Feature extraction and quantification to explore human vasculature

Li Chen
Department of Electrical and Computer Engineering
8/9/2021

UNIVERSITY of WASHINGTON

Thanks for coming to my dissertation defense

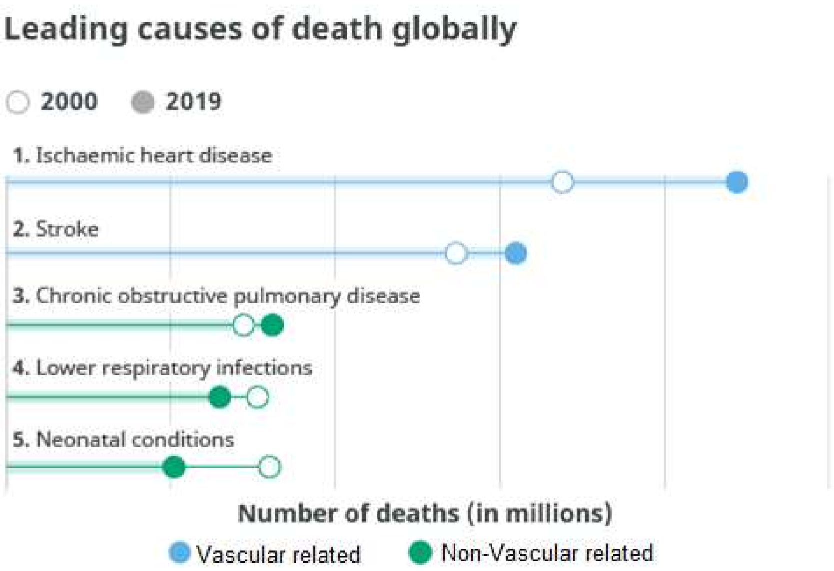
- Committee members:
- Co-chairs: Dr. Jenq-Neng Hwang (ECE) and Dr. Chun Yuan (BIOE, Radiology)
- GSR: Dr. Shuyi Chen (Atmospheric Sciences)
- Members: Dr. Linda Shapiro (ECE, CSE) and Dr. Ming-Ting Sun (ECE)
- All the audience

Overview

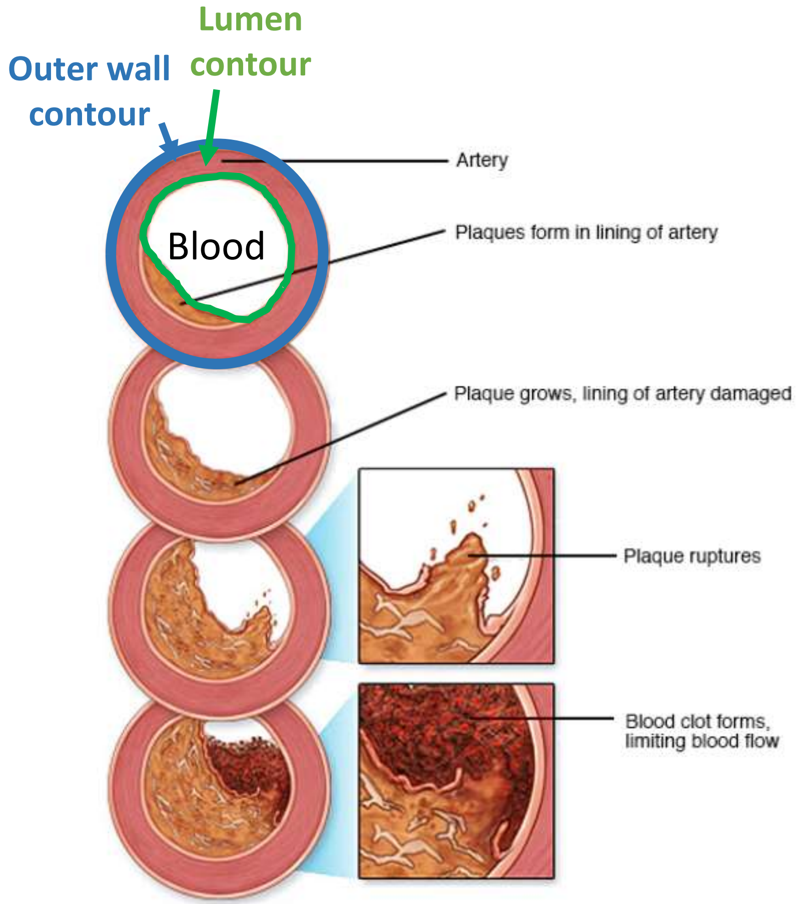
- > Background
- > Quantitative vasculature map construction
  - Artery centerline generation
  - Lumen and vessel wall segmentation
  - Atherosclerotic lesion identification and classification
- > Conclusions and future directions

Background: vascular health

> Vascular disease: top death causes worldwide
> Atherosclerosis: cause of ischemic strokes
  - Plaque growth -> Risk of rupture
  - Narrowing lumen -> Reduction in distal flow



Source: WHO Global Health Estimates. Link

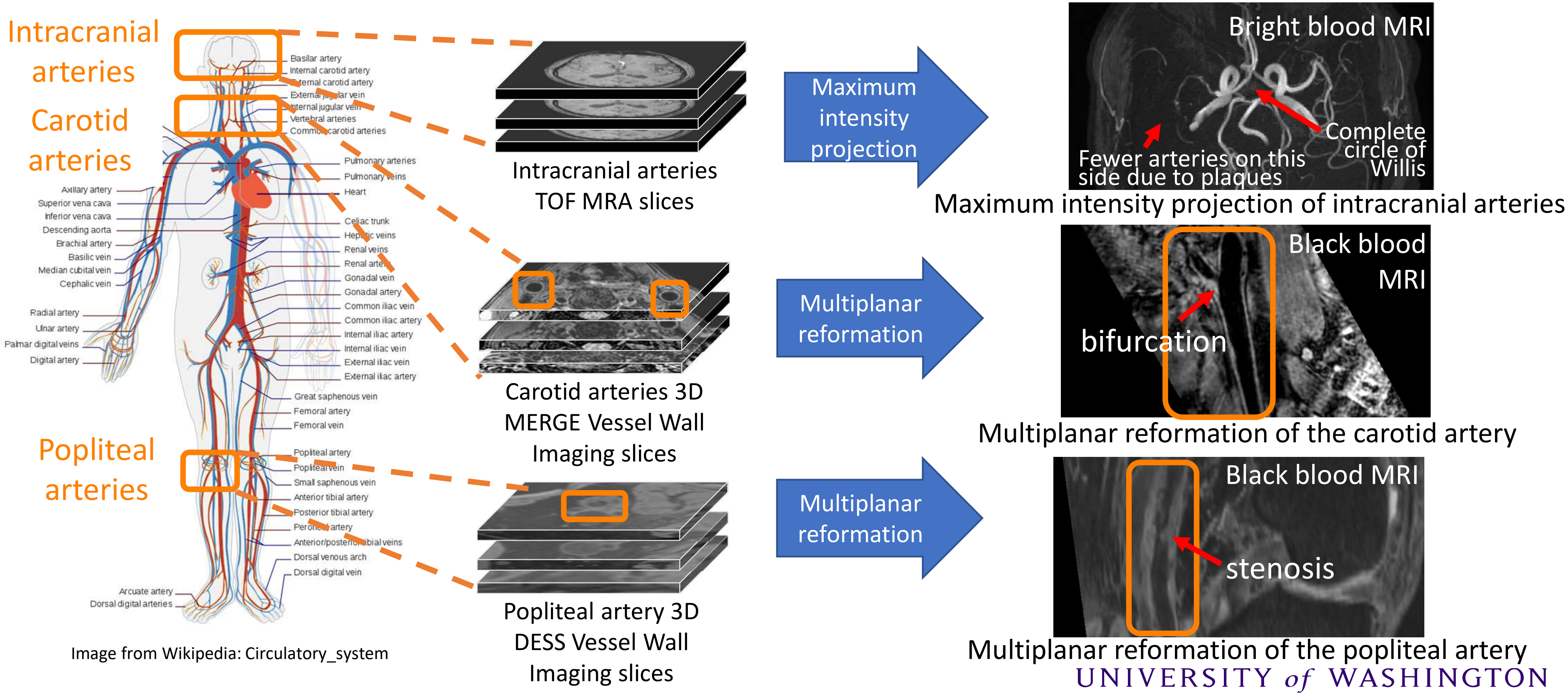


Cross sectional view of an artery with accumulating plaque

Image from mayoclinic

Background: MRI for human vasculature

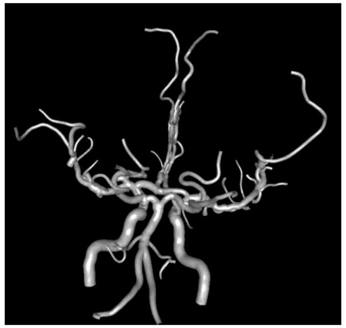
> A complex and vital system visualized by Magnetic Resonance Imaging (MRI)



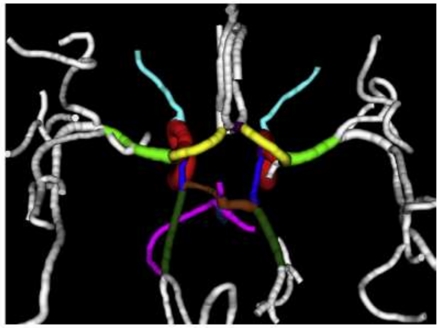
Background: existing vascular analysis techniques

> Focused on specific analysis tasks
  - Artery tracing
  - Artery anatomical labeling
  - Vessel wall segmentation

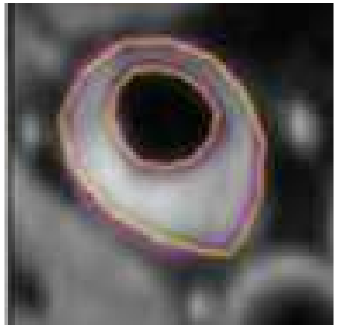
> Limited capability



Artery tracing for large arteries with good contrast alone [1]



Artery labeling on major arteries with little variations [2]



Vessel wall segmentation with rough contours [3]

[1] Volkau, 2005. [2] Robben, 2016. [3] Gao, 2017.

Aim: Quantitative vasculature map

> A *quantitative vasculature map* needed for comprehensive features
  - Construct centerlines to quantify artery structural features
  - Segment vessel wall to quantify plaque morphometry features
  - Locate disease regions and classify severity of plaques for lesion features

> Automation desired
  - Unbiased, fast and robust

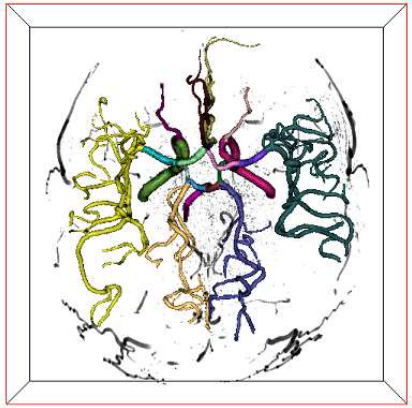
> Challenges
  - Tiny region, variable signals, limited samples

Overview

> Background

> Quantitative vasculature map construction
  - Artery centerline generation
  - Lumen and vessel wall segmentation
  - Atherosclerotic lesion identification and classification

> Summary and future directions



[A1] Li Chen, et. al, Magnetic resonance in medicine, 2018.

[A2] Li Chen, et. al, Magnetic resonance imaging, 2018.

[A3] Li Chen, et. al, RSNA, 2017.

[A4] Li Chen, et. al, MICCAI 2021.

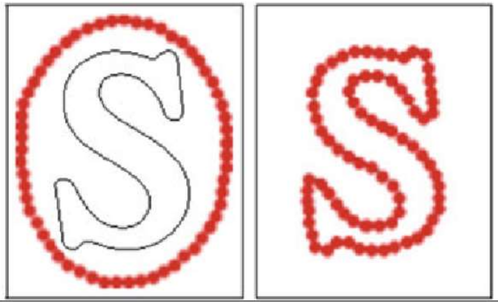
[A5] Li Chen, et. al, MICCAI 2020.

Related work: Snake (active contour model)

> Snake [1]
  - Initial closed contour slithers to find salient object
  - Internal energy: control contour shape
  - External energy: control contour fitness to objects

> Open curve snake [2] (OCS):
  - Stretch from seeds
  - Open curve

> iCafe [A1]: optimized on MRA intracranial artery tracing



Initial contour and final contour using snake

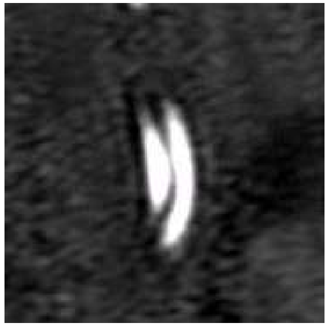
[1] Kass, 1988. [2] Wang, 2011.

Previous work: iCafe

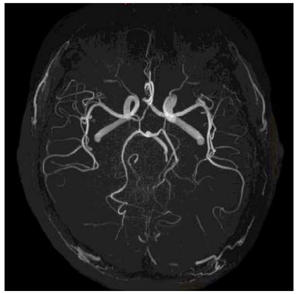
> Accurate [A2] but requires extensive human supervisions

> Existing problems:

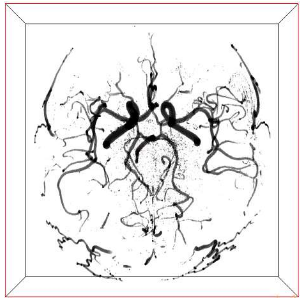
- Parallel arteries; Sensitive to initial contours; No global structure



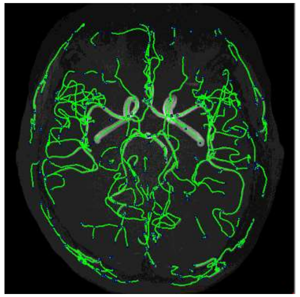
Two parallel arteries



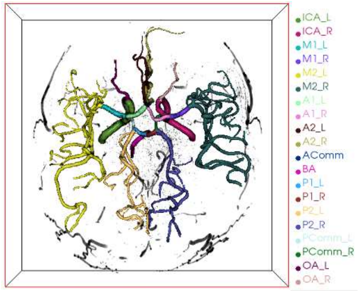
(a)



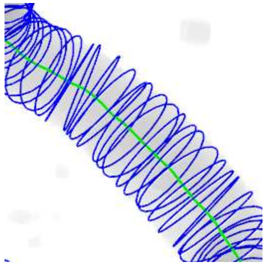
(b)



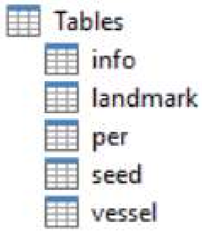
(c)



(d)



(e)



(f)

Image Preprocessing → **Lumen Segmentation** → **Vessel Tracing** → **Artery Labeling** → **Feature Calculation** → **Output and Analysis**

Lumen Segmentation:
- Phansalkar threshold [1]

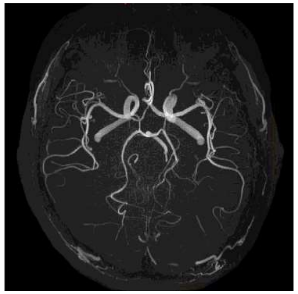
Vessel Tracing:
- Improved Open-Curve Snake
- **Manual editing**

Artery Labeling:
- Maximum a Posteriori [A3]
- **Manual correction**

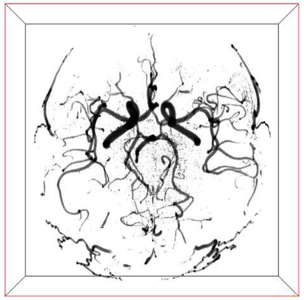
[1] Phansalkar, 2011.

AI+iCafe=AICafe for automated artery centerline generation

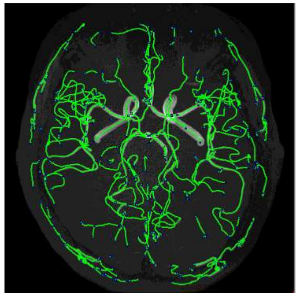
> Processed iCafe traces + artificial intelligence (AI) = automated process (AICafe)
> Same workflow but with AI modules



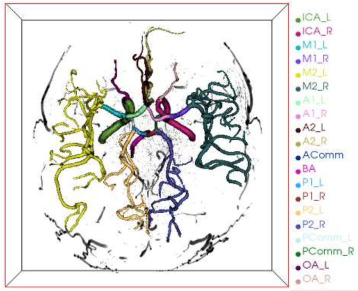
(a)



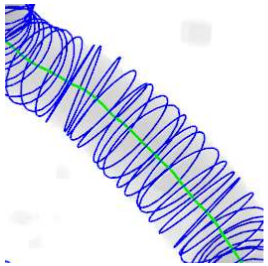
(b)



(c)



(d)



(e)

(f)

Image Preprocessing → **Lumen Segmentation** → **Vessel Tracing** → **Artery Labeling** → Feature Calculation → Output and Analysis

Lumen Segmentation
- Distance transform [1]
- Curve proposal from skeletonization [2]

Vessel Tracing
- Deep open snake tracing [A4]
- Global tree constraint [A4]

Artery Labeling
- Graph neural network [A5]
- Hierarchical refinement [A5]

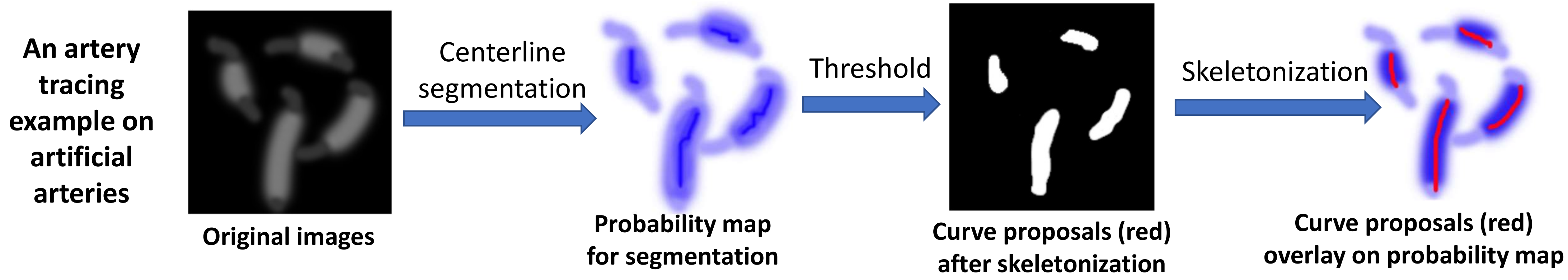
[1] Wang, 2020. [2] Zhang, 1984.

Step 1: Centerline segmentation and curve proposal

> Distance transform [1]: voxels near artery center have higher probability

> Segmentation network: U-Net [2] with two outputs
  - Probability map: distance transformed map (trained with L2 loss)
  - Binary mask: vascular region (trained with binary cross-entropy loss)

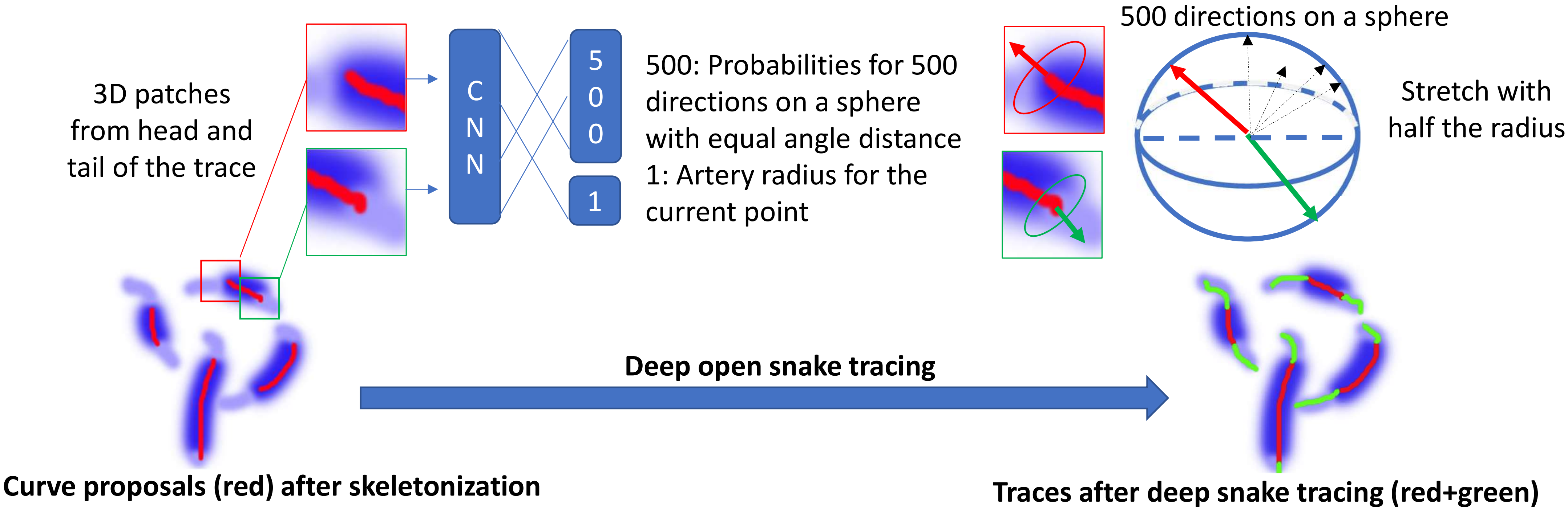
> When prediction, binarize the probability map and skeletonization



[1] Wang, 2020. [2] Ronneberger, 2015.

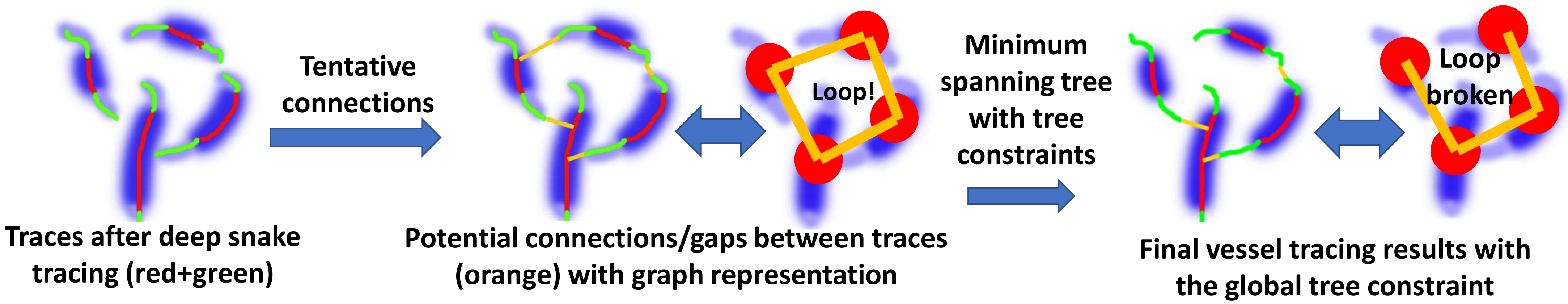
Step 2: Deep open snake tracing

- > Deep learning to decide stretching direction and estimate radius
- > Snake framework ensures smoothness and fitness

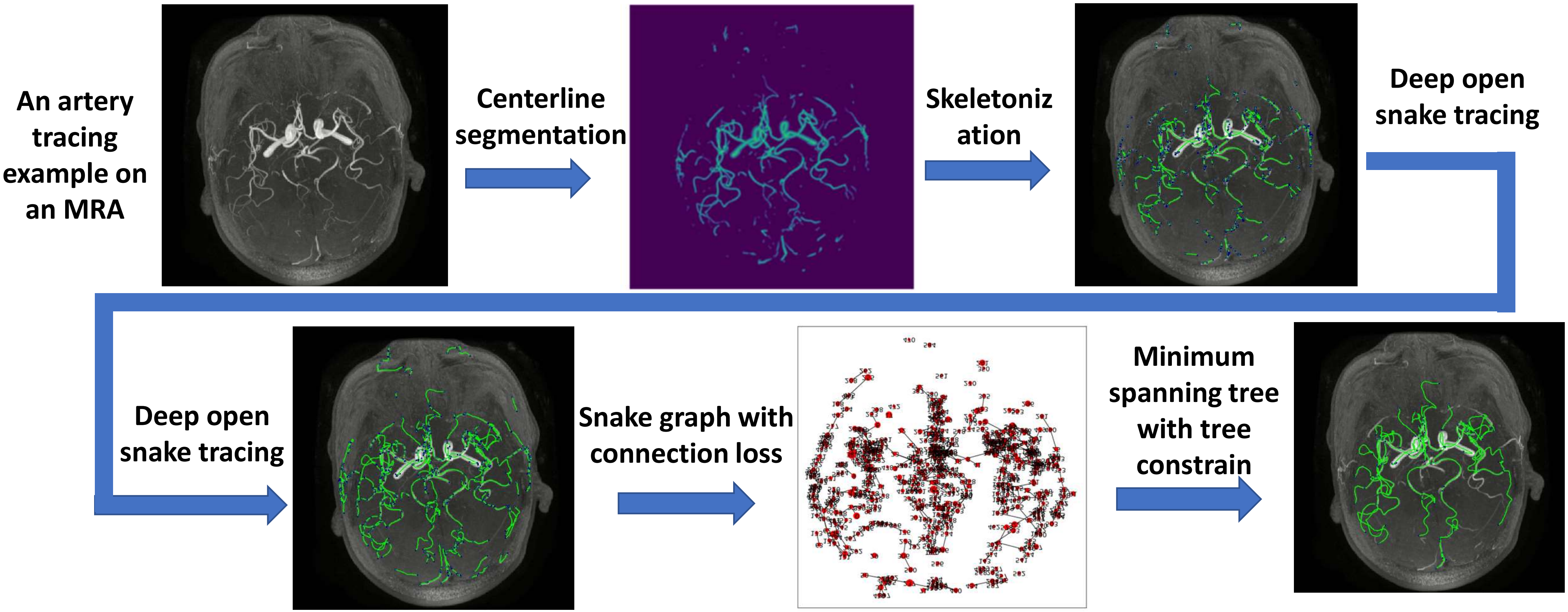


Step 3: Global tree constraint

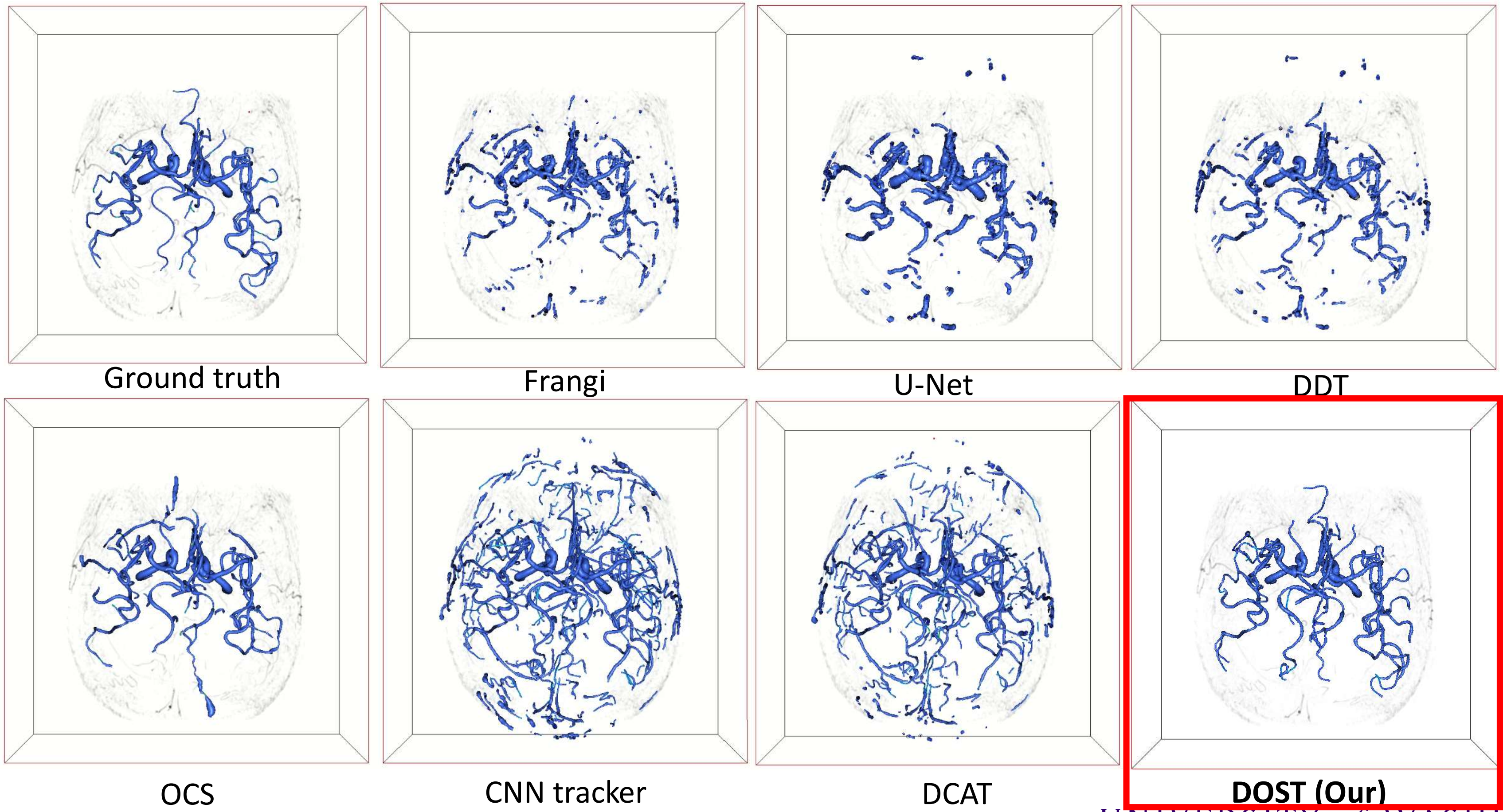
- Intracranial arteries: a tree without broken branches or loops
- 1. Tentative connections for neighboring snakes
- 2. Snake graph construction: nodes=traces, edges=connection loss (estimated by intensity fitness) between traces
- 3. Break loops in the snake graph by minimum spanning tree



Intracranial artery tracing using AICafe on an MRA



Qualitative comparisons with other tracing methods



Quantitative comparisons with other tracing methods

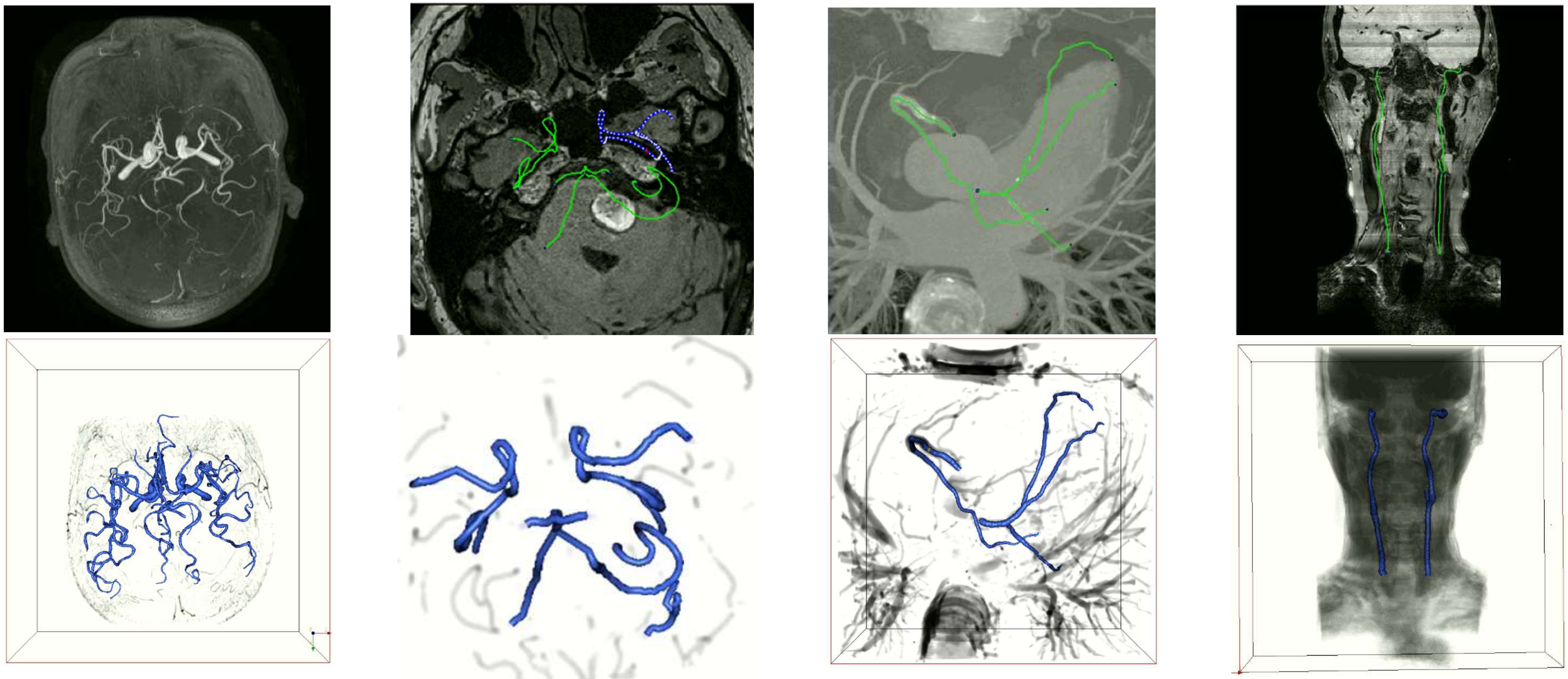
Tracing approach	Model name	Overlap↑	Mean distance↓	MOTA↑	IDF1↑	IDS↓
		Tracking accuracy metrics		Multi-object tracking metrics		
Traditional segmentation	Frangi	0.617	0.956	0.238	0.621	343.9
Deep learning segmentation	U-Net	0.662	0.724	0.300	0.696	398.3
Deep learning segmentation	DDT	0.683	0.703	0.281	0.712	423.0
Traditional tracking	OCS*	0.672	**0.356**	**0.372**	0.694	**74.8**
Deep learning tracking	CNN tracker	0.562	0.860	-0.312	0.595	108.5
Deep learning tracking	DCAT	0.564	0.943	-0.241	0.601	137.8
Hybrid	**DOST (Our)**	**0.732**	0.592	0.318	**0.731**	104.1

* Ground truth was modified manually based on OCS results

A broadly applicable artery tracing solution

Original image (MIP or Slice view)

Deep open snake tracer



Intracranial TOF MRA

Intracranial T1 VISTA (black blood)

Coronary CTA

Carotid MERGE (black blood)

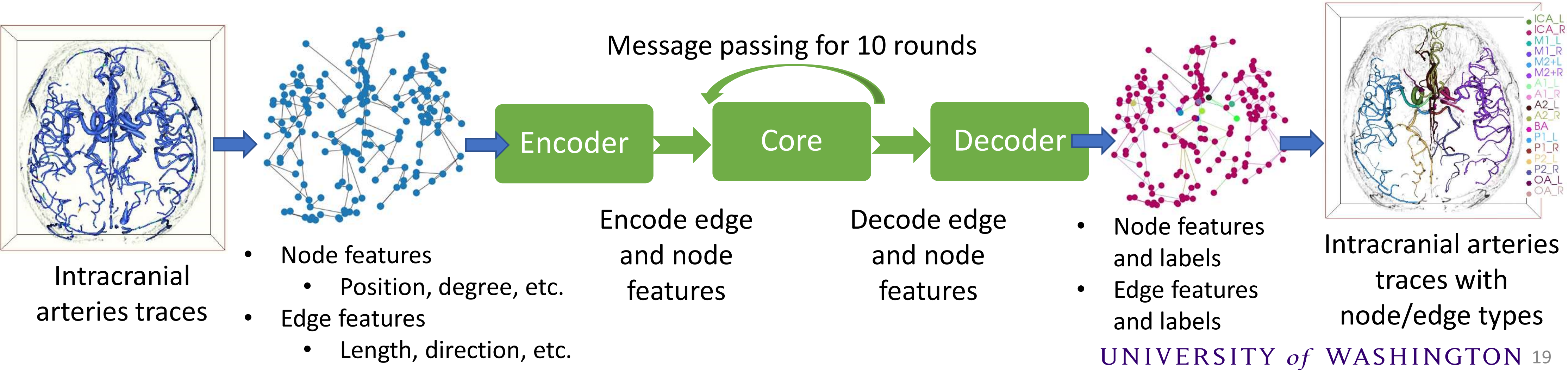
Step 4: Artery landmark prediction from graph neural network

> Intracranial artery centerlines: a natural graph
  - nodes=bifurcation/ending points, edges=having connections between nodes

> Input: a graph with node/edge features

> A message passing Graph Neural Network (GNN)

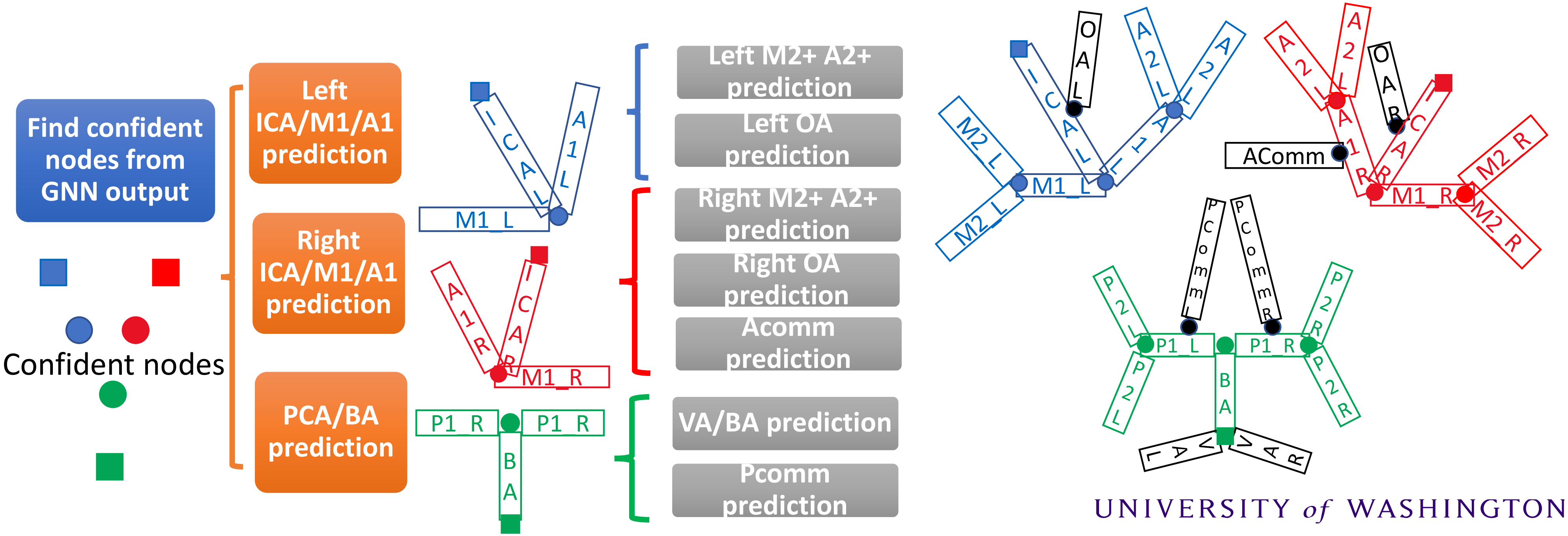
> Output: a graph with more features (including node and edge type)



Step 5: Hierarchical refinement on artery labels

> End-to-end prediction is not perfect

> Hierarchical labeling framework: human + machine knowledge
  - Three-layer labeling from most confident nodes to optional branches
  - Robust for anatomical variations

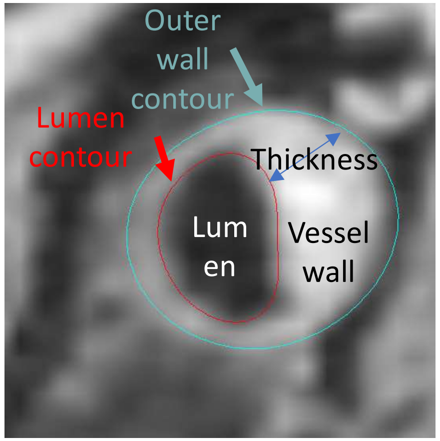


Quantitative comparisons with other labeling methods

Method	Node_Acc ↑	Node_Wrong↓	Node_Solve↑	CoW_Node_Solve↑	Edge_Acc ↑	Edge_Solve↑	Process time (s) ↓
MAP	0.9153	10.0	0	0.0476	0.3304	0	1.075
Template	0.7316	31.6	0	0.0476	0.7934	0	5.057
Atlas	0.8856	13.5	0	0.0095	0.7010	0	9.253
GNN	0.9637	4.3	0.0381	0.4286	0.9223	0	**0.020**
GNN+HR (Our)	**0.9746**	**3.0**	**0.3238**	**0.6381**	**0.9246**	**0.3238**	0.092

Overview

> Background
> Quantitative vasculature map construction
  - Artery centerline generation
  - Lumen and vessel wall segmentation
  - Atherosclerotic lesion identification and classification
> Summary and future directions



[B1] Li Chen, et. al, IEEE International Conference on Bioinformatics and Biomedicine (BIBM), 2017.

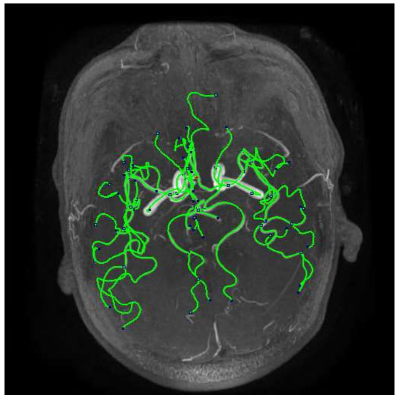
[B2] Li Chen, et. al, ISMRM, 2018.

[B3] Li Chen, et. al, IEEE Access, 2020.

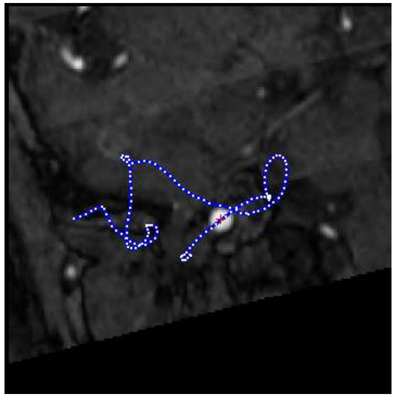
[B4] Li Chen, et. al, Magnetic resonance in medicine, 2020.

From centerlines to lumen/vessel wall feature extraction

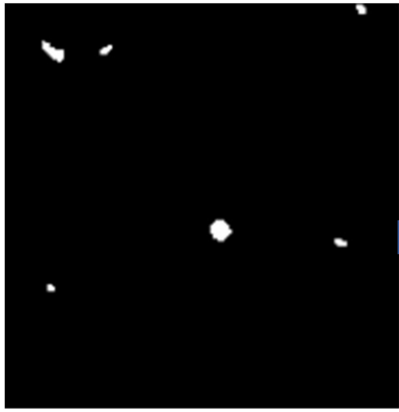
Bright blood MRA (MIP view)



Cross sectional slice

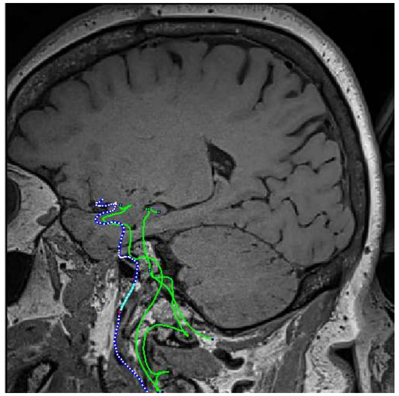


Lumen segmentati on [B1]

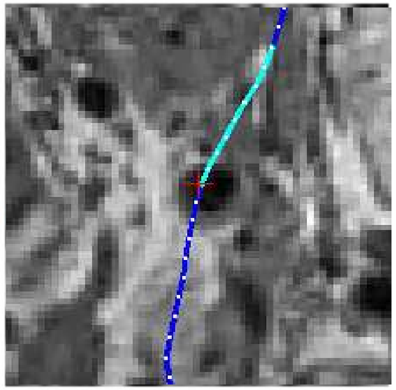


Lumen morphometry features:
- Cross-sectional area
- Volume
- etc.

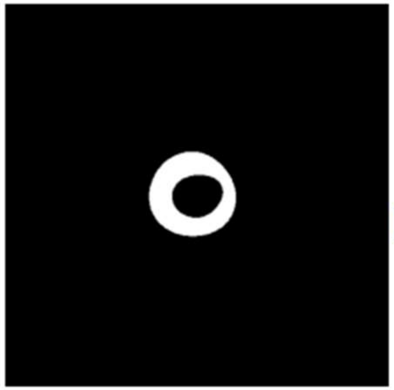
Black blood MR VWI (Slice view)



Cross sectional slice



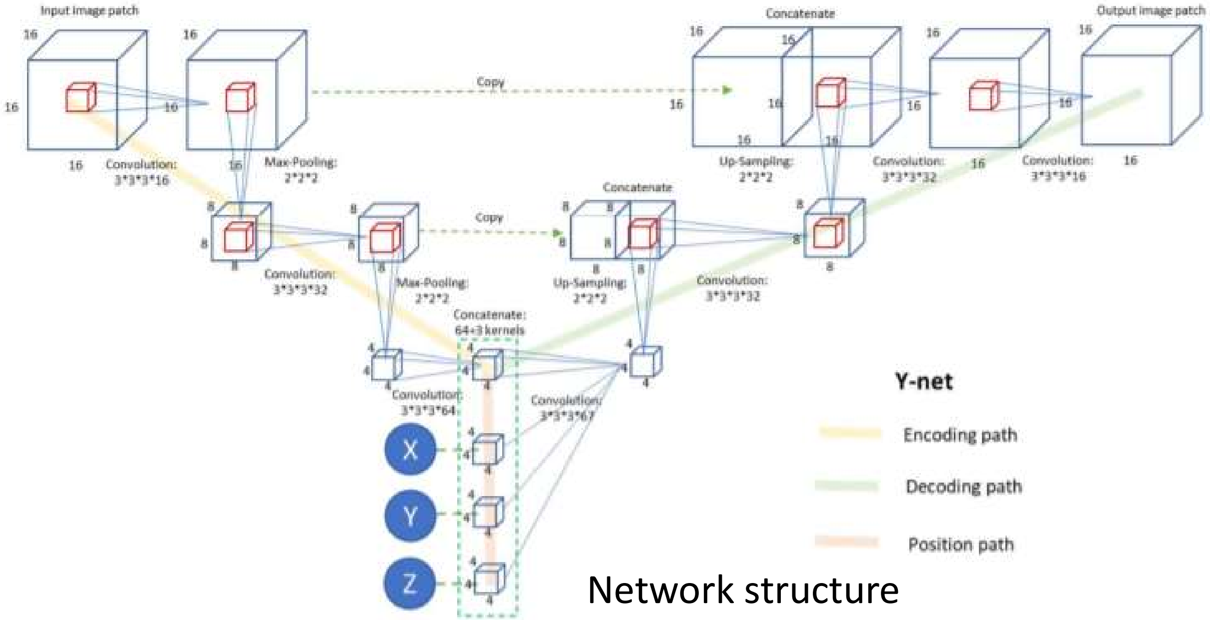
Polar vessel wall segmentati on [B2]



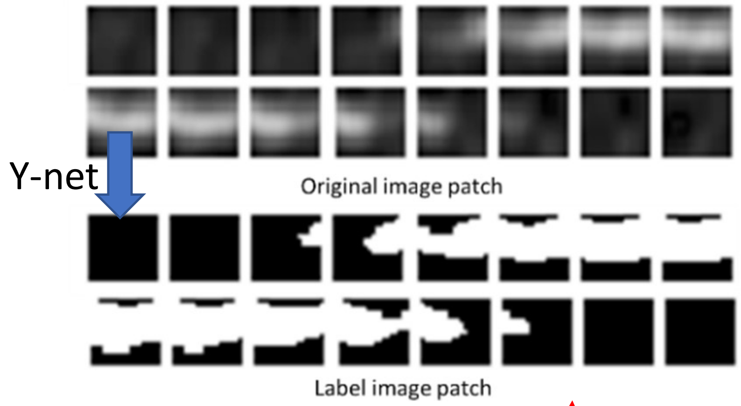
Plaque morphometry features:
- Vessel wall thickness
- Plaque region
- etc.

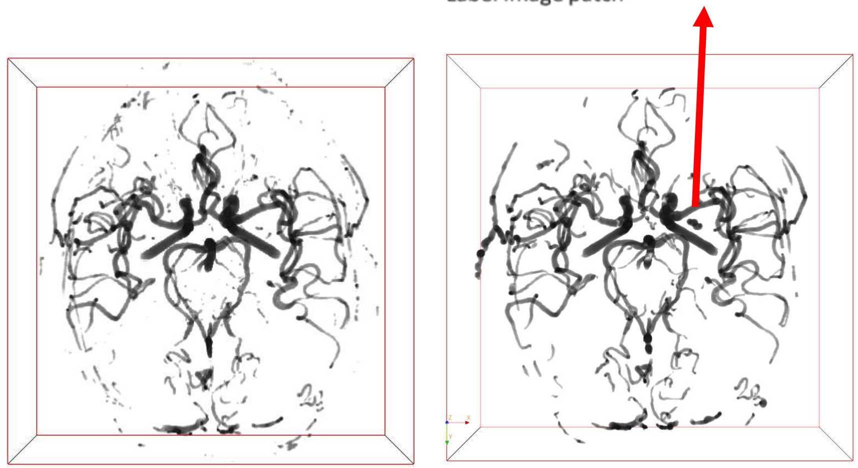
Segment lumen areas from bright blood MRA

- From iCafe traces to train lumen segmentation
- Y-net [B1]: 3D patch-based CNN segmentation
- Patch origin added as the additional information



Network structure

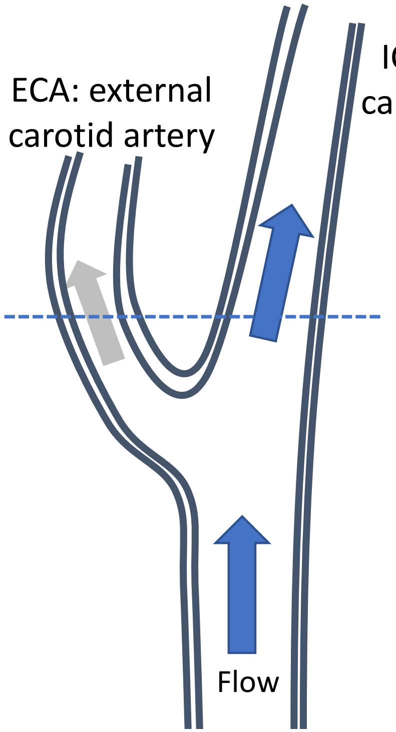




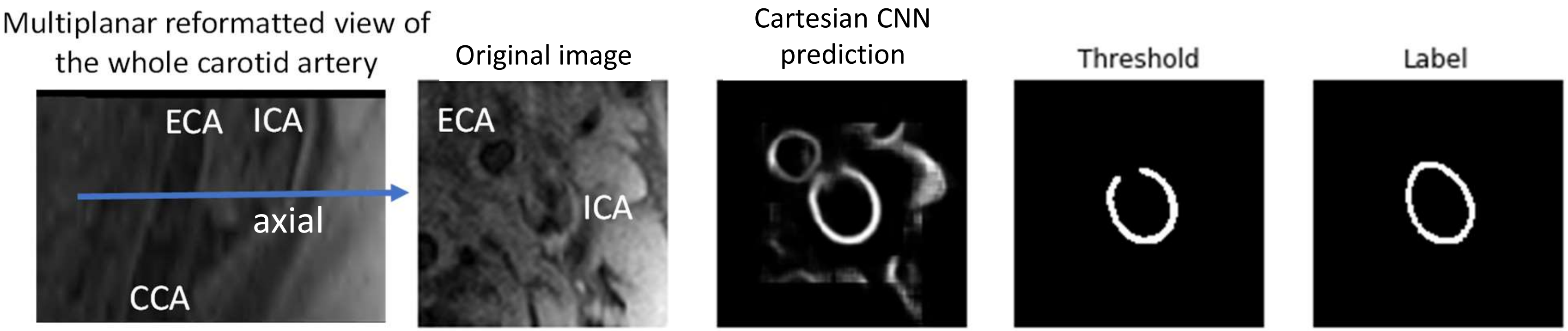
Y-net segmentation

iCafe (Ground truth) segmentation

Problem of vessel wall segmentation using Cartesian CNN



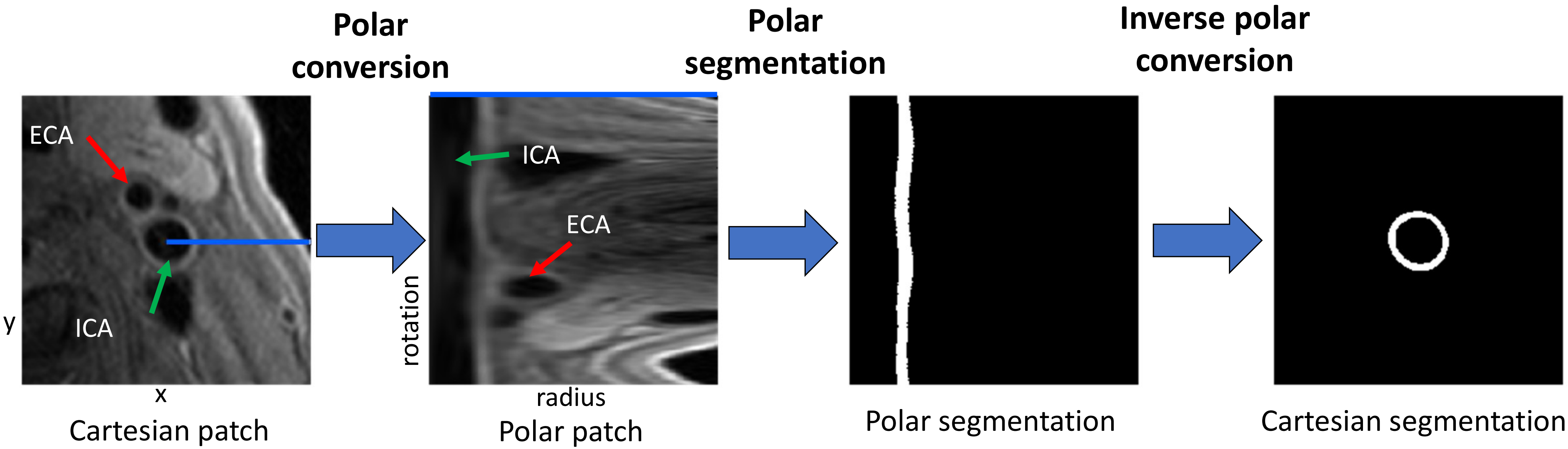
- Artery bifurcations cause many arteries coexist in the view
  - Traditional Cartesian CNN segments all vessel walls
- Wall signal drops/flow artifacts
  - Wall boundary continuity cannot be ensured



Exemplary problems encountered in Cartesian based neural network models [B2]

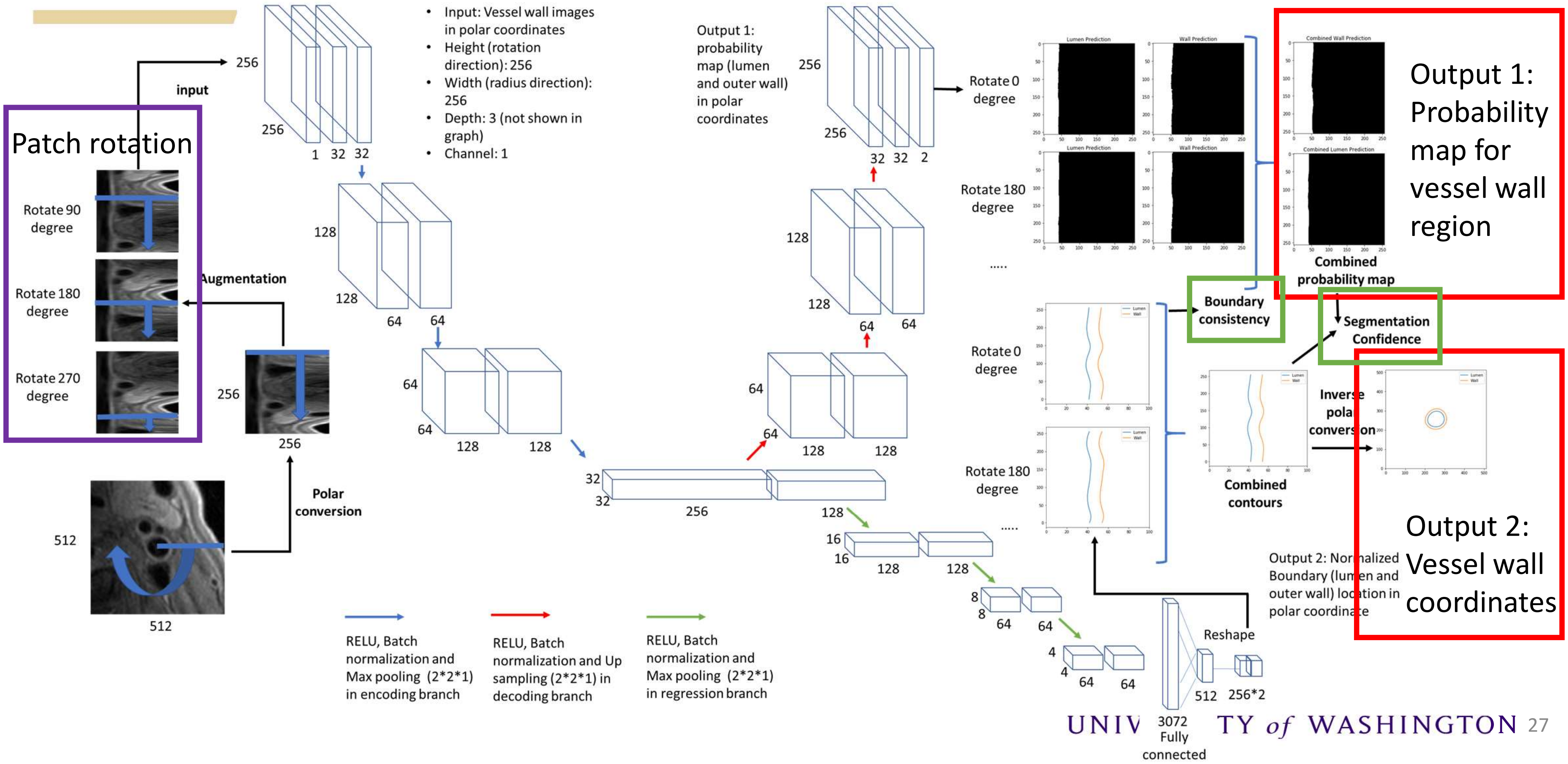
Polar vessel wall segmentation [B3]

> Benefits of polar segmentation
  - Neighboring arteries (ECA) are quite different from the artery of interest (ICA).
  - Contours are represented as two vertical lines, easy to ensure continuity.

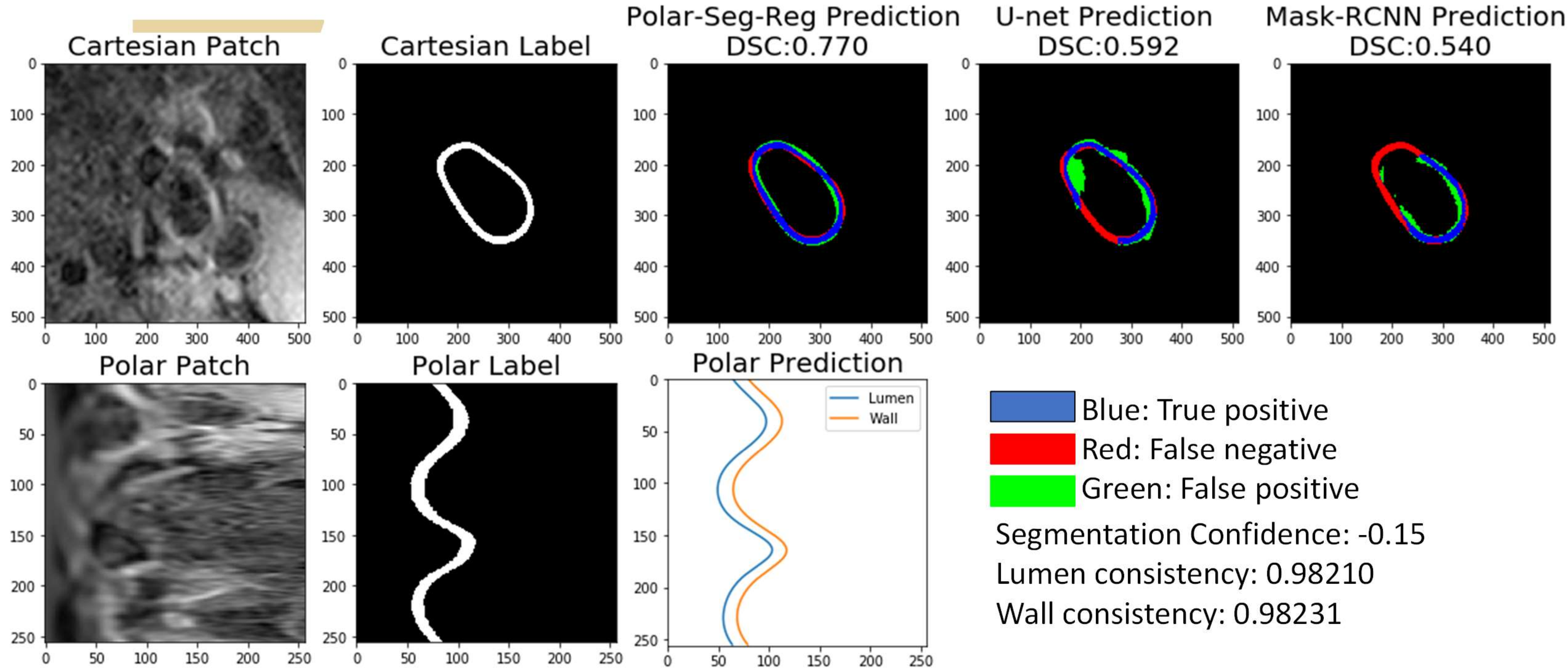


Example of polar segmentation in a carotid artery

Dual output network for segmentation **+ confidence**



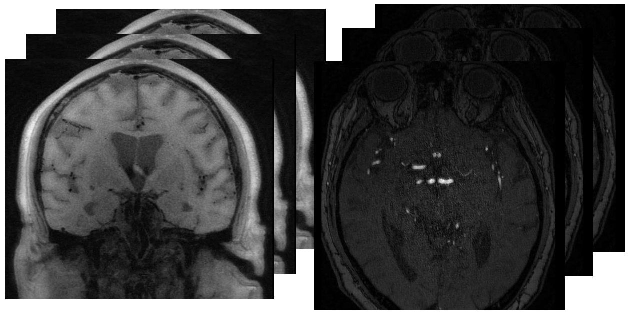
An example of polar segmentation at a challenging slice



[1] U-Net: Ronneberger, 2015. [2] Mask-RCNN: He, 2017.

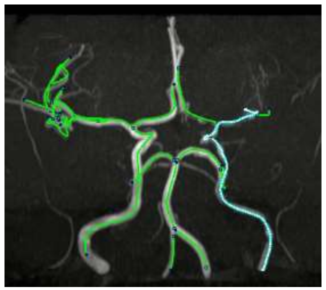
iCafe+: intracranial centerline + vessel wall feature

> With transfer learning and active learning from carotid segmentation model



MR VWI (and/or MRA) images for intracranial arteries

iCafe or AICafe tracing

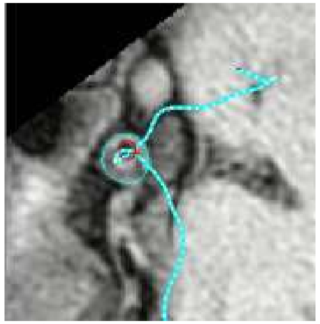


Artery centerlines

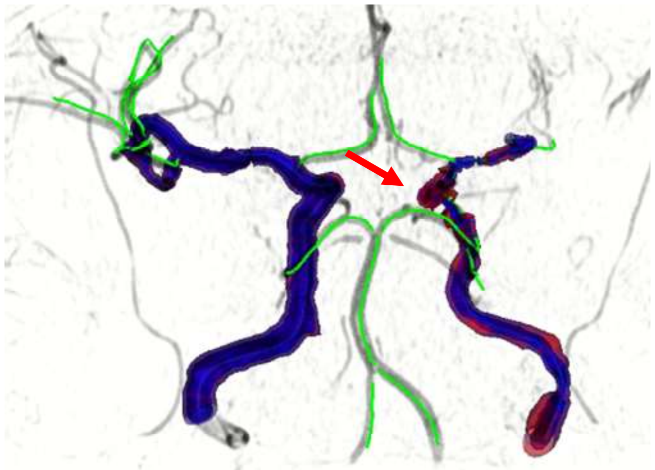
Extract patches along the centerlines

Cross-sectional slice

Vessel wall segmentation



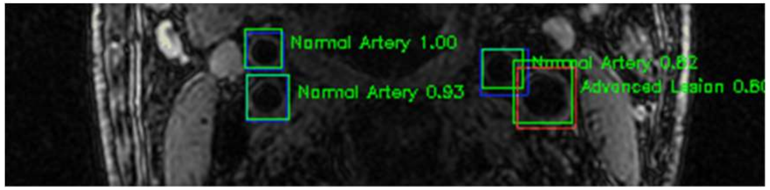
Combine segmentation results into color coded vascular map



Color coded vascular map (redder means thicker wall)
Red arrow indicate the example cross-sectional location

Overview

> Background
> Quantitative vasculature map construction
  - Artery centerline generation
  - Lumen and vessel wall segmentation
  - Atherosclerotic lesion identification and classification
> Summary and future directions



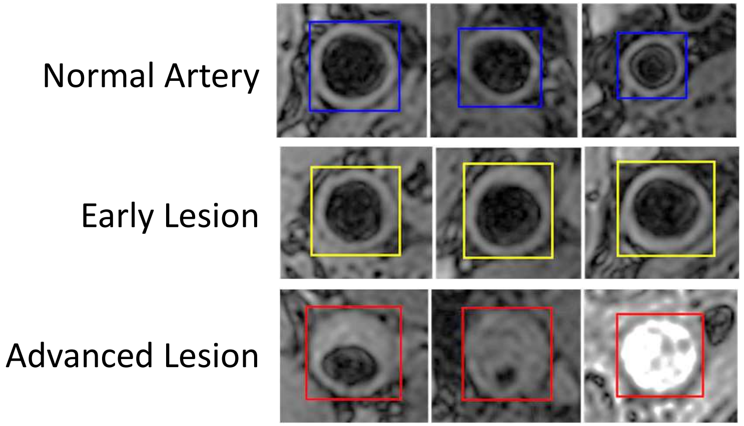
[C1] Li Chen, et. al, ISMRM 2019.

[C2] Li Chen, et. al, Magnetic resonance in medicine**,** 2021.

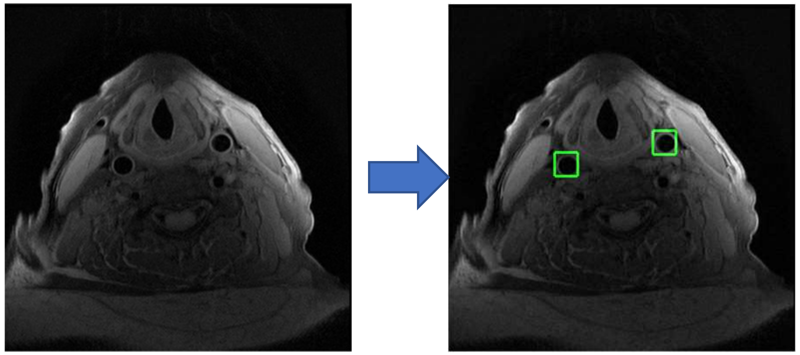
[C3] Hongjian Jiang, **Li Chen**, et. al, SPIE, 2020,

LATTE: Atherosclerotic lesion identification and classification

- Fast MR solution for carotid artery assessment
- Aims
  - Locate artery, vessel wall segmentation and classify severity of plaques
  - Large coverage with less imaging/process time
  - Deployable to multiple sites
- Existing technique: tracklet refinement [B3]
- Challenges
  - Exclude low quality slices/scans
  - Domain adaptive for multiple sites



Tracklet refinement

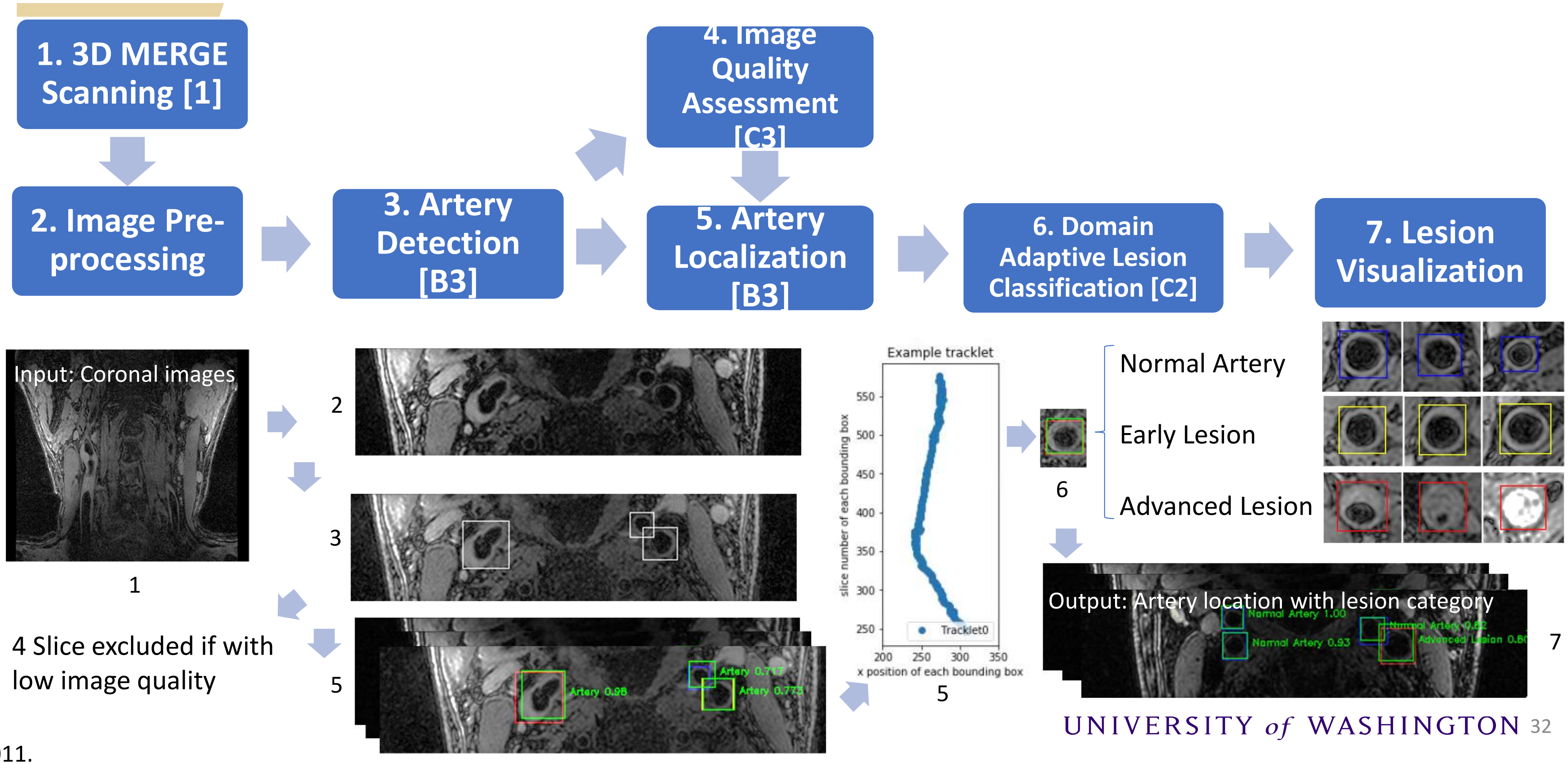


Carotid arteries identified by our Yolo [1] based tracklet refinement algorithm [B3]

[1] Redmon, 2017.

LATTE: **L**esion **A**ssessment **T**hrough **T**racklet **E**valuation [C1] [C2]

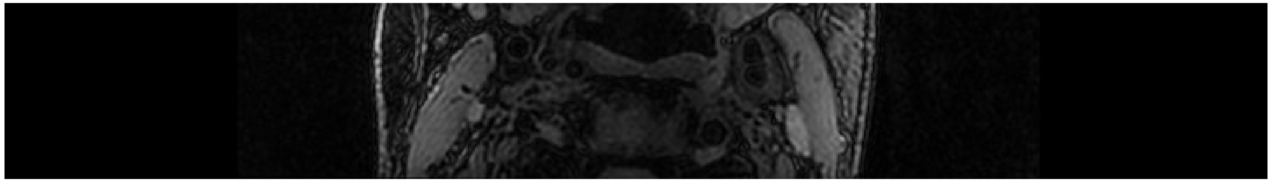
LATTE workflow



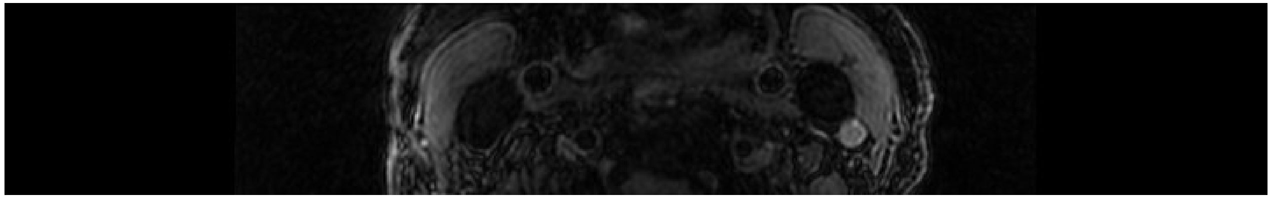
[1] Balu, 2011.

Domain shift among datasets

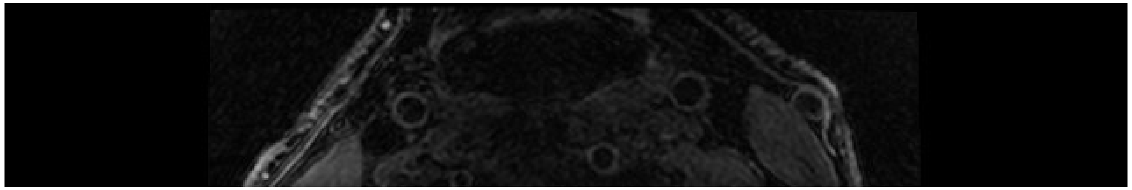
(a) Original domain:
CARE-II dataset



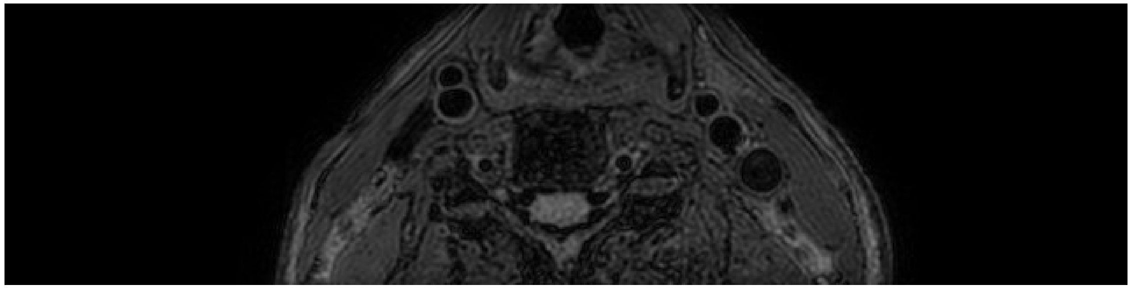
(b) Target domain:
CROP dataset



(c) Target domain:
IPH dataset



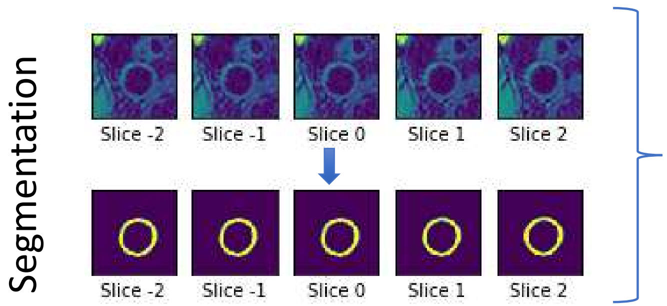
(d) Target domain:
Renji dataset



Causes of domain shift

- Scanner
- Image size
- Imaging resolution
- Coverage
- Coils
- Echo time / Repetition time in MR imaging
- etc.

Domain adaptive CNN with its training strategy



Patch of 64*64 in 5 neighboring slices, along with segmentation mask

Feature extractor

Convolution + Batch Normalization + Relu + Max Pool

4 concatenated blocks

Dropout | Dropout | Dropout

Node 512 → Node 128 → Node 1 + threshold

Source classifier
- Normal Artery
- Early Lesion
- Advanced Lesion

Node 32 → Node 2

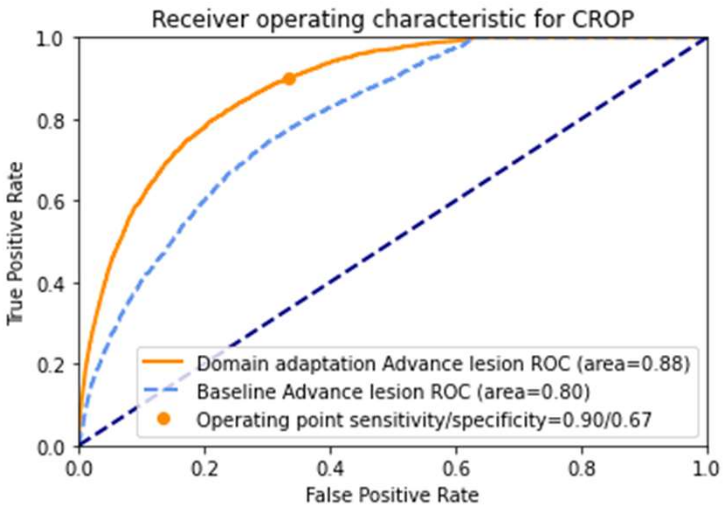
Domain classifier
- Source domain
- Target domain

	Input (each block is a batch)		**Source classifier output**		**Domain classifier output**	
Step1: Change weights on non-domain classifier branch	Source domain patches	Target domain patches	Source domain lesion classes	0 (Not in loss)	1	0
Step2: Change weights on domain classifier branch only	Source domain patches	Target domain patches			0	1

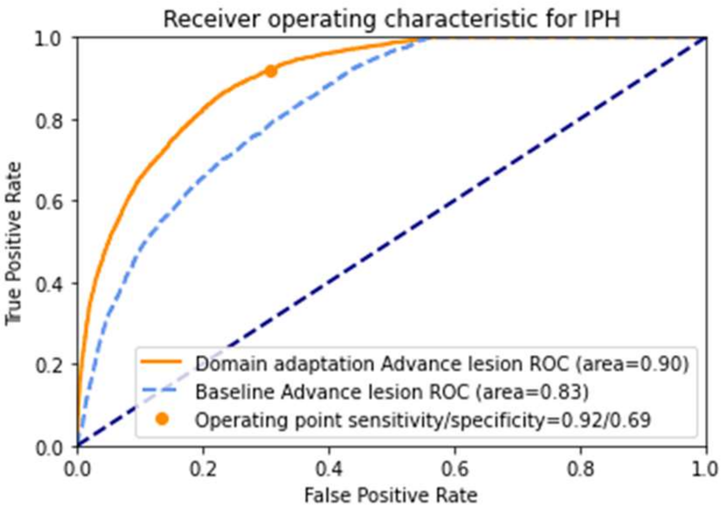
Enlighted from Ganin, 2015. Published in [C2]

Quantitative performance evaluation for domain adaptation

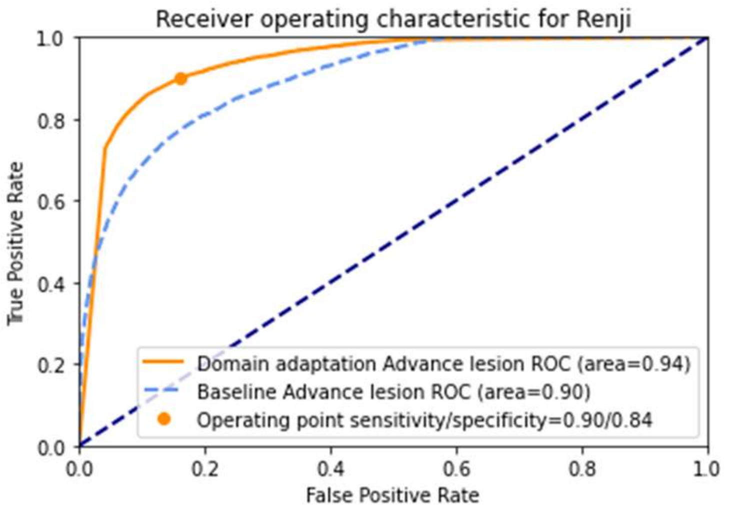
> Evaluation by area under the Receiver operating characteristic curves (AUC) before and after domain adaptation
> No additional annotations required for target datasets (CROP, IPH and Renji)



AUC improved from 0.80 to 0.88



AUC improved from 0.83 to 0.90



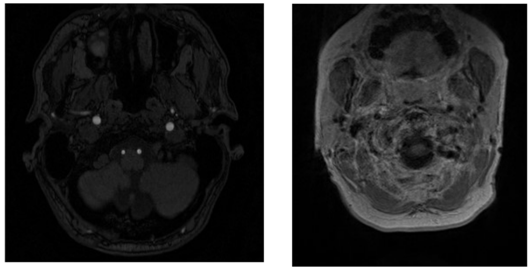
AUC improved from 0.90 to 0.94

Overview

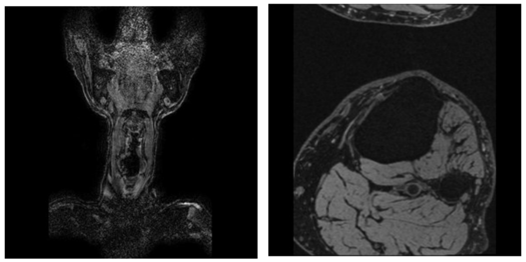
> Background
> Quantitative vasculature map construction
  - Artery centerline generation
  - Lumen and vessel wall segmentation
  - Atherosclerotic lesion identification and classification
> Summary and future directions

Conclusions

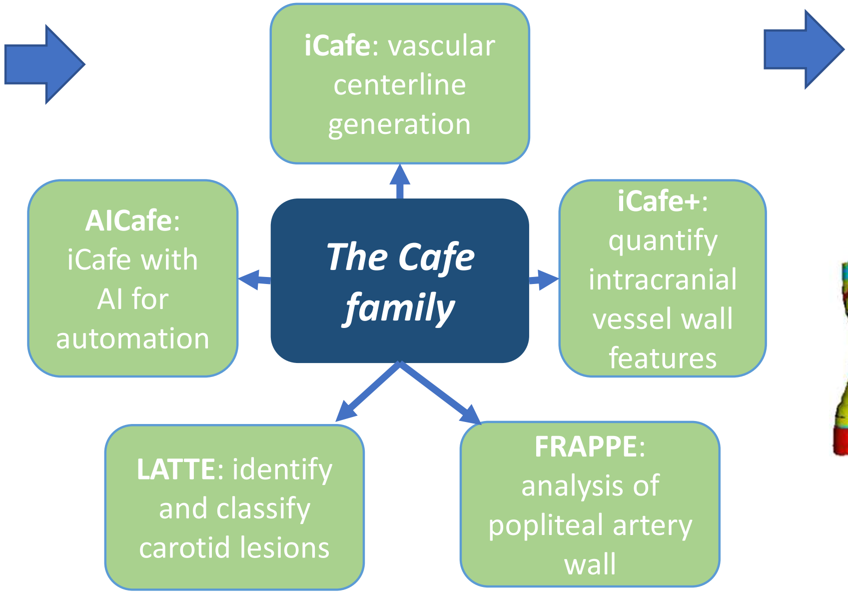
> Novel vascular analysis toolset (*the Cafe family*) for quantitative vasculature map:
- Comprehensive features: artery structure + plaque morphometry + lesion severity
- Automated and robust, suitable for large studies



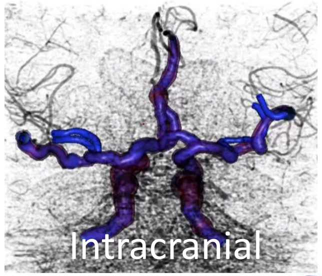
Intracranial arteries MRA/MR VWI

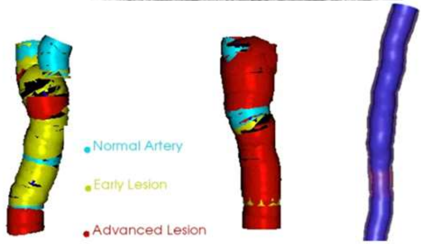


Carotid and popliteal artery MR VWI



The Cafe family toolset





Carotid Popliteal

- Length
- Tortuosity
- Volume
- Vessel wall thickness
- Plaque area
- Normalized wall index
- Lesion severity
- etc.

Quantitative vascular map with comprehensive features

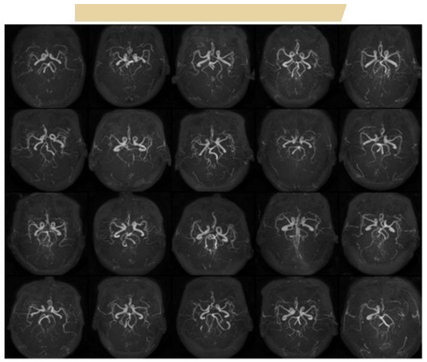
Conclusions

> Artificial intelligence on vascular image analysis
  - Extract subtle patterns not easily describable
  - Human and machine wisdom combined for better performance
  - Progressively improving performance

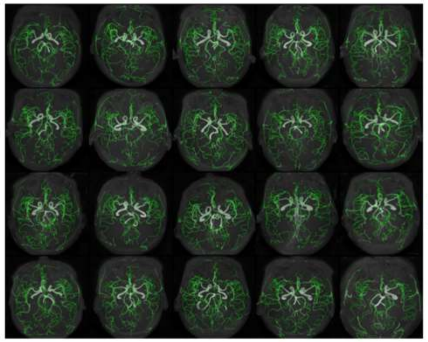
> Contribute to vascular research
  - iCafe tool distributed under academic licenses
  - Datasets for intracranial artery labeling [1] and vessel wall segmentation [2]
  - Vessel wall segmentation challenge (MICCAI/SMRA 2021) [3] with 200+ participants

[1] https://github.com/clatfd/GNN-ART-LABEL
[2] https://github.com/clatfd/OAI-Polar
[3] https://vessel-wall-segmentation.grand-challenge.org/

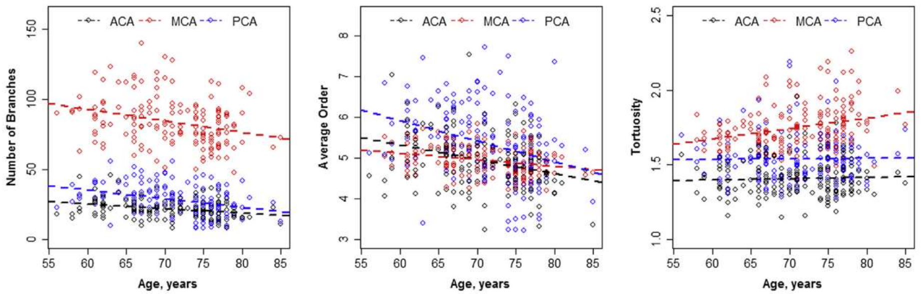
The Cafe family further our understanding on vascular disease



iCafe/
AICafe

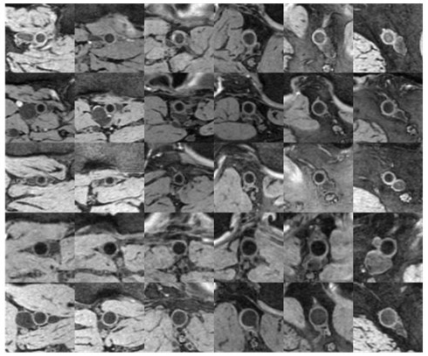


Statistical
analysis

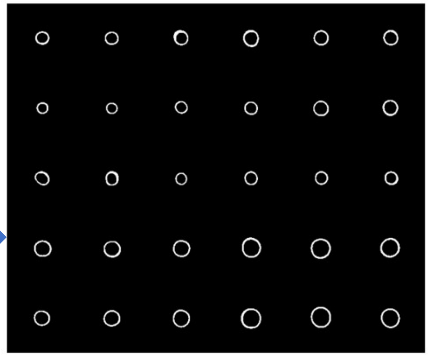


iCafe/AICafe processed 163 intracranial arteries

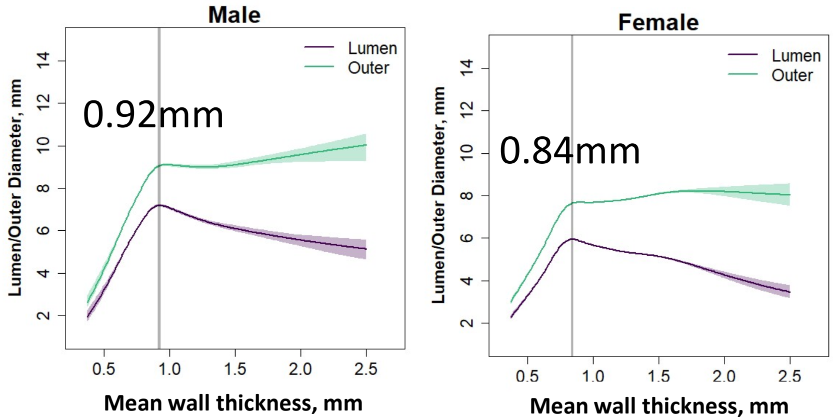
Vascular change through aging represented by decrease of branches (left), order (middle) and increase of tortuosity (right). Regional difference (color) also observed.



FRAPPE



Statistical
analysis



FRAPPE [B4] processed 235,152 and 319,953 popliteal images of men and women

Vessel wall remodeling patterns

From Chen, Neurobiology of Aging, 2019 and Canton, JAHA, 2021.

Future directions

- Further improve the performance
- Extend *the Cafe family* toolbox to more vascular beds with more imaging modalities
- Construct a vascular feature bank to store vascular features along with clinical data to provide reference for new patients with similar features in the feature bank
- Transforming *the Cafe family* toolbox to products with easy access for medical workers

Artery centerline generation related publications

iCafe development:

1. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Development of a quantitative intracranial vascular features extraction tool on 3D MRA using semiautomated open-curve active contour vessel tracing. Magnetic resonance in medicine (IF:3.9), 2018, 79 (6), Pages 3229-3238. Editor's pick.
2. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Quantification of morphometry and intensity features of intracranial arteries from 3D TOF MRA using the intracranial artery feature extraction (iCafe): A reproducibility study. Magnetic Resonance Imaging (IF:2.1), 2019, 57 (April 2019), Pages 293-302.
3. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. A Novel Algorithm for Refining Cerebral Vascular Measurements in Infants and Adults. Journal of Neuroscience Methods (IF:2.8), 2020, 340 (1 July 2020), Pages 108751.

AICafe development:

4. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Simultaneous Intracranial Artery Tracing and Segmentation from Magnetic Resonance Angiography by Joint Optimization from Multiplanar Reformation. MICCAI CVII-STENT 2019 workshop, 2019, Shenzhen, China (October 13), Pages 201-209.
5. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Automated Intracranial Artery Labeling using a Graph Neural Network and Hierarchical Refinement. MICCAI 2020, Lima, Peru.
6. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Deep Open Snake Tracker for Vessel Tracing. MICCAI 2021, Strasbourg, France.

Artery centerline generation related publications

iCafe applications:

7. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Quantitative Assessment of the Intracranial Vasculature in an Older Adult Population using iCafe (intraCranial Artery Feature Extraction). Neurobiology of Aging (IF:4.4), 2019, 79 (July 2019), Pages 59-65.
8. Li Chen, et. al, Jenq-Neng Hwang and Chun Yuan. Quantitative Assessment of the Intracranial Vasculature of Infants and Adults using iCafe (intraCranial Artery Feature Extraction). Frontiers in Neurology (IF:2.9), 2021, 28 May 2021.
9. Zhensen Chen, Li Chen, et. al, Chun Yuan. Intracranial vascular feature changes in time of flight MR angiography in patients undergoing carotid revascularization surgery. Magnetic Resonance Imaging (IF:2.1), 2020, 75 (January 2021), Pages 45-50.
10. Wenjin Liu, Xiaoqin Huang, Xuebing Liu, Dakota Ortega, Li Chen, et. al, Uncontrolled hypertension associates with subclinical cerebrovascular health globally: a multimodal imaging study. European Radiology (IF:4.1), 2020, 14 September 2020. DOI: 10.1007/s00330-020-07218-5

Lumen/vessel wall segmentation related publications

Lumen segmentation development

11. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. 3D intracranial artery segmentation using a convolutional autoencoder. 2017 IEEE International Conference on Bioinformatics and Biomedicine (BIBM), 2017, Kansas City, MO, USA

Lumen and outer wall segmentation development

12. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Automated Artery Localization and Vessel Wall Segmentation of Vessel Wall Images using Tracklet Refinement and Polar Conversion . IEEE Access, 2020, 8, Pages 217603-217614.
13. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Fully automated and Robust Analysis Technique for Popliteal Artery Vessel Wall Evaluation (FRAPPE) using Neural Network Models from Standardized Knee MRI. Magnetic resonance in medicine (IF:3.6), 2020, 84, Pages 2147–2160.

Vessel wall segmentation applications

14. Gador Canton, Daniel Hippe, Li Chen, et. al, Chun Yuan. Atherosclerotic Burden and Remodeling Patterns of the Popliteal Artery as detected in the MRI Osteoarthritis Initiative Dataset. JAHA: Journal of the American Heart Association (IF:4.67), 2021, 10 (11).
15. Daniel Hippe, Niranjan Balu, Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Confidence weighting for robust automated measurements of popliteal vessel wall MRI. Circulation: Genomic and Precision Medicine (IF:4.9), 2020, 13 (1), Pages 39-41.

Atherosclerotic plaque assessment related publications

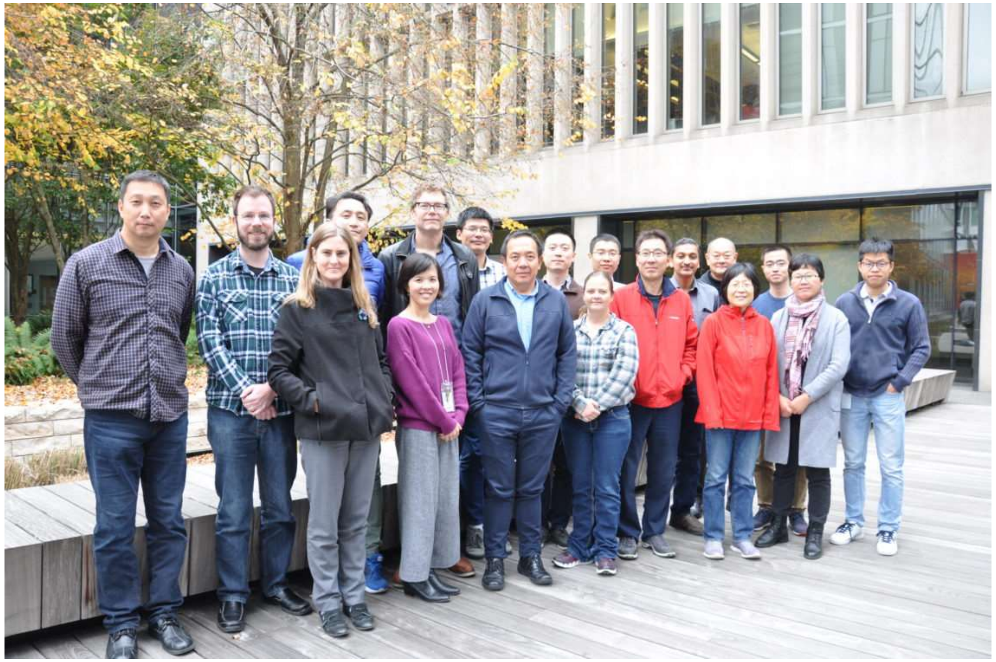
16. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Carotid Artery Localization and Lesion Detection on 3D-MERGE MRI through Online Learning. Society for Magnetic Resonance Angiography 30th Annual International Conference, SMRA 2018, University of Glasgow, Glasgow, Scotland.
17. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Carotid Artery Localization and Lesion Classification on 3D-MERGE MRI using Neural Network and Object Tracking methods. 2019 Annual Meeting of International Society for Magnetic Resonance in Medicine (ISMRM), 2019, Palais des congrès de Montréal, Montréal, QC, Canada
18. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Domain Adaptive and Fully Automated Carotid Artery Atherosclerotic Lesion Detection using an Artificial Intelligence Approach (LATTE) on 3D MRI. Magnetic resonance in medicine (IF:3.6), 2021, 86 (3), Pages 1662-1673.
19. Hongjian Jiang, Li Chen, et. al, Chun Yuan. A Target-Oriented and Multi-Patch Based Framework for Image Quality Assessment on Carotid Artery MRI. Medical Imaging 2020: Image Processing. SPIE, 2020, Marriott Marquis Houston, Houston, Texas, United States (February 15 - 20).
20. Duygu Geleri, Hiroko Watase, Baocheng Chu, Li Chen, et. al, Chun Yuan. Detection of Advanced Lesions on Carotid Arteries using 3D-MERGE Magnetic Resonance Imaging as a Screening Tool. Stroke (IF:7.2), 2021,

Acknowledgements

- Thanks for the advices from advisors and committee members.
- Thanks for the support from Information Processing Lab and Vascular Imaging Lab.
- We acknowledge the contributions from
  - Our collaborators: CARE-II, CROP, Kowa, OAI, BRAVE, University of Arizona researchers, etc.
  - Open-source resources owners: Dr. Yu Wang from Rensselaer Polytechnic Institute, Dr. Elizabeth Bullitt from UNC, the DeepMind group, etc.
- Thanks for the funding supports from Philips healthcare, National Institute of Health, and American Heart Association.
- We gratefully acknowledge the support of NVIDIA Corporation for donating the Titan GPUs.

Thanks for your attention!

Information Processing Lab
Department of Electrical and Computer Engineering
University of Washington



Vascular Imaging Lab
Department of Radiology
University of Washington

Questions and answers

Thanks for your attention