REFERENCES

[1] G. Guidoboni, A. Harris, S. Cassani, J. Arciero, B. Siesky, A. Amireskandari, L. Tobe, P. Egan, I. Januleviciene, and J. Park, "Intraocular pressure, blood pressure, and retinal blood flow autoregulation: a mathematical model to clarify their relationship and clinical relevance," *Investigative ophthalmology visual science*, vol. 55, no. 7, p. 4105—4118, May 2014.

[2] P. Saeedi, I. Petersohn, P. Salpea, B. Malanda, S. Karuranga, N. Unwin, S. Colagiuri, L. Guariguata, A. A. Motala, K. Ogurtsova, J. E. Shaw, D. Bright, R. Williams, and I. D. A. Committee, "Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the international diabetes federation diabetes atlas, 9th edition," *Diabetes Res Clin Pract.*, 2019.

[3] M. B. Sasangko, T. Y. Wong, T. T. Ngyuyen, C. Y. Cheung, J. E. Shaw, and J. J. Wang, "Retinal vascular tortuosity in persons with diabetes and diabetic retinopathy," *Diabetologia*, vol. 54, no. 9, pp. 2409–2416, 2011.

[4] S. Ciurică, M. Lopez-sublet, B. L. Loeys, I. Radhouani, N. Natarajan, M. Vikkula, A. H. Maas, D. Adlam, and A. Persu, "Arterial tortuosity: Novel implications for an old phenotype," *Hypertension*, vol. 73, p. 951–960, 2019. [Online]. Available: https://api.semanticscholar.org/CorpusID:73726760

[5] M. Abdalla, A. Hunter, and B. Al-Diri, "Quantifying retinal blood vessels' tortuosity — review," in *2015 Science and Information Conference (SAI)*, 2015, pp. 687–693.

[6] C. G. Owen, R. S. B. Newsom, A. R. Rudnicka, T. J. Ellis, and E. G. Woodward, "Vascular response of the bulbar conjunctiva to diabetes and elevated blood pressure," *Ophthalmology*, vol. 112, no. 10, p. 1801–1808, 2005.

[7] M. M. Khansari, W. O'Neill, R. Penn, F. Chau, N. P. Blair, and M. Shahidi, "Automated fine structure image analysis method for discrimination of diabetic retinopathy stage using conjunctival microvasculature images," *Biomed. Opt. Express*, vol. 7, no. 7, p. 2597, 2016.

[8] Y. Atiskova, J. Wildner, M. S. Spitzer, C. Aries, N. Muschol, and S. Dulz, "Retinal vessel tortuosity as a prognostic marker for disease severity in fabry

disease," *Orphanet Journal of Rare Diseases*, vol. 16, no. 1, p. 485, 2021. [Online]. Available: https://doi.org/10.1186/s13023-021-02080-0

[9] C. G. Owen, R. S. B. Newsom, A. R. Rudnicka, S. A. Barman, E. G. Woodward, and T. J. Ellis, "Diabetes and the tortuosity of vessels of the bulbar conjunctiva," *Ophthalmology*, vol. 115, no. 6, pp. 27–32, 2008.

[10] K. A. Iroshan, A. D. N. De Zoysa, C. L. Warnapura, M. A. Wijesuriya, S. Jayasinghe, N. D. Nanayakkara, and A. C. De Silva, "Detection of diabetes by macrovascular tortuosity of superior bulbar conjunctiva," *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EM)*, p. 2732–2735, 2018.

[11] Y. Song, Z. Zhou, H. Liu, R. Du, Y. Zhou, S. Zhu, and S. Chen, "Tortuosity of branch retinal artery is more associated with the genesis and progress of diabetic retinopathy," *Frontiers in Endocrinology*, vol. 13, 2022.

[12] T. Y. Wong, T. T. Nguyen, C. Y. Cheung, J. E. Shaw, and J. J. Wang, "Retinal vascular tortuosity in persons with diabetes and diabetic retinopathy." *Diabetologia*, vol. 54, no. 9, 2012.

[13] M. Iorga and G. Dougherty, *Tortuosity as an Indicator of the Severity of Diabetic Retinopathy*. Springer New York, 2011, pp. 269–290.

[14] S. M. Zabihi, H. R. Pourreza, and T. Banaee, "Vessel extraction of conjunctival images using lbps and anfis," *International Scholarly Research Notices*, vol. 2012, no. 1, pp. 1–6, 2012.

[15] P. K. Yu, I. L. McAllister, W. H. Morgan, S. J. Cringle, and D. Y. Yu, "Interrelationship of arterial supply to human retina, choroid, and optic nerve head using micro perfusion and labeling," *Investig. Ophthalmol. Vis. Sci.*, vol. 58, no. 9, p. 3565–3574, 2017.

[16] J. W. Kiel, "Chapter 2, anatomy," in *The Ocular Circulation*. Morgan and Claypool Life Sciences, 2010.

[17] B. Anand-Apte and J. G. Hollyfield, "Developmental anatomy of the retinal and choroidal vasculature," 2010. [Online]. Available: https://api.semanticscholar.org/CorpusID:80736154

[18] M. B. Sasongko, P. B. Aguirre, J. J. Wang, N. Cheung, A. Jenkins, and T. Y. Wong, "Alterations in retinal microvascular geometry in young type 1 diabetes," *Invest.Ophthalmol. Vis. Sci.*, vol. 51, no. 13, p. 1240, 2010.

[19] M. B. Sasongko, J. J. Wang, K. C. Donaghue, N. Cheung, P. Benitez-Aguirre, A. Jenkins, W. Hsu, M. L. Lee, and T. Y. Wong, "Alterations in retinal microvascular geometry in young type 1 diabetes." *Diabetes Care*, vol. 33, no. 6, pp. 1331–1336, 2010.

[20] J. Ditzel, "Angioscopic changes in the smaller blood vessels in diabetes mellitus andtheir relationship to aging," *Circulation*, vol. 14, no. 3, p. 386–397, 1956.

[21] P. Pancera, M. Ribul, B. Presciuttini, and A. Lechi, "Prevalence of carotid artery kinking in 590 consecutive subjects evaluated by echocolordoppler. is there a correlation with arterial hypertension?" *Journal of Internal Medicine*, vol. 248, no. 1, pp. 7–12, 2000.

[22] P. Pancera, M. Ribul, S. De Marchi, E. Arosio, and A. Lechi, "Prevalence of morphological alterations in cervical vessels: a colour duplex ultrasonographic study in a series of 3300 subjects." *International Angiology: a Journal of the International Union of Angiology*, vol. 17, no. 1, pp. 22–27, 1998.

[23] S. M. Factor, T. Minase, S. Cho, F. Fein, J. M. Capasso, and E. H. Sonnenblick, "Coronary microvascular abnormalities in the hypertensive-diabetic rat. a primary cause of cardiomyopathy?" *Am J Pathol.*, vol. 116, no. 1, pp. 9–20, 1984.

[24] C. Y. Cheung, E. Lamoureux, M. K. Ikram, M. B. Sasongko, Y. Zheng, P. Mitchell, J. J. Wang, and T. Y. Wong, "Retinal vascular geometry in asian persons with diabetes and retinopathy," *Journal of diabetes science and technology*, vol. 6, no. 3, pp. 596–605, 2012.

[25] A. Te, E. Sistermans, and R. A. Wevers, "Familial retinal arterial tortuosity associated with tortuosity in nail bed capillaries," *Arch Ophthalmol.*, vol. 124, pp. 1492–1494, 2016.

[26] A. R. Pries, A. J. M. Cornelissen, A. A. Sloot, M. Hinkeldey, M. R. Dreher, M. Höpfner, M. W. Dewhirst, and T. W. Secomb, "Structural adaptation and heterogeneity of normal and tumor microvascular networks," *PLoS Computational Biology*, vol. 5, no. 5, 2009.

[27] G. Azzopardi, N. Strisciuglio, M. Vento, and N. Petkov, "Trainable cosfire filters for vessel delineation with application to retinal images," *Medical Image Analysis*, vol. 19, no. 6, pp. 46–57, 2015.

[28] A. M. Reza, "Realization of the contrast limited adaptive histogram equalization (clahe) for real-time image enhancement," *Journal of VLSI signal processing systems for signal, image and video technology*, vol. 28, no. 1, pp. 35–44, 2004.

[29] E. S. Zegers, B. T. J. Meursing, E. B. Zegers, and A. J. M. Oude Ophuis, "Coronary tortuosity: A long and winding road," *Netherlands Hear. J.*, vol. 15, no. 5, pp. 191–195, 2007.

[30] T. J. Jebaseeli, C. A. D. Durai, and J. D. Peter, "Extraction of retinal blood vessels on fundus images by kirsch's template and fuzzy c-means," *J Med Phys*, vol. 44, no. 1, pp. 21–26, 2019.

[31] J. Dash and N. Bhoi, "A thresholding based technique to extract retinal blood vessels from fundus images," *Future Computing and Informatics Journal*, vol. 2, no. 2, pp. 103–109, 2017.

[32] Z. Yavuz and C. Köse, "Blood vessel extraction in color retinal fundus images with enhancement filtering and unsupervised classification," *J Healthc Eng.*, 2017.

[33] M. Singla, S. Soni, P. Saini, A. Chaudhary, and K. K. Shukla, "Diabetic retinopathy detection using twin support vector machines," in *Advances in Bioinformatics, Multimedia, and Electronics Circuits and Signals*. Springer Singapore, 2020, pp. 91–104.

[34] M. Badar, M. Haris, and A. Fatima, "Application of deep learning for retinal image analysis: A review," *Comput. Sci. Rev.*, vol. 35, no. C, 2020.

[35] O. Ronneberger, P. Fischer, and T. Brox, "U-net: Convolutional networks for biomedical image segmentation," in *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015*. Springer International Publishing, 2015, pp. 234–241.

[36] Z. Jin, Q.and Meng, T. D. Pham, Q. Chen, L. Wei, and R. Su, "Dunet: A deformable network for retinal vessel segmentation," *Knowledge-Based Systems*, vol. 178, pp. 149–162, 2019.

[37] L. Li, M. Verma, Y. Nakashima, H. Nagahara, and R. Kawasaki, "Iternet: Retinal image segmentation utilizing structural redundancy in vessel networks," in *2020 IEEE Winter Conference on Applications of Computer Vision (WACV)*, 2020, pp. 3645–3654.

[38] A. Sodi, C. Lenzetti, D. Bacherini, L. Finocchio, T. Verdina, I. Borg, F. Cipollini, F. U. Patwary, I. Tanini, C. Zopetti, S. Rizzo, and G. Virgili, "Quantitative analysis of conjunctival and retinal vessels in fabry disease," *Journal of Ophthalmology*, 2019.

[39] Y. Xu, M. Kong, W. Xie, R. Duan, Z. Fang, Y. Lin, Q. Zhu, S. Tang, F. Wu, and Y. Yao, "Deep sequential feature learning in clinical image classification of infectious keratitis," *Engineering*, vol. 7, no. 7, pp. 1002–1010, 2021.

[40] A. Awuah, J. S. Moore, M. A. Nesbit, M. W. Ruddock, P. F. Brennan, J. A. Mailey, A. J. McNeil, M. Jing, D. D. Finlay, E. Trucco, M. J. Kurth, J. Watt, J. V. Lamont, P. Fitzgerald, M. S. Spence, J. A. D. McLaughlin, and T. C. B. Moore, "A novel algorithm for cardiovascular screening using conjunctival microcirculatory parameters and blood biomarkers," *Scientific Reports 12*, no. 6545, 2022.

[41] S. Das, I. De Ghosh, and A. Chattopadhyay, "An efficient deep sclera recognition framework with novel sclera segmentation, vessel extraction and gaze detection," *Signal Processing: Image Communication*, vol. 97, 2021.

[42] S. M. Zabihi, H. R. Pourreza, and T. Banaee, "Vessel extraction of conjunctival images using lbps and anfis," *ISRN Machine Vision*, 2011.

[43] H. Bai, Z. Ma, C. Gao, and J. Zhu, "Svsnet: Scleral vessel segmentation with a cnn-transformer hybrid network," *Journal of Innovative Optical Health Sciences*, vol. 18, no. 06, p. 2550017, 2025. [Online]. Available: https://doi.org/10.1142/S1793545825500178

[44] T. King and A. Ayuba, "Deep learning in retinal image analysis: A review," *British Journal of Healthcare and Medical Research*, vol. 6, no. 3, p. 30–60, 2019.

[45] S. Shit, J. C. Paetzold, A. Sekuboyina, I. Ezhov, A. Unger, A. Zhylka, J. P. W. Pluim, U. Bauer, and B. H. Menze, "cldice - a novel topology-preserving loss function for tubular structure segmentation," in *2021 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR)*, 2021, pp. 16 555–16 564.

[46] H. C. Han, "Twisted blood vessels: Symptoms, etiology and biomechanical mechanisms," *Journal of Vascular Research*, vol. 49, no. 3, pp. 185–197, 2012.

[47] C. R. Thore, J. A. Anstrom, D. M. Moody, V. R. Challa, M. C. Marion, and W. R. Brown, "Morphometric analysis of arteriolar tortuosity in human cerebral white matter of preterm, young, and aged subjects," *Journal of Neuropathology and Experimental Neurology*, vol. 66, no. 5, pp. 337–345, 05 2007.

[48] M. Hiroki, K. Miyashita, and M. Oda, "Tortuosity of the white matter medullary arterioles is related to the severity of hypertension," *Cerebrovascular Diseases*, vol. 13, no. 4, pp. 242–250, 05 2002.

[49] H. Azegrouz, E. Trucco, B. Dhillon, T. MacGillivray, and I. J. MacCormick, "Thickness dependent tortuosity estimation for retinal blood vessels," *Annual International Conference of the IEEE Engineering in Medicine and Biology - Proceedings*, p. 4675–4678, 2006.

[50] E. Grisan, M. Foracchia, and A. Ruggeri, "A novel method for the automatic grading ofretinal vessel tortuosity," *EEE Trans. Med. Imaging*, vol. 27, no. 3, pp. 310–319, 2008.

[51] D. De Zoysa, A. Kondarage, C. Warnapura, M. Wijesuriya, S. Jayasinghe, N. Nanayakkara, and A. De Silva, "Eccentricity based quantification of retinal vascular tortuosity for early detection of diabetes and diabetic retinopathy," in *2018 IEEE International Conference on Systems, Man, and Cybernetics (SMC)*, 2018, pp. 3280–3284.

[52] L. Zhou, C. Zhang, and M. Wu, "D-linknet: Linknet with pretrained encoder and dilated convolution for high resolution satellite imagery road extraction," in *2018 IEEE/CVF Conference on Computer Vision and Pattern Recognition Workshops (CVPRW)*, 2018, pp. 192–1924.

[53] P. Rot, M. Vitek, K. Grm, v. Emeršič, P. Peer, and V. Štruc, "Deep sclera segmentation and recognition," in *Handbook of Vascular Biometrics (HVB)*, A. Uhl, C. Busch, S. Marcel, and R. N. J. Veldhuis, Eds. Springer, 2020, pp. 395–432.

[54] P. Rot, Žiga Emeršič, V. Struc, and P. Peer, "Deep multi-class eye segmentation for ocular biometrics," *2018 IEEE International Work Conference on Bioinspired Intelligence (IWOBI)*, pp. 1–8, 2018.

[55] A. De Silva, M. V. Perera, N. Wijethilake, S. Jayasinghe, N. D. Nanayakkara, and A. De Silva, "A thickness sensitive vessel extraction framework for retinal and conjunctival vascular tortuosity analysis," 2021. [Online]. Available: https://arxiv.org/abs/2101.00435

[56] W. P. S. N. Pathiratna, H. M. H. T. Munasinghe, K. R. H. M. D. M. Kularatne, K. R. Jeyanthan, A. M. Naim, S. Jayasinghe, and A. D. Silva, "Conjunctival and retinal images of healthy subjects and subjects with diabetes," 2025. [Online]. Available: https://dx.doi.org/10.21227/6583-ay07

[57] V. Badrinarayanan, A. Kendall, and R. Cipolla, "Segnet: A deep convolutional encoder-decoder architecture for image segmentation," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, vol. 39, no. 12, pp. 2481–2495, 2017. [Online]. Available: https://ieeexplore.ieee.org/document/7803544

[58] H. Noh, S. Hong, and B. Han, "Learning deconvolution network for semantic segmentation," in *Proceedings of the IEEE International Conference on Computer Vision (ICCV)*. IEEE, 2015, pp. 1520–1528. [Online]. Available: https://ieeexplore.ieee.org/document/7410535

[59] O. Oktay, J. Schlemper, L. L. Folgoc, M. C. H. Lee, M. P. Heinrich, K. Misawa, K. Mori, S. G. McDonagh, N. Y. Hammerla, B. Kainz, B. Glocker, and D. Rueckert, "Attention u-net: Learning where to look for the pancreas," *CoRR*, vol. abs/1804.03999, 2018. [Online]. Available: http://arxiv.org/abs/1804.03999

[60] J. Schindelin, I. Arganda-Carreras, E. Frise, V. Kaynig, M. Longair, T. Pietzsch, S. Preibisch, C. Rueden, S. Saalfeld, B. Schmid, J. Tinevez, D. J. White, V. Hartenstein, K. Eliceiri, P. Tomancak, and A. Cardona, "Fiji: an open-source platform for biological-image analysis," *Nature Methods*, vol. 9, no. 7, pp. 676–682, 2012.

[61] J. Staal, M. D. Abramoff, M. Niemeijer, M. A. Viergever, and B. van Ginneken, "Ridge-based vessel segmentation in color images of the retina," *IEEE Transactions on Medical Imaging*, vol. 23, no. 4, pp. 501–509, 2004.

[62] T. M. Inc., "Matlab version: 8.5.0.197613 (r2015a)," Natick, Massachusetts, United States, 2015. [Online]. Available: https://www.mathworks.com

[63] J. Dash and N. Bhoi, "An unsupervised approach for extraction of blood vessels from fundus images," *Journal of Digital Imaging*, vol. 31,

no. 6, pp. 857–868, December 2018, pMC6261194. [Online]. Available: https://doi.org/10.1007/s10278-018-0059-x

[64] K. BahadarKhan, A. A Khaliq, and M. Shahid, "A morphological hessian based approach for retinal blood vessels segmentation and denoising using region based otsu thresholding," *PLOS ONE*, vol. 11, pp. 1–19, 07 2016. [Online]. Available: https://doi.org/10.1371/journal.pone.0158996

[65] J. Almotiri, K. Elleithy, and A. Elleithy, "Retinal vessels segmentation techniques and algorithms: A survey," *Applied Sciences*, vol. 8, no. 2, 2018. [Online]. Available: https://www.mdpi.com/2076-3417/8/2/155

[66] R. B. Forster, E. S. Garcia, A. J. Sluiman, S. M. Grecian, S. McLachlan, T. J. MacGillivray, M. W. J. Strachan, and J. F. Price, "Retinal venular tortuosity and fractal dimension predict incident retinopathy in adults with type 2 diabetes: the edinburgh type 2 diabetes study." *Diabetologia*, vol. 64, no. 5, p. 1103–1112, 2021.

[67] R. J. Tapp, C. G. Owen, S. A. Barman, D. P. Strachan, R. A. Welikala, P. J. Foster, P. H. Whincup, and A. R. Rudnicka, "Retinal microvascular associations with cardiometabolic risk factors differ by diabetes status: results from the uk biobank," *Diabetologia*, vol. 65, no. 10, p. 1652–1663, 2022.

[68] W. E. Hart, M. Goldbaum, B. Côté, P. Kube, and M. R. Nelson, "Automated measurement of retinal vascular tortuosity," in *Proceedings: a conference of the American Medical Informatics Association. AMIA Fall Symposium*, 1997, pp. 459–463.

[69] J. Chen, J. Mei, X. Li, Y. Lu, Q. Yu, Q. Wei, X. Luo, Y. Xie, E. Adeli, Y. Wang, M. P. Lungren, S. Zhang, L. Xing, L. Lu, A. Yuille, and Y. Zhou, "Transunet: Rethinking the u-net architecture design for medical image segmentation through the lens of transformers," *Medical Image Analysis*, vol. 97, p. 103280, 2024. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S1361841524002056

[70] X. Qin, Z. Zhang, C. Huang, M. Dehghan, O. R. Zaiane, and M. Jagersand, "U2-net: Going deeper with nested u-structure for salient object detection," *Pattern Recognition*, vol. 106, p. 107404, 2020. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0031320320302077

[71] H. Cao, Y. Wang, J. Chen, D. Jiang, X. Zhang, Q. Tian, and M. Wang, "Swin-unet: Unet-like pure transformer for medical image segmentation," 2021. [Online]. Available: https://arxiv.org/abs/2105.05537

[72] C. Li, Z. Li, and W. Liu, "Tdcau-net: retinal vessel segmentation using transformer dilated convolutional attention-based u-net method," *Physics in Medicine & Biology*, vol. 69, 2023. [Online]. Available: https://api.semanticscholar.org/CorpusID:265702649

[73] Y. Chu, Y. Zhang, Z. Han, C. Yang, L. Zhou, G. Luo, C. Huang, and X. Gao, "Improving representation of high-frequency components for medical visual foundation models," *IEEE Transactions on Medical Imaging*, vol. 44, no. 8, pp. 3196–3209, 2025.

[74] Y. Chu, G. Luo, L. Zhou, S. Cao, G. Ma, X. Meng, J. Zhou, C. Yang, D. Xie, D. Mu, R. Henao, G. Setti, X. Xiao, L. Wu, Z. Qiu, and X. Gao, "Deep learning-driven pulmonary artery and vein segmentation reveals demography-associated vasculature anatomical differences," *Nature Communications*, vol. 16, no. 1, p. 2262, 2025. [Online]. Available: https://doi.org/10.1038/s41467-025-56505-6