

FEATURE EXTRACTION AND QUANTIFICATION TO EXPLORE HUMAN VASCULATURE

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Thanks for coming to my general exam

- 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
- Completed work
 - Vasculature centerline generation
 - Vasculature segmentation
- Future directions
 - Automated intracranial artery tracing
 - Comprehensive vasculature map generation
 - Vascular feature bank construction

Background: Human vasculature

- A complicated and important system
- Arteries visible from Magnetic Resonance Imaging (MRI) techniques
 - MR angiography (MRA), MR vessel wall imaging



Left: Maximum intensity projection of intracranial arteries

Bottom: One slice of carotid arteries pointed by the arrow Right: One slice of popliteal

artery pointed by the arrow





Image from Wikipedia: Circulatory_system ⁴

Background: atherosclerosis

- Cholesterol accumulates on vessel wall, forming atherosclerotic plaque
- Plaque may narrow/block arteries, may also burst, causing ischemic stroke
- A systemic disease affecting multiple vascular beds
- Quantitative analysis of all human vasculature
 - Monitor vascular health
 - Help vascular research



Image from https://www.mayoclinic.org/diseases-conditions/arteriosclerosisatherosclerosis/symptoms-causes/syc-20350569

Aim: comprehensive vasculature analysis

- Comprehensive vasculature analysis needed
 - Lumen: identify artery centerlines to extract artery structures and blood flow features
 - Outer wall: identify vessel wall contours to extract plaque features
 - Automated solutions for all human vasculature
- Challenges
 - Tiny structure of artery and vessel wall (<1mm)
 - Signal low, contrast weak, artifacts in vascular images
 - Limited samples, expensive manual labeling



Lumen (red) and outer wall (blue) contours on a slice of popliteal vessel wall

Related research on luminal region analysis

- Limited features available
- Limited ability for human correction
- Insufficient automation



Lumen segmentation only, no topological features [1]

Large arteries with good contrast only [2]

[1] Zhao, et.al, IEEE TMI, 2017 [2] Volkau, et.al, IEEE TMI, 2005
[3] Wright, et.al, NeuroImage, 2013 [4] Marchenko, et al, J of Digital Imaging, 2010



No radius features and limited anatomical regions [3]



Long time manual processing [4]

Related research on vessel wall segmentation

- Deformable model
 - Active contour models [1,2,3]
- Model fitting
 - Active shape model [4]
 - Ellipse fitting [5]
 - 3D NURBS surface fitting [6]
 - Tree model fitting [7]
- Learning-based classification
 - Fuzzy clustering [5]
 - AdaBoost [8]
 - K-nearest neighbors [7]
- Graph-based methods
 - Coupled graph cut [9,10,11]

- Remaining problems:
 - Robustness
 - Automation

[1] Yuan, et al. Magnetic Resonance Imaging, 1999.
[2] Adams, et al. Proc. SPIE medical imaging, 2002.
[3] Kerwin, et.al. Topics in Magnetic Resonance Imaging, 2007.
[4] Hunter, et.al. J Magn Reson Imaging, 2006.
[5] Adame, et al. Proc. SPIE medical imaging, 2004.
[6] Van't Klooster, et. al. Journal of Magnetic Resonance Imaging, 2012.
[7] Gao, et. al. Medical Physics, 2017.
[8] K Hameeteman, et. al. Physics in medicine and biology, 2013.
[9] Ukwatta, et. al. IEEE Transactions on Medical Imaging, 2016.
[11] Petersen, et.al. IEEE Transactions on Medical Imaging, 2019.

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Completed work Part I: Vasculature centerline generation

- Centerline: a list of points along the center of artery (with radius)
- Generate centerline from vascular images in 3D space
 - Extract vascular structure features: length, tortuosity, etc.
 - Identify region of interest for detailed analysis: vessel wall segmentation
- Start with relatively straight arteries



MR scan of knee with relatively straight popliteal artery (displayed in a reconstructed tube)

Centerline generation for relatively straight arteries

- Time dimension in video equivalent to depth dimension in 3D medical image
- Centerline generation: tracking by detection
 - Detection of bounding boxes from each axial image slice
 - Combining detections using **tracklet refinement** algorithm



Tracking cars (in bounding boxes) from traffic videos in NVIDIA AI City Challenge [1]



Finding popliteal artery from 3D vascular images



Popliteal artery shown in knee scan

Similarity of artery region among axial slices





Three axial slices of popliteal arteries

[1] Tang, et. al, CVPR, 2018

Artery localization: detection + tracklet refinement

- Detection of arteries in each slice using Yolo V2 [1] detector
 - Predict objects in bounding boxes with a confidence score
 - Pretrained weights from natural images
 - Further tuned on vascular images using vascular labels
- Problems
 - Noise detections
 - Missing detections
- Solution
 - Use detections from neighboring slices



Example bounding boxes (with confidence score) on a slice of carotid artery image Bounding boxes: minimum encompassing rectangle around the artery

[1] Redmon, et.al, CVPR, 2017.

Artery localization: detection + tracklet refinement



Tail box $TB_i = (x_i, y_i, w_i, h_i, z_i, c_i)$ in tracklet i Head box $HB_i = (x_i, y_i, w_i, h_i, z_i, c_i)$ in tracklet j x, y, z: 3D coordinates of box center, w, h: width and height of box c: confidence score

Combined loss $L_{i,i} = a_1 \cdot \max(0, z_i - z_i) - a_2 \cdot$ $IoU(TB_i, HB_i) + a_3 \cdot (|w_i - w_j| + |h_i - h_j|)$ Weights of $a_{1,2,3}$ decided from validation set 13

Artery localization: detection + tracklet refinement



Smooth remaining tracklets, using a median filter and a mean filter

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Tracklet refinement results

Dataset with #slices		Mean IoU	Miss detection	False detection
Carotid N=3406	Before refinement	0.779	5.8%	1.0%
	After refinement	0.798	4.3%	0.0%
Popliteal N=588	Before refinement	0.783	0.0%	6.6%
	After refinement	0.861	0.0%	0.0%

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Centerline generation results



Bounding boxes along carotid artery (16 slices, 2mm thickness)

Bounding boxes along popliteal artery (76 slices, 1.5mm thickness)

Completed work Part 2: Vessel wall segmentation

- A novel vessel wall segmentation algorithm
 - Polar segmentation [1] to generate vessel wall contours for vessel wall thickness measurements
- Clinical applications using vascular segmentation
 - Automated vessel wall analysis for popliteal arteries [2]
 - Fast MR screening system for carotid lesion detection [3]

[1] Chen, et. al, submitted to IEEE Trans on Med Img, Under review

[2] Chen, et. al, submitted to Magn Reson In Medicine, Under review

[3] Chen, et. al, submitted to Scientific Reports, Under review

Metrics for evaluating segmentation performance

• Dice Similarity Coefficient (DSC) [1]

 $-DSC = \frac{2(A \cap B)}{A+B}$

- A is the ground truth, B is the segmentation
- Higher better, range from 0-1
- DSC>0.7 considered excellent



Illustration of DSC

[1] Dice, et. al, Ecology, 1945.[2] Angelie, et. al, Invest. Radiol, 2007.

Metrics for evaluating segmentation performance

• Degree of Similarity (DoS) [1]

$$- DoS = \frac{\sum_{n=0}^{N} p_n(d)}{N} \text{ where } p_n(d) = \begin{cases} 1, if \ d \leq T\\ 0, if \ d > T \end{cases}$$

- N: sample pair of points on contours
- T: distance error allowed in the prediction
- d: distance of each pair of points
- Higher better, range from 0-1

Example of DoS =0.73. Solid line: ground truth, grey band T=0.27 mm margin, dashed line: prediction contour. 73% of the solid line coincides with the dashed line. [2]

Segmentation using Cartesian convolutional neural network (CNN)

- Convolutional autoencoder (CAE) works well for normal vessel walls with regular shapes (DSC: 0.86) [1]
- Problems:
 - Neighboring arteries will also be segmented.
 - Closed contours are not ensured.
 - Region of interest need to be manually selected.
 - Feedback from segmentation is unavailable.



Examples for challenging slices for vessel wall segmentation using Cartesian convolutional neural network with poor performance

Solution: Segment vessel wall in polar coordinate system

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



Polar segmentation system



Carotid image as example, but is a generic system for vessel wall segmentation











Polar segmentation with rotated patches



Segmentation uncertainty scores

- Segmentation confidence
 - I. Probability image (0-1) from output I: S[t, r]
 - 2. Binary fill within contours from output 2: M[t, r]
 - 3. Sum of probability inside vessel wall contours: $\sum_t \sum_r S \cdot M$
 - 4. Sum of probability map outside vessel wall contours: $\sum_t \sum_r (1-S) \cdot M$
 - 5. Pixels number inside vessel wall contours: $\sum_t \sum_r M$
 - 6. Segmentation Confidence: $Conf = \frac{\sum_{t} \sum_{r} S \cdot M - \sum_{t} \sum_{r} (1 - S) \cdot M}{\sum_{t} \sum_{r} M}$
 - Boundary sharpness evaluation. Up to 1, no lower limit. Higher value more confidence.



Example for calculating the segmentation confidence. Intuitively it is reflecting the sharpness of boundaries.

Segmentation uncertainty scores

- Lumen and wall boundary consistency
 - I. Lumen/Wall contours from rotated patch *i* at polar angle *t* from output 2: $L_i[t]$, $W_i[t]$
 - 2. Standard deviation of contour predictions at angle $t: BL_t = SD(L_{1,2...i}[t]), BW_t = SD(W_{1,2,...i}[t])$
 - 3. Normalize to the worst case when all predictions are random BL_t/W , BW_t/W
 - 4. One minus mean of all h boundary points

$$CS_{L} = 1 - \frac{1}{h} * \sum_{t}^{h} BL_{t} / W, CS_{W} = 1 - \frac{1}{h} * \sum_{t}^{h} BW_{t} / W$$

Consistency for predictions from rotated patches.
 Range from 0-1. Higher value more consistency



Example of consistency at angle t = 128 (red line) with 3 rotations i = 0,80,160 ²⁹

Validation of uncertainty scores

- Uncertainty scores correlates with DSC for vessel wall \bullet
- With added noise, both DSC for vessel wall and uncertainty scores decrease ۲



Segmentation confidence with DSC^{VW} from the Polar-Seg CNN architecture from the Polar-Reg CNN architecture

Contour consistency with DSC^{VW}

Segmentation results



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

Segmentation results



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

Comparison on segmentation quality (#slices = 3406)

Model	DSC ^{vw}	DSC ^{INNE} R	DSC ^{Outer}	DoS ^{Lumen}	DoS ^{Wall}	# failed segmentation	Processing time (s)	# paramete rs in network
Polar-Res-Reg	0.860	0.961	0.962	0.921	0.864	0	0.757±0.072	44,989,224
Polar-Reg	0.848	0.957	0.959	0.907	0.843	0	0.738±0.058	5,642,016
Polar-Seg-Reg	0.852	0.958	0.959	0.912	0.840	0	1.264±0.066	7,386,914
Polar-Seg	0.811	0.942	0.945	0.866	0.747	0	0.886±0.059	4,095,682
Mask R-CNN [1]	0.792	0.940	0.940	0.654	0.565	81	0.138±0.027	63,733,406
Cartesian U-Net [2]	0.774	0.922	0.941	0.647	0.517	194	0.103±0.032	4,094,817

DSC: Dice Similarity Coefficient, DoS: Degree of Similarity, higher better

[1] He, et. al, ICCV, 2017. [2] Ronneberger, et. al, arXiv, 2015. [3] Petersen, et.al, Trans on Medical imaging, 2019.

Comparison on vascular feature accuracy

Model	Max Wall Thickness		Mean Wall Thickness		Lumen Area		Wall Area	
	MAD	ICC (CI)	MAD	ICC (CI)	MAD	ICC (CI)	MAD	ICC (CI)
Polar-Res- Reg	0.890	0.896 (0.887- 0.904)	0.484	0.886 (0.878- 0.893)	25.715	0.985 (0.984- 0.986)	40.404	0.984 (0.983- 0.985)
Polar-Reg	0.964	0.874 (0.864- 0.883)	0.521	0.870 (0.862- 0.878)	28.439	0.981 (0.979- 0.982)	42.703	0.981 (0.979- 0.983)
Polar-Reg- Seg	0.916	0.893 (0.886- 0.900)	0.507	0.879 (0.871- 0.887)	27.221	0.983 (0.982- 0.984)	43.625	0.983 (0.982- 0.984)
Polar-Seg	1.353	0.760 (0.717- 0.794)	0.692	0.762 (0.644- 0.832)	31.338	0.965 (0.963- 0.968)	59.100	0.971 (0.961- 0.978)
Mask R- CNN [1]	1.264	0.653 (0.632- 0.672)	0.701	0.509 (0.473- 0.543)	32.171	0.942 (0.938- 0.945)	62.567	0.907 (0.885- 0.924)
Cartesian U-Net [2]	1.071	0.810 (0.798- 0.822)	0.565	0.808 (0.728- 0.859)	45.065	0.935 (0.923- 0.945)	52.460	0.949 (0.945- 0.952)

MAD: mean absolute difference, lower better.

ICC (CI): intraclass correlation coefficient (with 95% confidence interval), higher better.

[1] He, et. al, ICCV, 2017. [2] Ronneberger, et. al, arXiv, 2015.

Application I: Automated popliteal vessel wall analysis

- FRAPPE (fully automated and robust analysis technique for popliteal artery evaluation):
 - Locate popliteal artery, segment vessel wall, and quantify vessel wall features
- Transfer from carotid model
 - Only 25 scans labeled as the training set
- Successfully processed 48,716 knee scans, 3,490,998 slices, 70 years for manual review
 - Qualitative check 0.88% failure. Quantitative check DSC of 0.79.
- Useful features (mean wall thickness, etc) extracted for clinical research
- Open dataset

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Example slices Original Image



Application 2: Fast MR screening system for carotid lesion

- LATTE for Carotid atherosclerotic lesion screening
 - Fast scan + Automated vessel wall analysis
 - Highlight artery segments with early/advanced lesions
- Advance lesion classification
 - Sensitivity: 0.924
 - Specificity: 0.919

Balu, et.al, Magn. Reson. Med, 2011.
 Jiang, et.al, SPIE Medical Imaging, 2020.



Workflow of LATTE (Lesion Assessment Through Tracklet Evaluation)

Summary for completed work

- Achievement: A robust solution for vessel wall analysis
 - Automated artery centerline generation + vessel wall segmentation
 - From development to applications
- Innovations
 - Tracking by detection approach on 3D vascular images
 - Polar segmentation methods
 - Segmentation uncertainty scores
- Technically and clinically useful

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Direction I: Automated intracranial artery tracing

- Problems
 - Intracranial arteries are complicated and tortuous
 - Automated tracing is challenging
- Proposal
 - Extend the tracklet approach for intracranial artery tracing
 - Supervised learning from 1,000+ human corrected intracranial artery traces by iCafe[1]



MR scan of brain with complicated and tortuous intracranial arteries (displayed in reconstructed tubes)



[1] Chen, et. al, Magn Reson Med, 2018. [2] Chen, et. al, IEEE BIBM, 2017. [3] Chen, et.al, MICCAI CVII-STENT Workshop, 2019

Intracranial artery centerline labeling tool: iCafe [1]

- iCafe: an interactive tool to label tortuous arteries
 - Each artery: centerline, with various radius and certain anatomical type
 - Tracing by open-curve active contour algorithm [2]
 - Manual editing to correct mistakes
- Feature extraction
 - Structural and flow features of arteries: length, tortuosity, mean intensity, etc.
 - Reproducibility validated [3]

User interface of iCafe (implemented in C++ with ~60k lines of codes)

[1] Chen, et. al, Magn Reson Med, 2018[2] Wang, et.al. Neuroinformatics, 2011[3] Chen, et. al, Magn Reson Img, 2018

From Chen, et. al, IEEE BIBM, 2017

Segment luminal area with patch-based CNN

- Y-net: Patch based segmentation to better use similarity between arteries
- Training labels from corrected iCafe traces
- DSC of 0.83 on testing set



Multiplanar reformation (MPR) on artery refinement

- MPR by straightening arteries using interpolation for better visualization
- Easier to correct mistake by incorporating global information
- In MPR view, optimization on
 - Centerline positions
 - Lumen radii
 - Centerline deviations



after refinement Centerline deviations (red arrows) have been corrected ⁴³

Direction 2: Comprehensive vasculature map generation



Comprehensive features of cerebral vasculature

- Topology and blood flow features from generated centerline [1]
- Artery radius feature from lumen segmentation [2]
- Plaque burdens features from vessel wall segmentation [3]
- Plaque/stenosis features from vascular disease detection models [4]
- Plaque risks feature from plaque component and signal analysis [5]
- Longitudinal changes of features

[1] Chen, et. al, Magn Reson Med, 2018. [2] Chen, et. al, IEEE BIBM, 2017.
[3] Chen, et. al, submitted to IEEE Trans on Med Img, Under review.
[4] Han, et.al, [5] Li, et.al, submitted to ISMRM 2020, under review.

iCafe visualization of multiplex features



Intracranial arteries with centerline and radius/ lumen segmentation and outer wall segmentation and detected plaque/stenosis locations and plaque components and plaque signal pattern and longitudinal changes

Direction 3: Vascular feature bank construction

- With large amount of vascular features and clinical data of patients
- Build a vascular feature bank to
 - Manage features
 - Understand features
 - Utilize features

Direction 3: Vascular feature bank construction: manage



Direction 3: Vascular feature bank construction: Understand

Vascular feature bank



- Clustering algorithm to discover patterns from features of population
 - Explore the clinical implication of clusters.
 - Which features are correlated?
- Explore the relation between features and clinical outcomes
 - Whether patients in certain cluster are likely to have for certain vascular disease?
 - Construct a vascular risk score to assess vascular health.

Direction 3: Vascular feature bank construction: utilize



Feature map generation for plaque identification





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Summary for future directions

- Automated -> Fast and applicable to large population
- Comprehensive -> Comprehensive vascular features analysis, extraction and visualization
- Informative -> Understand vascular disease pattern & Deliver more precise medical care

Conclusions

- Goal:
 - Automated construction of comprehensive vascular map for vascular assessment
- Innovative achievements:
 - A centerline generation solution for all vasculature
 - Polar segmentation architecture for robust vessel wall segmentation
- Future directions:
 - Automated, comprehensive, and informative vascular feature extraction
- Significances:
 - Novel imaging features as imaging biomarkers for vascular research
 - Clinically applicable workflow to assist clinicians to provide better health care

Related Journal Publications

iCafe trilogy: development \rightarrow validation \rightarrow application

- 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. DOI: 10.1002/mrm.26961. Editor's pick.
- 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. DOI: 10.1016/j.mri.2018.12.007
- 3. 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. DOI: 10.1016/j.neurobiolaging.2019.02.027

Related Journal Publications

Vessel wall analysis trilogy: segmentation \rightarrow quantification \rightarrow detection

- 4. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Automated Artery Localization and Vessel Wall Segmentation of Magnetic Resonance Vessel Wall Images using Tracklet Refinement and Polar Conversion. (under review)
- 5. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Fully automated and Robust Vessel Wall Feature Extraction from Standardized Knee MRI. (under review)
- 6. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Carotid Artery Atherosclerotic Lesion Detection using an AI based Fully automated Workflow Based on 3D MRI. (under review)

Centerline refinement

7. Li Chen, et. al, Jenq-Neng Hwang, Chun Yuan. Automated Cerebral Vascular Measurements Refinement in Clinically Challenging Patient Populations. (under review)

Related Conference Publications

- 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. Machine Learning and Medical Engineering for Cardiovascular Health and Intravascular Imaging and Computer Assisted Stenting, First International Workshop, MLMECH 2019, and 8th Joint International Workshop, CVII-STENT 2019, Held in Conjunction with MICCAI, 2019, Shenzhen, China (October 13), Pages 201-209. DOI: 10.1007/978-3-030-33327-0
- 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 (November 13 - 16). DOI: 10.1109/BIBM.2017.8217741

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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