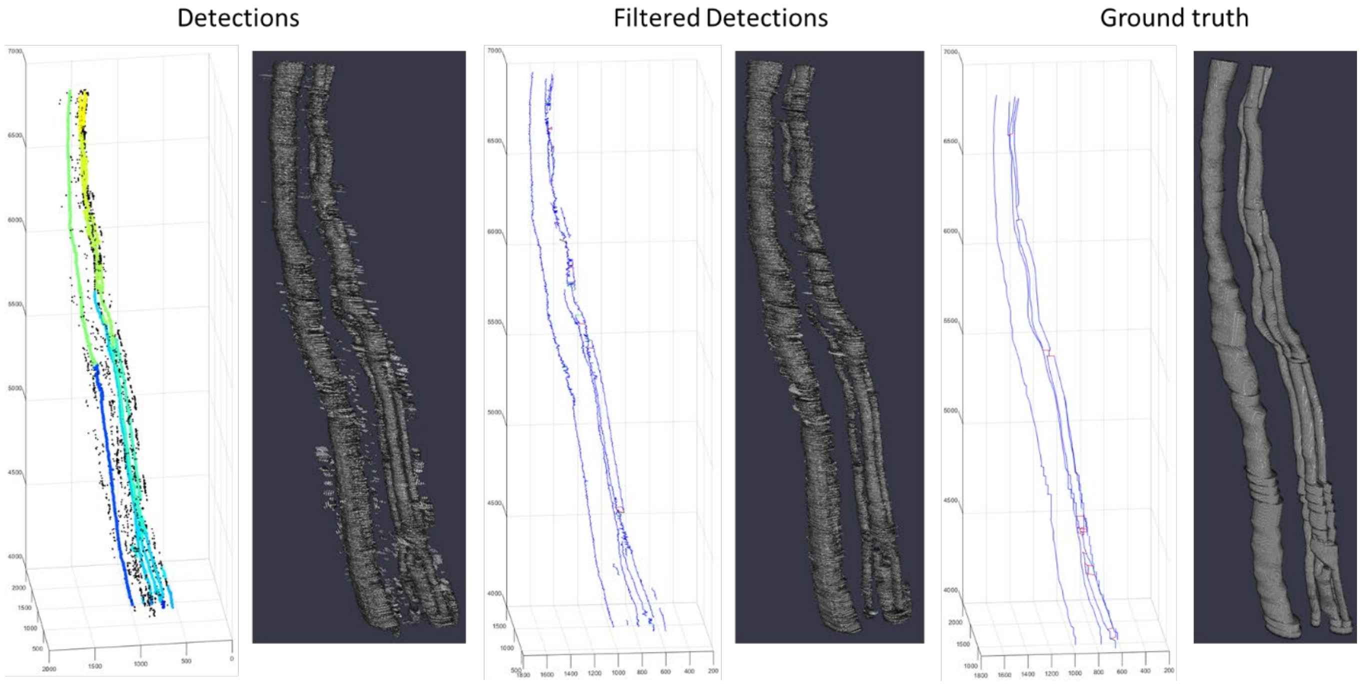


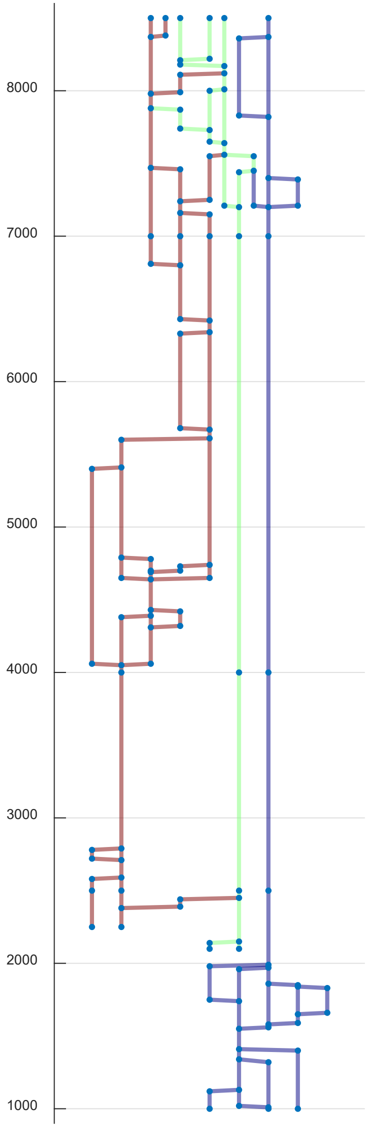


Deep Learning for micro-CT imaging data

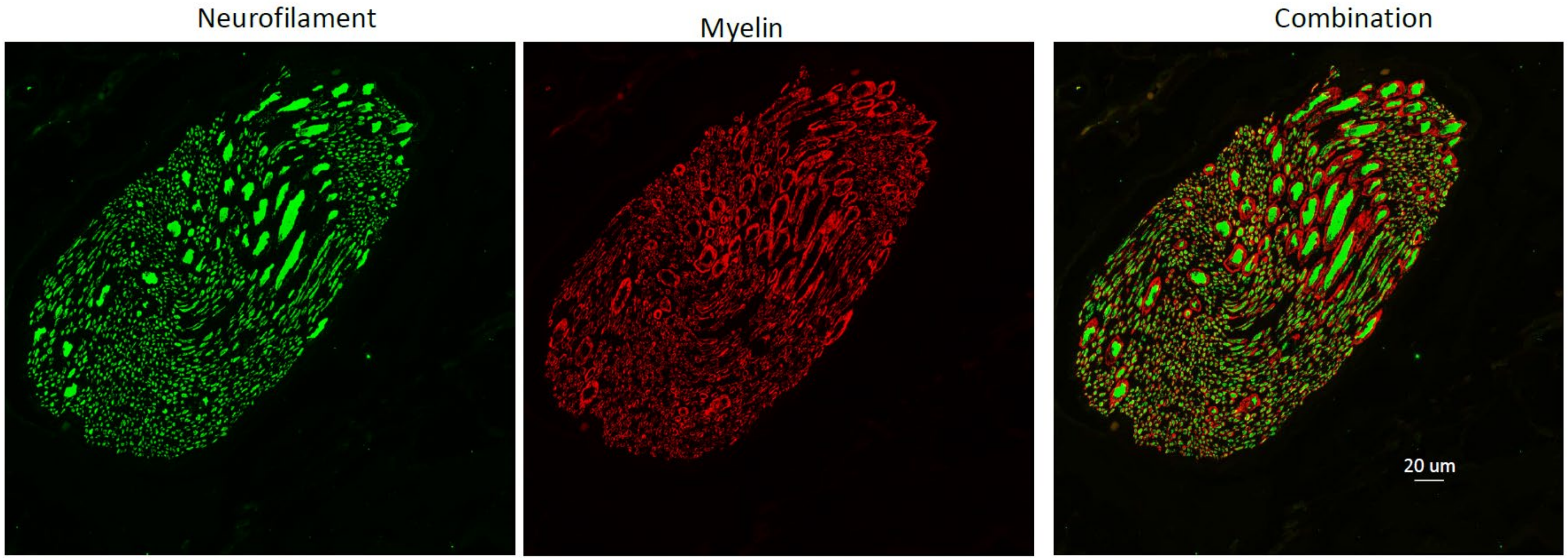








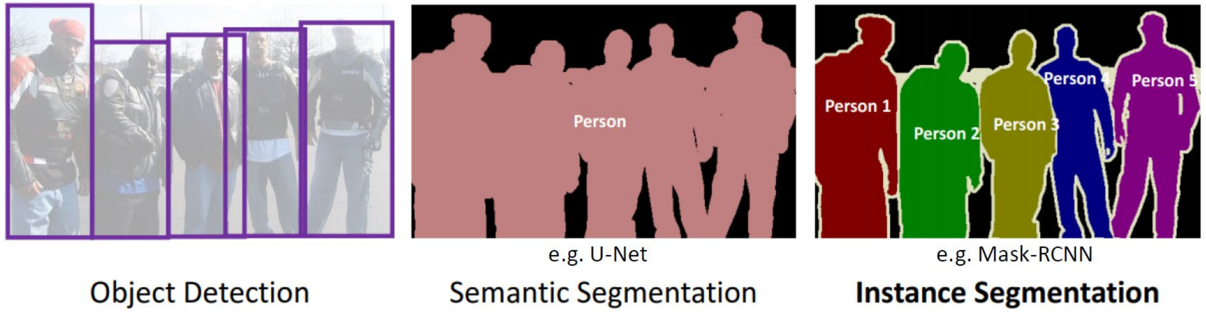
Deep Learning for IHC imaging data



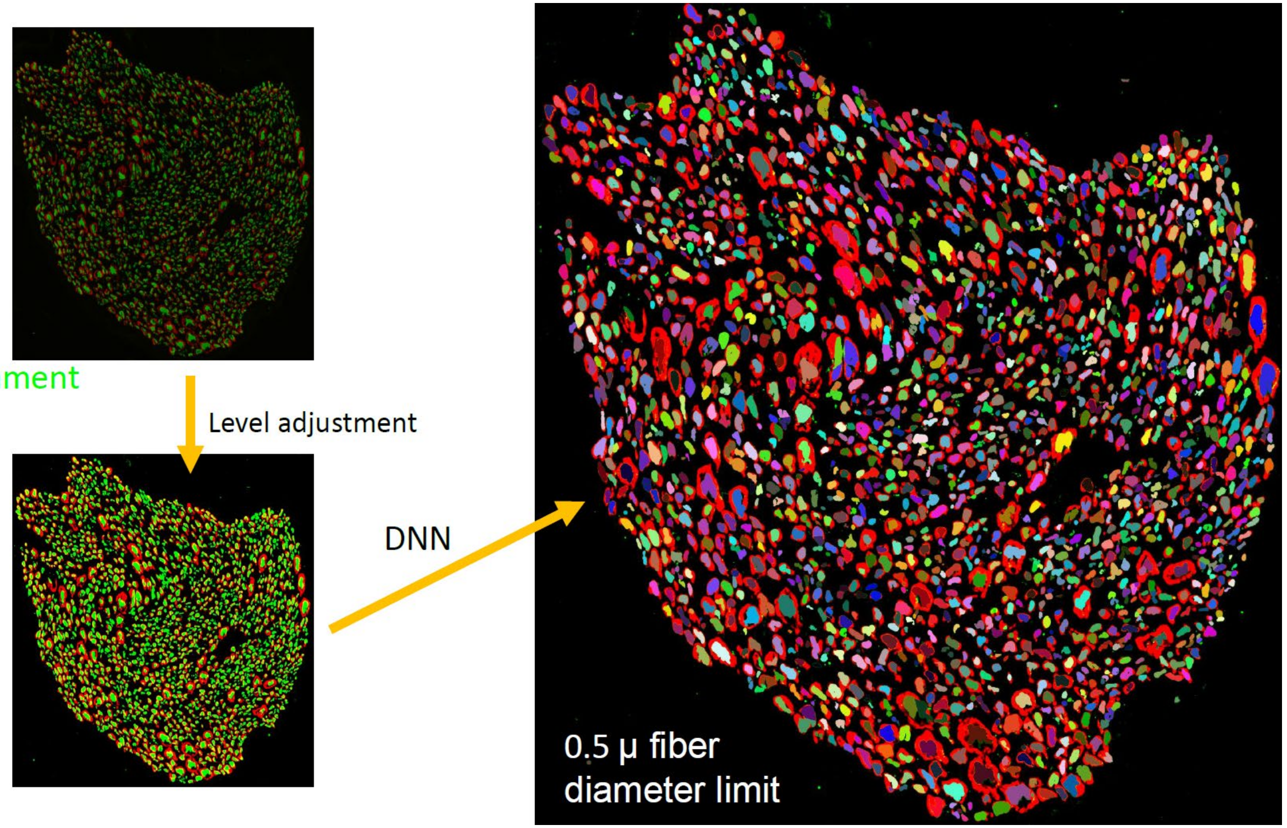
Tóth et al. 2020, EMBC

Trained an instance segmentation ML method: deep mask-RCNN (He et al. 2017) to detect *and* separate neurofilament blobs

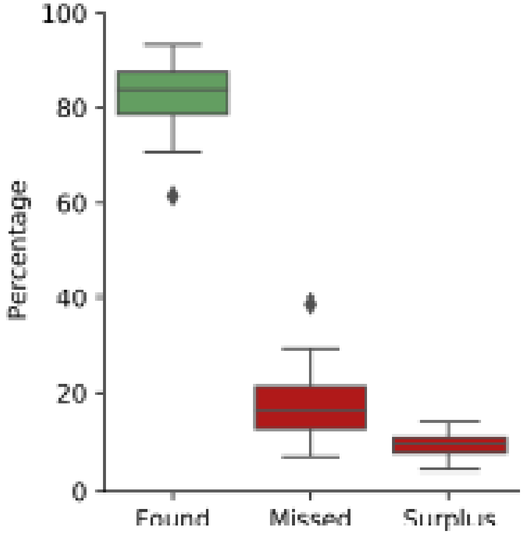
- ResNet-50 backbone network
- Pretrained on the COCO dataset
- Ground truth – 70 fascicles annotated by humans (36 training, 34 testing)
- ~1400 fibers per fascicle on average



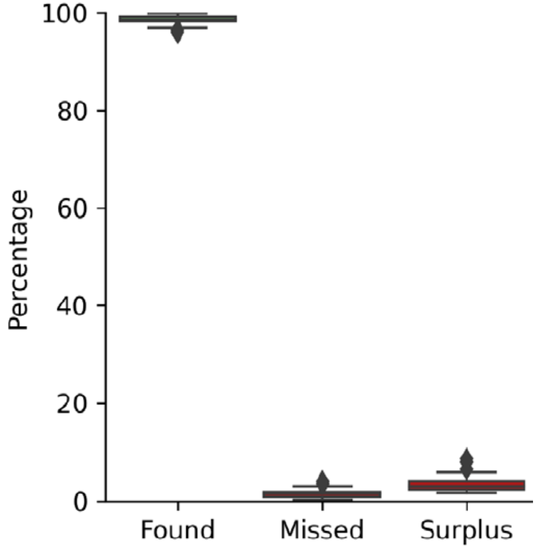
Deep Learning for IHC imaging data



Gaussian Mixture Models + Voronoi decomposition



Mask R-CNN



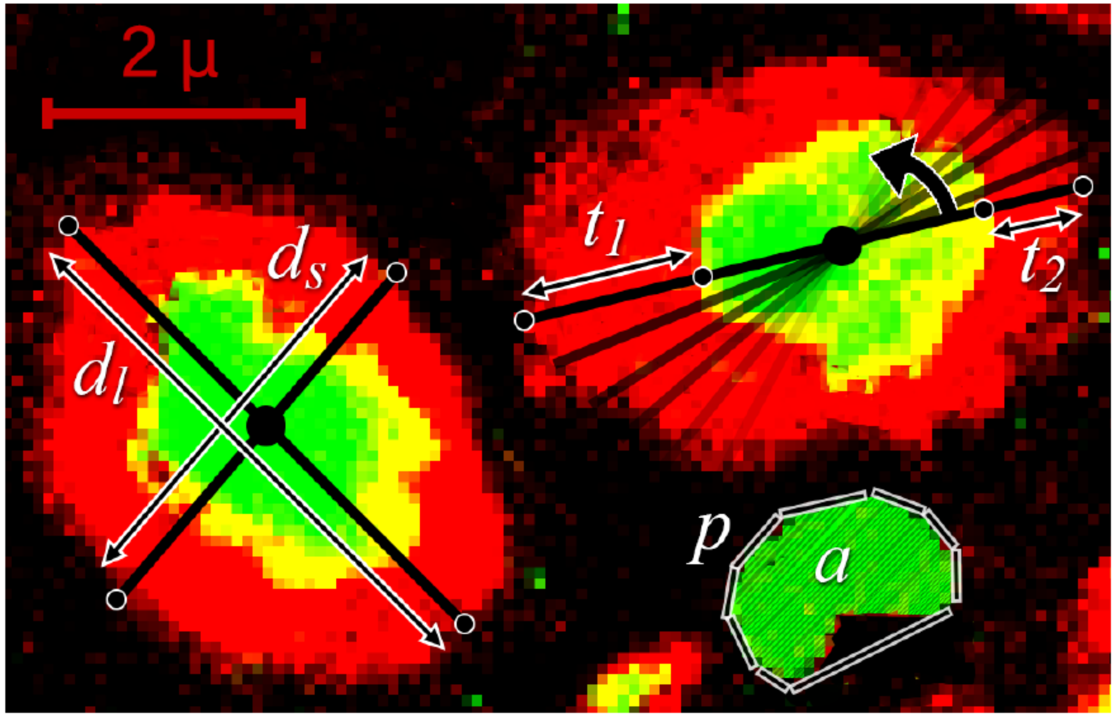
Tóth et al. 2020, EMBC
Jayaprakash et al. 2022 Brain Stim

Feinstein Institutes for Medical Research
Northwell Health

Deep Learning for IHC imaging data

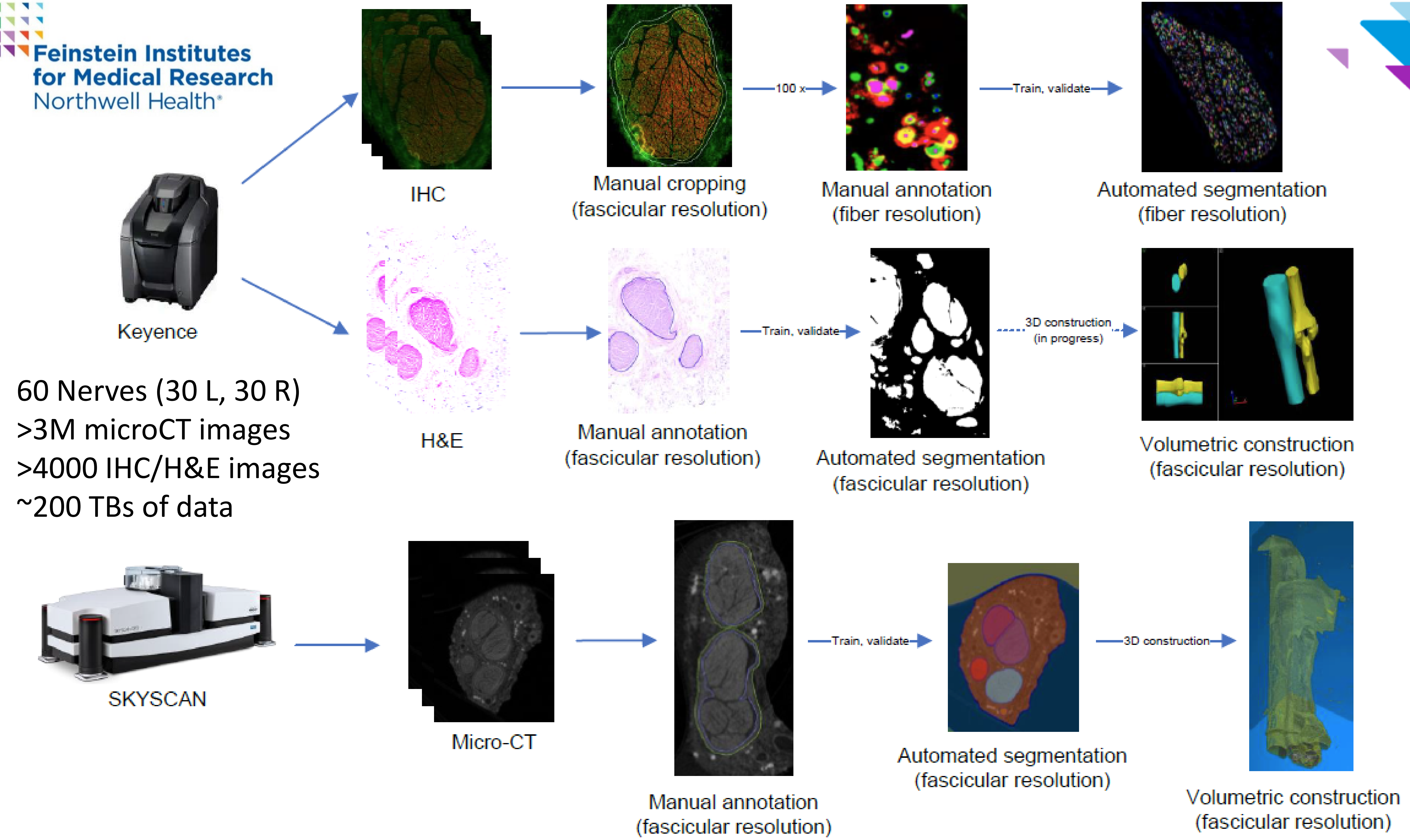
Features extracted

- Location
  - Cartesian and polar coordinates
- Neurofilament and myelin area
- Perimeter
- Shortest/longest diameter
- Median/max myelin thickness



x	y	fiber_area	myelin_area	eccentricity	angles	perimeters	shortest_diameters	longest_diameters	median_myelin_thickness	max_myelin_thickness
828.222222	165.958333	72	543	2167.69659	0.120397871	30.9664008	7.552522969	10.5946782	4.54849243	35.72256828
1454.72297	280.033149	1267	4329	2070.56014	-0.17776849	176.638596	33.88555159	62.83801836	22.73623278	43.06796846
1049.10231	279.301601	1124	4846	2039.04337	0.019361217	142.01436	28.40612876	56.7484743	19.54409173	165.5670892
944.67931	335.082759	290	296	1988.09461	0.072443655	60.0557262	17.8955333	19.72119943	4.960168413	8.113218391
921.145803	368.053019	679	393	1957.08503	0.085656638	135.02203	17.56919772	55.31655765	11.53964613	52.89832661
1407.3357	448.14032	563	520	1896.79796	-0.16885152	106.013759	14.45270026	44.99644387	5.397960658	10.65977332
1518.74045	463.727528	1780	3997	1903.47788	-0.22795666	189.837336	41.91775628	70.94949637	22.14902134	112.4996833

Measurements in pixels – 1 pixel = 0.15µ

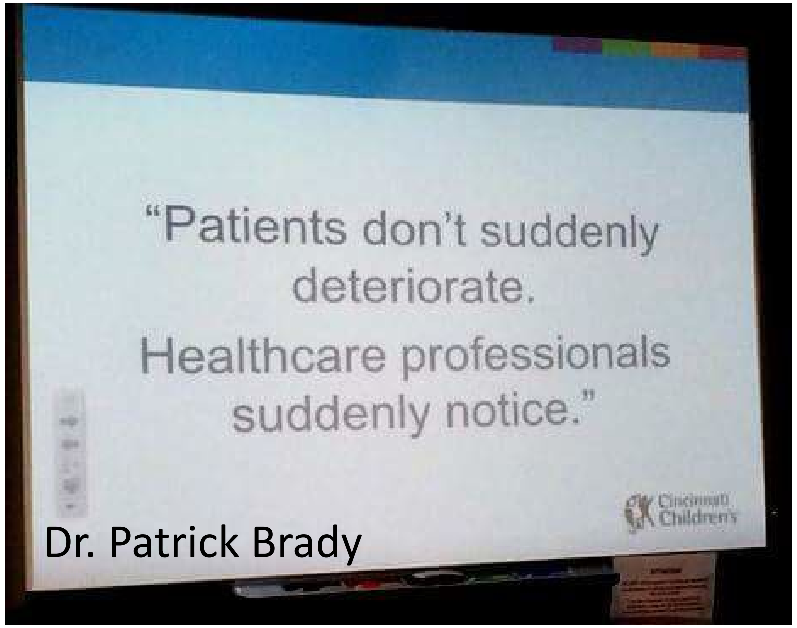

Keyence
IHC
Manual cropping
(fascicular resolution)
100 x
Manual annotation
(fiber resolution)
Train, validate
Automated segmentation
(fiber resolution)
H&E
Manual annotation
(fascicular resolution)
Train, validate
Automated segmentation
(fascicular resolution)
3D construction
(in progress)
Volumetric construction
(fascicular resolution)
60 Nerves (30 L, 30 R)
>3M microCT images
>4000 IHC/H&E images
~200 TBs of data
SKYSCAN
Micro-CT
Manual annotation
(fascicular resolution)
Train, validate
Automated segmentation
(fascicular resolution)
3D construction
Volumetric construction
(fascicular resolution)

Bringing AI to the bedside

Feinstein Institutes for Medical Research
Northwell Health

The case for AI in clinical decision support

- ER setting: Nurses undertriage 17% and overtriage 12% of cases - Doctors undertriage 14% and overtriage 14% of cases*
- Up to 5% of patients in medical-surgical wards deteriorate requiring intensive care



Dr. Patrick Brady

Labs

Vitals

Radiographs


nso.com

Demographics

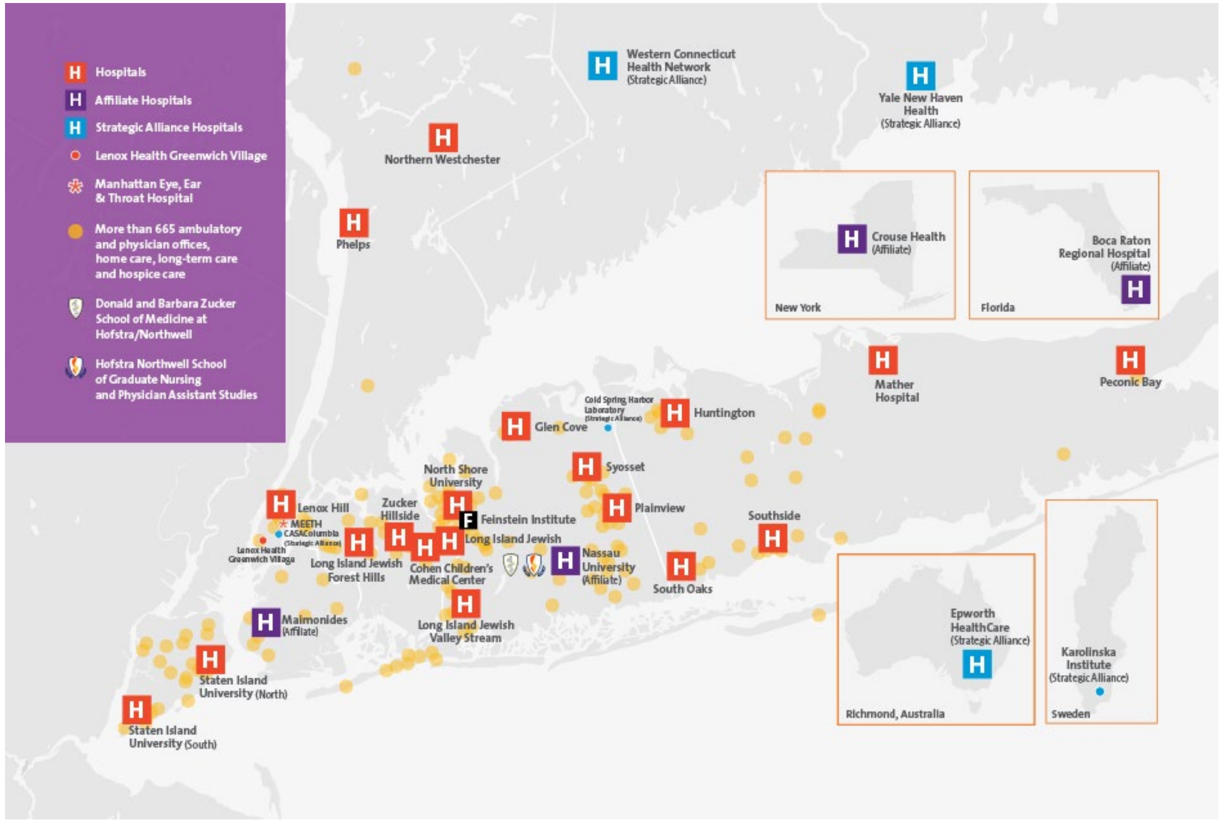
Comorbidities

Medical notes

*Ruttanaseeha et al. 2020

Northwell's Advantage

- Largest health system in NY
- 23 Hospitals
- >700 Outpatient clinics
- >2M patients treated annually, over 5.5M patient encounters
- One of the most ethnically, culturally, genetically, socially and economically diverse population in the US (likely the world)



Continuously monitoring vitals in-hospital

VitalConnect VitalPatch

Biobeat Chest Monitor

Isansys Lifetemp

NIH National Institute of Nursing Research

4-year, $3.2M grant

- 3 different devices
- >1.2k patients, >4k days of data collected already
- Goal of 4k, >20k days patients in 2 years

Shubham Debnath

Michael Scheid

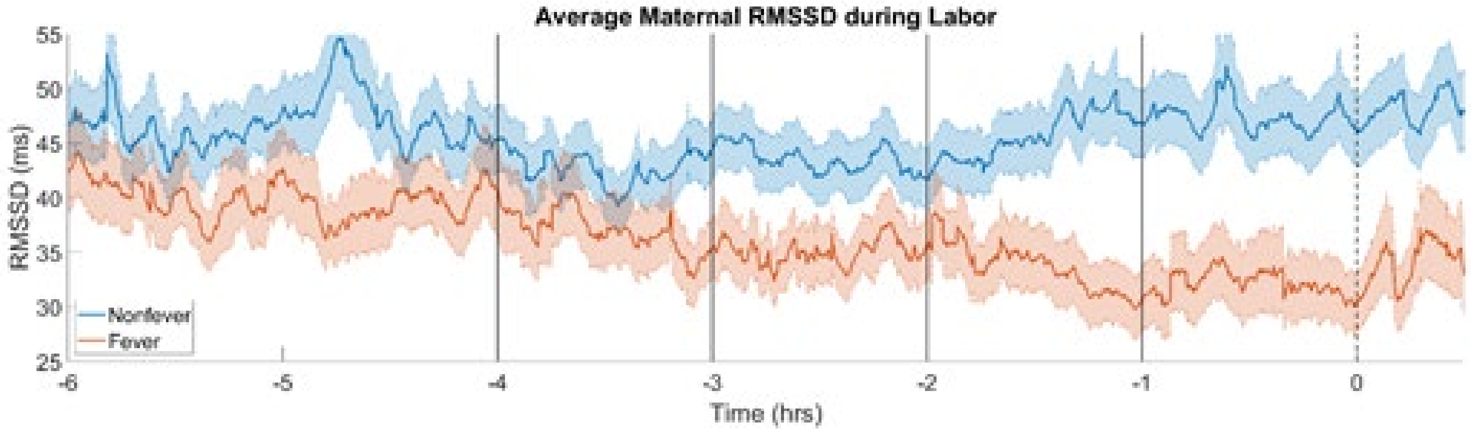
Barry Weinberger, MD
Rob Koppel, MD

Beth Friedmann, RN
Mike Oppenheim, MD

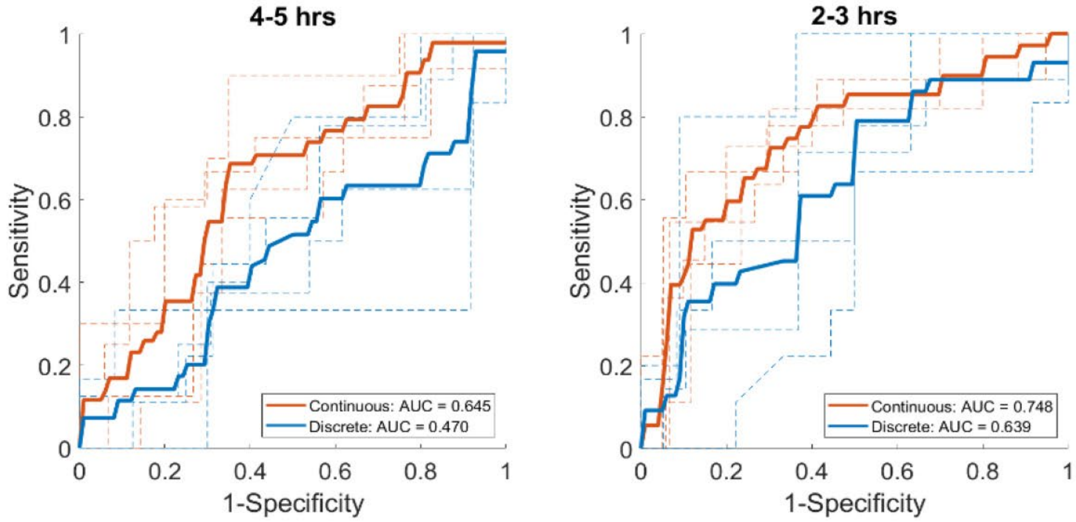
Monitoring during labor

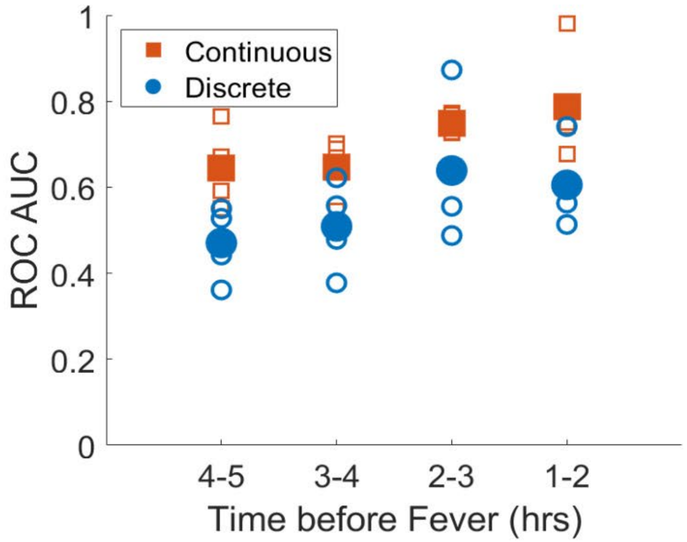
Neonatal early onset sepsis

- Major cause of morbidity/mortality
- Maternal fever during labor is the strongest predictor
- Continuous vital data from 336 women during labor, including HRV
- Model predicts fever 2-3h before onset
    - HRV one of the most important predictors



Debnath et al. 2023 Digital Health



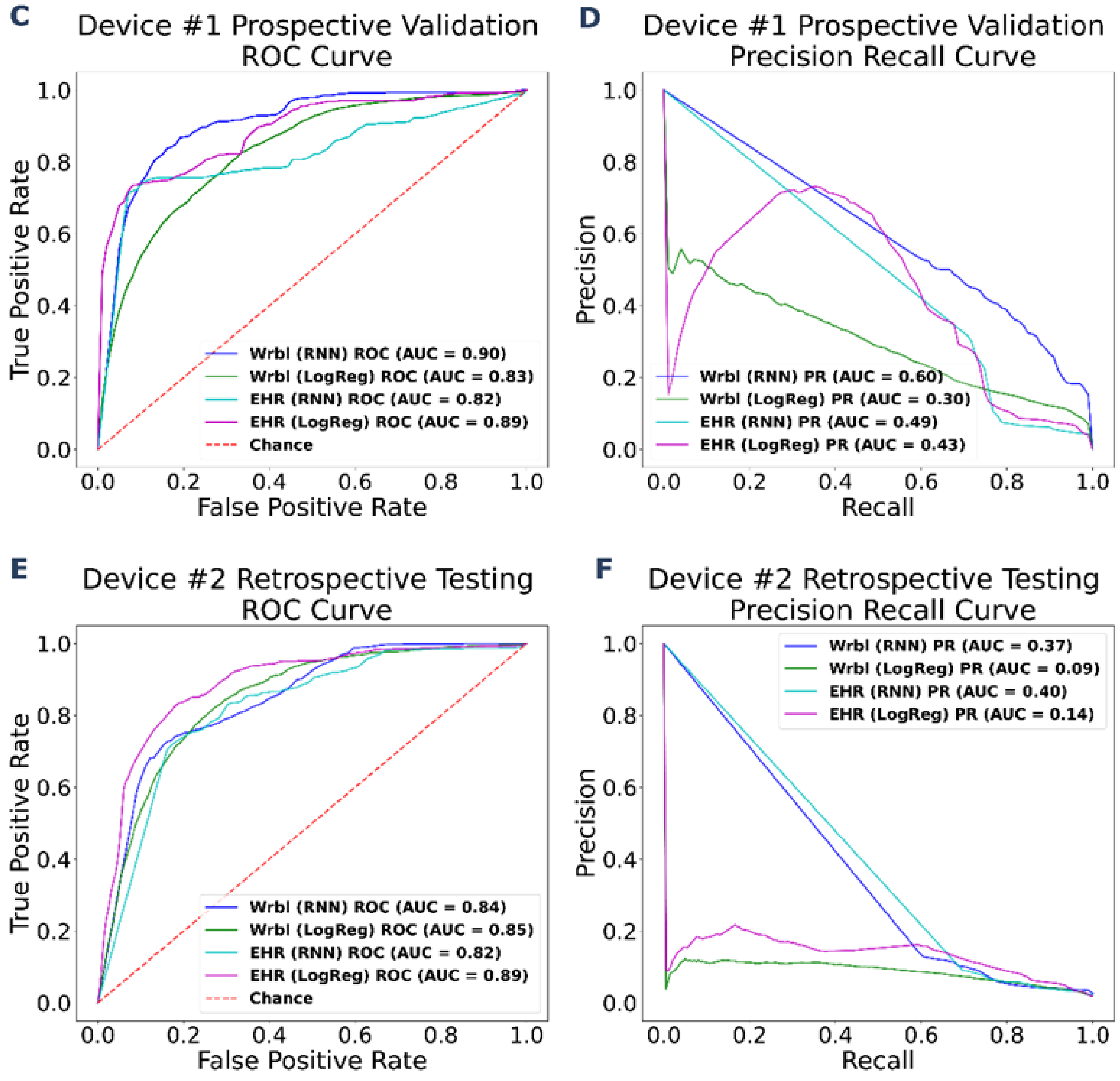


Shubham Debnath

Barry Weinberger, MD
Rob Koppel, MD
Beth Friedmann, RN

Deep Learning to predict alerts

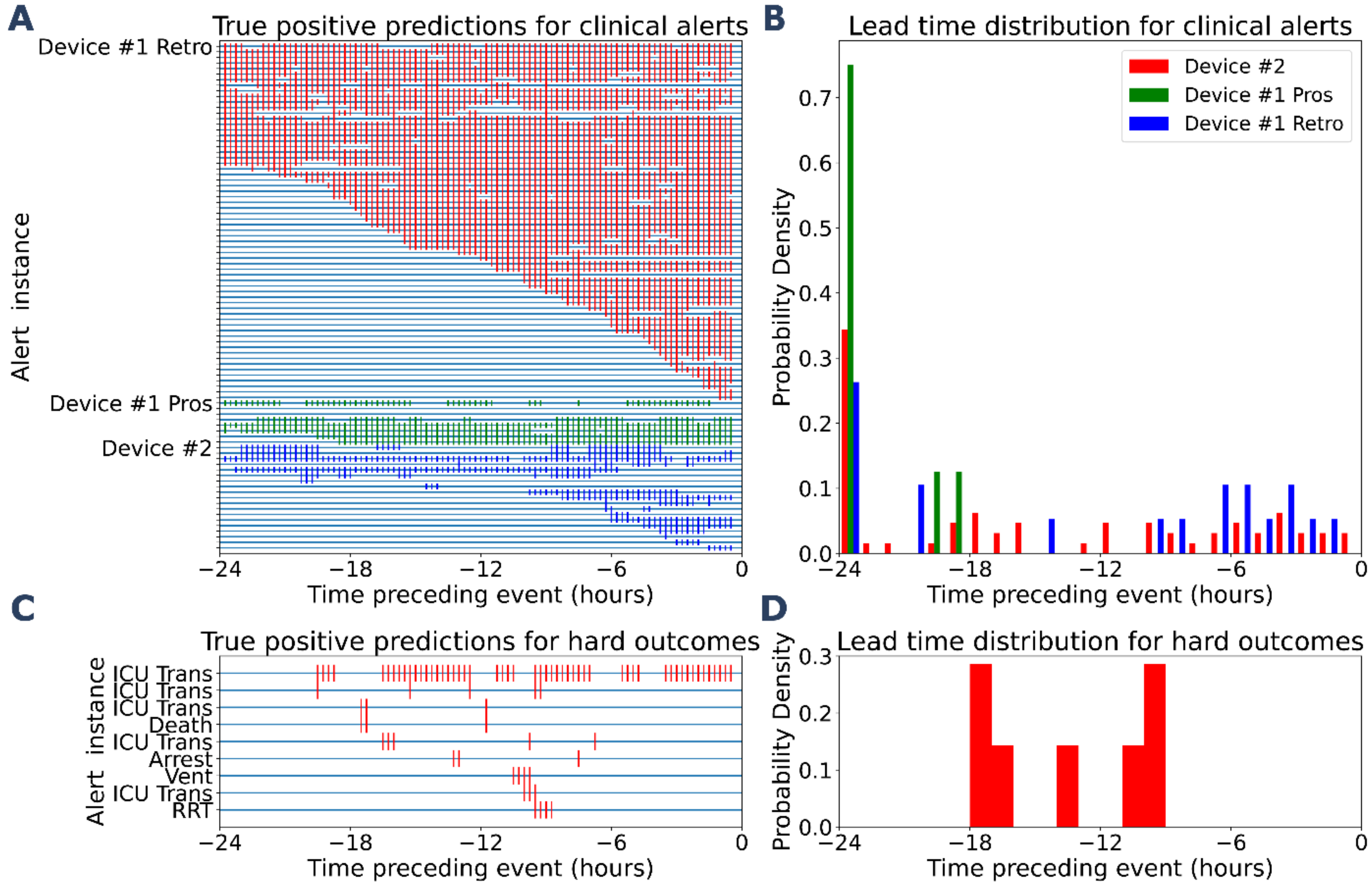
- LSTM RNN developed using data from 888 hospitalized patients, >1300 devices
- Tested on the same device (VitalConnect Vitalpatch) that was used to produce training data prospectively on a different hospital and patients
- Tested on a different device (Biobeat Chest Monitor) on a different hospital and patients



Scheid et al. (under review)

Deep Learning to predict alerts

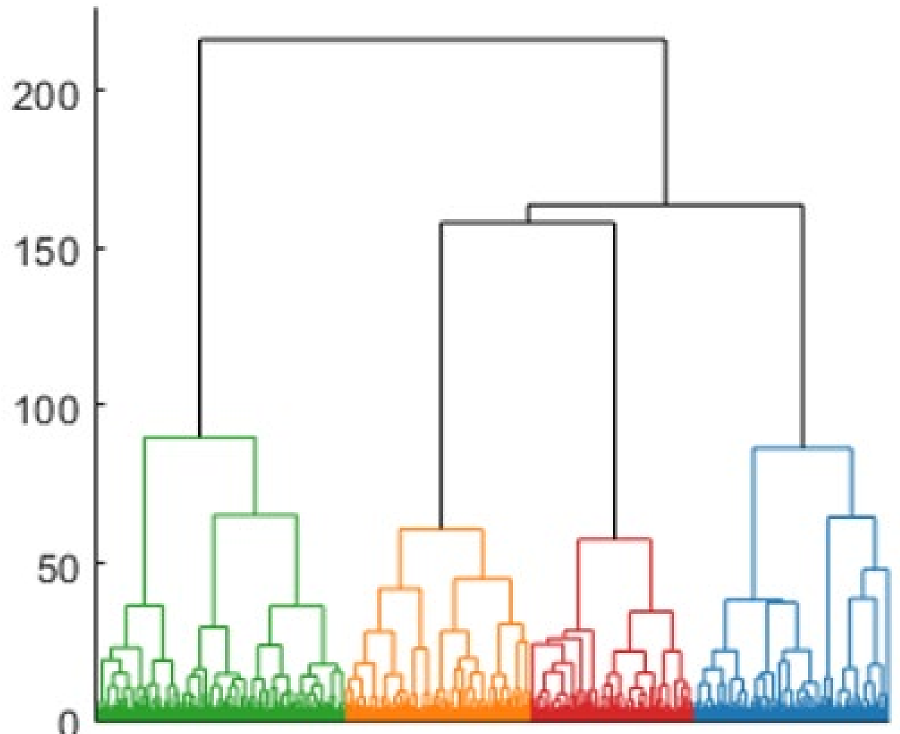
- Average lead time for clinical alers: 17h in advance
- Predicted 9/11 hard outcomes
- Average lead time for hard outcomes: 15h in advance
- 2000 clinical wearable patches to select patients



Scheid et al. (under review)

Answering Why

- Unsupervised learning
- Major clinical phenotypes should cluster patients to unique groups
- Initial application on COVID-19 patients presenting to the ED
- Applicable to optimizing clinical trial recruitment



High Lung inflammation

Poor kidney function

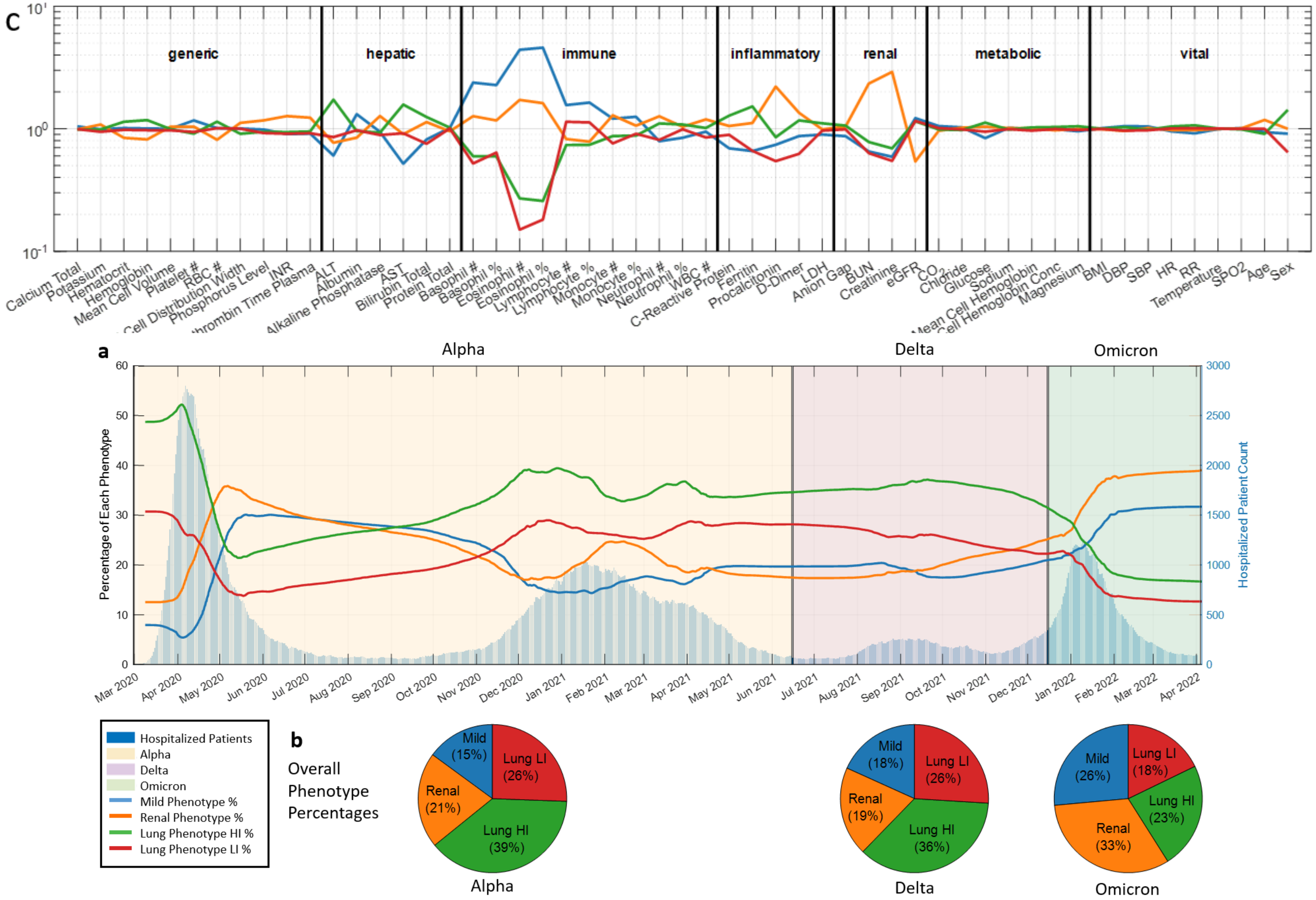
Low Lung inflammation

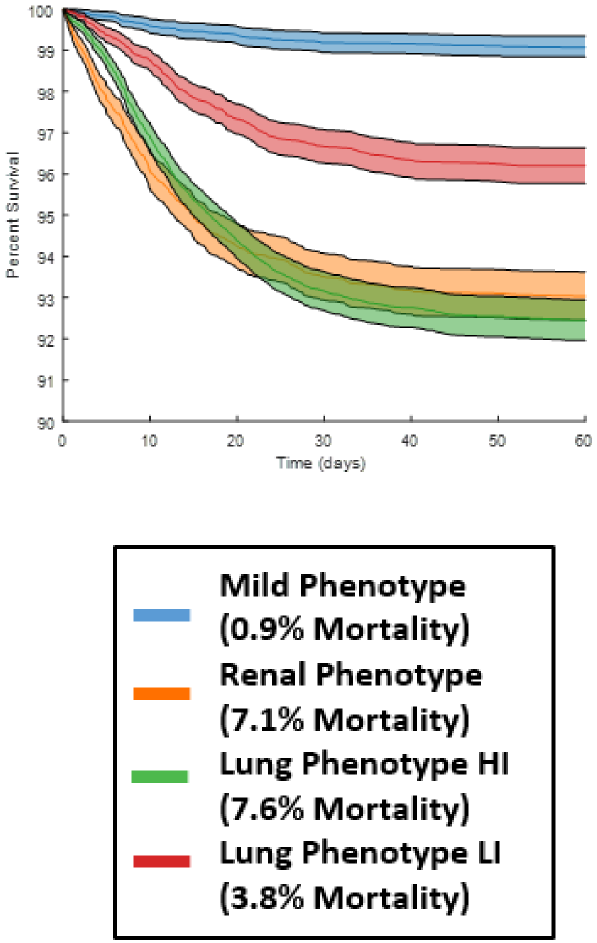
Mild phenotype, elevated immune cell counts

Matthew Ho

Ho et al. (IJMI 2023)

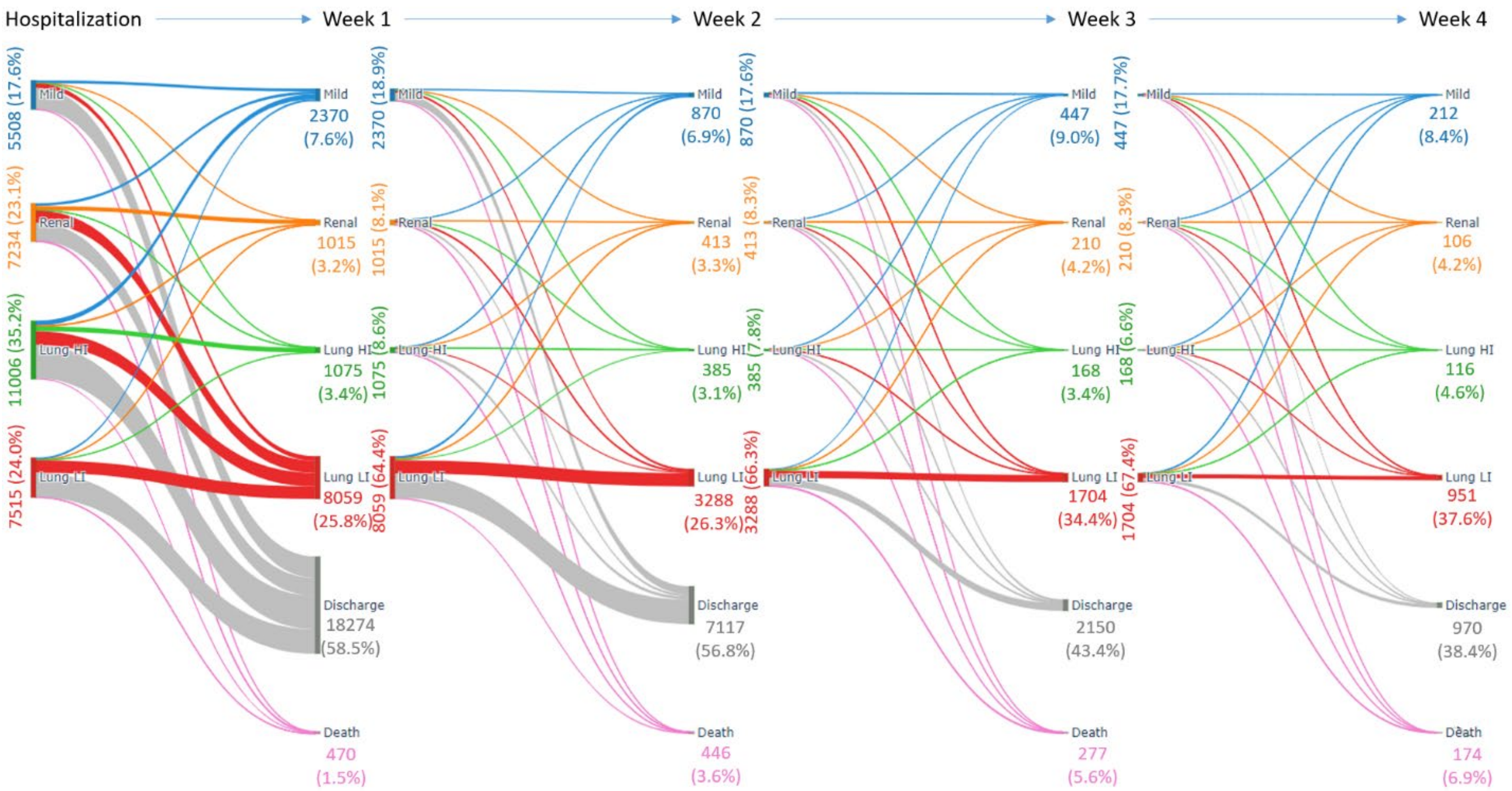
Answering Why





Ho et al. (IJMI 2023)

Answering Why and when



Ho et al. (IJMI 2023)

Feinstein Institutes for Medical Research
Northwell Health®

Questions?

tzanos@northwell.edu

Neuraldatascience.org
mlmd.org