

Supplementary information

Ophthalmic OCT-based image generation using GANs; A scoping review

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1. Derivation of clinical proximity and methodological novelty scores

1.1. Overview

To quantify each study's position in the generative model landscape (Figure 5), we developed a semi-quantitative scoring framework that integrates both clinical relevance and technical innovation. Each study S_i was assigned two primary indices, the first one is the clinical proximity (C_i), how closely the work aligns with real-world translational or clinical endpoints. While the second one is focused on methodological novelty (N_i), how technically advanced or conceptually original the generative model is. Both indices were normalised to a 0–1 range for cross-study comparison.

1.2. Calculation of clinical proximity (C_i)

Clinical proximity reflects how readily the proposed model could support clinical or translational application. It is computed as (equations 2 and 3 are from the main manuscript):

$$C_i = 0.4U_i + 0.3V_i + 0.3E_i \quad (2)$$

U_i is the clinical feasibility or clinical interpretability and is given based on the inclusion of features such as explainable outputs, privacy preservation, or annotation efficiency. V_i is the dataset origin and diversity. This score is given based on single-centre = low; multi-centre, public benchmark, or cross-device = high. E_i is the endpoint validation, where the quality and clinical relevance of the evaluation (e.g., expert grading, correlation with clinical biomarkers, lesion-level sensitivity) is considered. Each component was rated from 0 (low) to 1 (high) based on study design and reporting detail.

1.3. Calculation of methodological novelty (N_i)

Methodological novelty quantifies the innovation of model architecture and training approach:

$$N_i = 0.4M_i + 0.3C'_i + 0.3R_i \quad (3)$$

Where M_i is the model innovation, judged by the degree of architectural advancement (e.g., baseline cGAN = low; Fourier- or diffusion-based = high). C'_i is the conditioning and learning strategy, where the incorporation of multimodal input, semantic conditioning, spectral priors, or hybrid learning schemes ends in a higher score. R_i is the research originality, which is based on the novelty of the application domain (e.g., first OCTA synthesis vs. incremental variation). Table S1 shows these parameters in short. These components collectively determine the bubble placement and size in Figure 5 as detailed in Table S2.

Table S1. Definitions and scoring ranges for all quantitative variables used to derive the clinical proximity and methodological novelty indices.

Symbol	Meaning	Typical Range	Description
U_i	Utility in clinical workflow	0–1	Degree to which outputs can assist clinical decisions
V_i	Dataset size/diversity	0–1	Scaled by $\log(\text{dataset size}) \times \text{diversity factor}$
E_i	Endpoint or clinical evaluation	0–1	Quantifies use of clinical outcomes or expert validation
M_i	Model innovation	0–1	Architectural novelty (GAN < Fourier < Diffusion < Hybrid)
C'_i	Conditioning sophistication	0–1	Reflects multimodal or context-aware learning
R_i	Research originality	0–1	Novelty of the target problem or imaging domain

Table S2. Quantitative mapping of clinical proximity (C_i) and methodological novelty (N_i) for all reviewed studies. Each row lists the study reference, model type, computed indices, and contributing sub-scores ($U_i, V_i, E_i, M_i, C'_i, R_i$). Scores were assigned on a 0–1 scale by consensus review and normalised across all included publications. Bubble positions in Figure 5 – in the main manuscript - correspond directly to the (C_i, N_i) coordinates.

Study	Model(s)	(U_i) Endpoint validation	(V_i) Dataset scale/diversity	(E_i) Clinical feasibility	(C_i) (clinical proximity)	(M_i) Model innovation	(C'_i) Conditioning/architecture	(R_i) Research novelty	(N_i) (method novelty)
Zha [1]	cGAN+SSIM	0.3 (image quality)	0.2 (small dataset)	0.25 (moderate interpretability)	0.25	0.2 (baseline GAN)	0.3 (PatchGAN/SSIM)	0.4 (early adaptation)	0.30
Han [2]	cGAN	0.35 (quality assess)	0.25 (private dataset)	0.35 (interpretability)	0.32	0.25 (cGAN)	0.3 (transfer learning)	0.55 (application-driven)	0.36
Lazaridis [3]	WGAN ensemble	0.4 (trial outcome)	0.35 (UKGTS dataset)	0.4 (statistical power)	0.38	0.3 (WGAN)	0.45 (ensemble approach)	0.7 (improves trial design)	0.48
Ge [4]	FOF-GAN	0.15 (technical demo)	0.25 (private dataset)	0.2 (low clinical use)	0.20	0.7 (Fourier GAN)	0.6 (frequency conditioning)	0.7 (first in domain)	0.66
Tajmirriahi [5]	Dual-disc. Fourier GAN	0.3 (technical eval)	0.3 (medium dataset)	0.35	0.42	0.6 (dual-disc GAN)	0.55	0.65 (novel architecture)	0.60
Baek [6]	CycleGAN/UNIT/RegGAN	0.55 (outcome pred.)	0.45 (KINGFISHER)	0.65 (treatment monitoring)	0.56	0.4 (CycleGAN baseline)	0.55 (UNIT/RegGAN hybrid)	0.7 (AMD/DME focus)	0.56
Lee [7]	cGAN multimodal	0.65 (AMD pred.)	0.55	0.8 (clinical endpoint)	0.66	0.35 (cGAN)	0.4 (multimodal inputs)	0.55	0.46
Liu [8]	Pix2PixHD	0.75 (nAMD treatment)	0.7 (large dataset)	0.7	0.72	0.45 (Pix2PixHD)	0.5 (post-treatment focus)	0.55	0.50
Xu [9]	Pix2PixHD	0.65 (RVO treatment)	0.55	0.65	0.61	0.4	0.45	0.4	0.41
Vidal [10]	Pix2Pix	0.25	0.2	0.3	0.25	0.25	0.25	0.2	0.23

Zhao [11]	Multi-GAN	0.1	0.25	0.1	0.15	0.35 (multi-GAN setup)	0.25	0.3	0.32
Kumar [12]	PGGAN	0.35	0.3	0.40	0.30	0.5 (progressive GAN)	0.55	0.6	0.54
Zheng [13]	PGGAN	0.25	0.2	0.2	0.21	0.45	0.55	0.5	0.49
Kreitner [14]	OCTA synth. (PatchGAN)	0.45 (segm. augmentation)	0.35	0.45	0.42	0.35	0.45	0.5	0.44
Abdelmotal [15]	Pix2Pix OCT \leftrightarrow FA	0.55	0.45	0.65	0.55	0.25	0.35	0.45	0.34
Coronado [16]	cGAN fundus \rightarrow OCTA	0.6	0.55	0.65	0.60	0.2	0.3	0.35	0.28
Lin [17]	U-Net (OCT \rightarrow OCTA)	0.75	0.7	0.75	0.74	0.4	0.45	0.55	0.54
Makita [18]	Neural net OCT \rightarrow PS-OCT	0.75	0.7	0.8	0.75	0.25	0.35	0.55	0.35
Sun [19]	DL OCT \rightarrow PS-OCT	0.8	0.75	0.85	0.80	0.35	0.4	0.55	0.46
Pan [20]	DL PS-OCT \rightarrow PS-OCTA	0.6	0.55	0.6	0.58	0.55	0.6	0.7	0.62
Melo [21]	ESRGAN, SRFlow	0.55	0.6	0.55	0.56	0.65 (SRFlow advanced)	0.6	0.7	0.66

Supplementary section references

- [1] X. Zha, F. Shi, Y. Ma, W. Zhu, X. Chen, Generation of retinal OCT images with diseases based on cGAN, in: *Medical Imaging 2019: Image Processing*, SPIE, 2019: pp. 544–549. <https://doi.org/10.1117/12.2510967>.
- [2] K. Han, Y. Yu, T. Lu, Transfer Learning and Interpretable Analysis-Based Quality Assessment of Synthetic Optical Coherence Tomography Images by CGAN Model for Retinal Diseases, *Processes* 12 (2024) 182.
- [3] G. Lazaridis, M. Lorenzi, S. Ourselin, D. Garway-Heath, Improving statistical power of glaucoma clinical trials using an ensemble of cyclical generative adversarial networks, *Medical Image Analysis* 68 (2021) 101906. <https://doi.org/10.1016/j.media.2020.101906>.
- [4] N. Ge, Y. Liu, X. Xu, X. Zhang, M. Jiang, A Fast Generative Adversarial Network for High-Fidelity Optical Coherence Tomography Image Synthesis, *Photonics* 9 (2022) 944. <https://doi.org/10.3390/photonics9120944>.
- [5] M. Tajmirriahi, R. Kafieh, Z. Amini, V. Lakshminarayanan, A Dual-Discriminator Fourier Acquisitive GAN for Generating Retinal Optical Coherence Tomography Images, *IEEE Transactions on Instrumentation and Measurement* 71 (2022) 1–8. <https://doi.org/10.1109/TIM.2022.3189735>.
- [6] J. Baek, Y. He, M. Emamverdi, A. Mahmoudi, M.G. Nittala, G. Corradetti, M. Ip, S.R. Sadda, Prediction of Long-Term Treatment Outcomes for Diabetic Macular Edema Using a Generative Adversarial Network, *Trans. Vis. Sci. Tech.* 13 (2024) 4. <https://doi.org/10.1167/tvst.13.7.4>.
- [7] H. Lee, S. Kim, M.A. Kim, H. Chung, H.C. Kim, POST-TREATMENT PREDICTION OF OPTICAL COHERENCE TOMOGRAPHY USING A CONDITIONAL GENERATIVE ADVERSARIAL NETWORK IN AGE-RELATED MACULAR DEGENERATION, *RETINA* 41 (2021) 572. <https://doi.org/10.1097/IAE.0000000000002898>.
- [8] Y. Liu, J. Yang, Y. Zhou, W. Wang, J. Zhao, W. Yu, D. Zhang, D. Ding, X. Li, Y. Chen, Prediction of OCT images of short-term response to anti-VEGF treatment for neovascular age-related macular degeneration using generative adversarial network, *British Journal of Ophthalmology* 104 (2020) 1735–1740. <https://doi.org/10.1136/bjophthalmol-2019-315338>.
- [9] F. Xu, X. Yu, Y. Gao, X. Ning, Z. Huang, M. Wei, W. Zhai, R. Zhang, S. Wang, J. Li, Predicting OCT images of short-term response to anti-VEGF treatment for retinal vein occlusion using generative adversarial network, *Front Bioeng Biotechnol* 10 (2022) 914964. <https://doi.org/10.3389/fbioe.2022.914964>.
- [10] P.L. Vidal, J. de Moura, J. Novo, M.G. Penedo, M. Ortega, Image-to-image translation with Generative Adversarial Networks via retinal masks for realistic Optical Coherence Tomography imaging of Diabetic Macular Edema disorders, *Biomedical Signal Processing and Control* 79 (2023) 104098. <https://doi.org/10.1016/j.bspc.2022.104098>.
- [11] M. Zhao, Z. Lu, S. Zhu, X. Wang, J. Feng, Automatic generation of retinal optical coherence tomography images based on generative adversarial networks, *Medical Physics* 49 (2022) 7357–7367. <https://doi.org/10.1002/mp.15988>.
- [12] A.J. Sreejith Kumar, R.S. Chong, J.G. Crowston, J. Chua, I. Bujor, R. Husain, E.N. Vithana, M.J.A. Girard, D.S.W. Ting, C.-Y. Cheng, T. Aung, A. Popa-Cherecheanu, L. Schmetterer, D. Wong, Evaluation of Generative Adversarial Networks for High-Resolution Synthetic Image Generation of Circumpapillary Optical Coherence Tomography Images for Glaucoma, *JAMA Ophthalmol* 140 (2022) 974–981. <https://doi.org/10.1001/jamaophthalmol.2022.3375>.

- [13] C. Zheng, X. Xie, K. Zhou, B. Chen, J. Chen, H. Ye, W. Li, T. Qiao, S. Gao, J. Yang, J. Liu, Assessment of Generative Adversarial Networks Model for Synthetic Optical Coherence Tomography Images of Retinal Disorders, *Trans. Vis. Sci. Tech.* 9 (2020) 29. <https://doi.org/10.1167/tvst.9.2.29>.
- [14] L. Kreitner, J.C. Paetzold, N. Rauch, C. Chen, A.M. Hagag, A.E. Fayed, S. Sivaprasad, S. Rausch, J. Weichsel, B.H. Menze, M. Harders, B. Knier, D. Rueckert, M.J. Menten, Synthetic Optical Coherence Tomography Angiographs for Detailed Retinal Vessel Segmentation Without Human Annotations, *IEEE Transactions on Medical Imaging* 43 (2024) 2061–2073. <https://doi.org/10.1109/TMI.2024.3354408>.
- [15] H. Abdelmotaal, M. Sharaf, W. Soliman, E. Wasfi, S.M. Kedwany, Bridging the resources gap: deep learning for fluorescein angiography and optical coherence tomography macular thickness map image translation, *BMC Ophthalmology* 22 (2022) 355. <https://doi.org/10.1186/s12886-022-02577-7>.
- [16] I. Coronado, S. Pachade, E. Trucco, R. Abdelkhaleq, J. Yan, S. Salazar-Marioni, A. Jagolino-Cole, M. Bahrainian, R. Channa, S.A. Sheth, L. Giancardo, Synthetic OCT-A blood vessel maps using fundus images and generative adversarial networks, *Sci Rep* 13 (2023) 15325. <https://doi.org/10.1038/s41598-023-42062-9>.
- [17] Z. Lin, Q. Zhang, G. Lan, J. Xu, J. Qin, L. An, Y. Huang, Deep Learning for Motion Artifact-Suppressed OCTA Image Generation from Both Repeated and Adjacent OCT Scans, *Mathematics* 12 (2024) 446. <https://doi.org/10.3390/math12030446>.
- [18] S. Makita, M. Miura, S. Azuma, T. Mino, Y. Yasuno, Synthesizing the degree of polarization uniformity from non-polarization-sensitive optical coherence tomography signals using a neural network, *Biomed. Opt. Express*, *BOE* 14 (2023) 1522–1543. <https://doi.org/10.1364/BOE.482199>.
- [19] Y. Sun, J. Wang, J. Shi, S.A. Boppart, Synthetic polarization-sensitive optical coherence tomography by deep learning, *Npj Digit. Med.* 4 (2021) 105. <https://doi.org/10.1038/s41746-021-00475-8>.
- [20] M. Pan, Y. Wang, P. Gong, Q. Wang, B. Cense, Feasibility of deep learning-based polarization-sensitive optical coherence tomography angiography for imaging cutaneous microvasculature, *Biomed. Opt. Express*, *BOE* 14 (2023) 3856–3870. <https://doi.org/10.1364/BOE.488822>.
- [21] T. Melo, J. Cardoso, Â. Carneiro, A. Campilho, A.M. Mendonça, OCT Image Synthesis through Deep Generative Models, in: *2023 IEEE 36th International Symposium on Computer-Based Medical Systems (CBMS)*, 2023: pp. 561–566. <https://doi.org/10.1109/CBMS58004.2023.00279>.