Guest Editorial
Generative Adversarial Networks in Biomedical Image Computing

THE field of biomedical imaging has obtained great progress from Roentgen's original discovery of the X-ray to the current imaging tools, including Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Computed Tomography (CT), and Ultrasound (US) [1]. The benefits of using these non-invasive imaging technologies are to assess the current condition of an organ or tissue, which can be used to monitor a patient over time over time for accurate and timely diagnosis and treatment. With the development of imaging technologies, developing advanced artificial intelligence algorithms for automated image analysis has shown the potential to change many aspects of clinical applications within the next decade. Meanwhile, these advanced technologies have also brought new issues and challenges. Thus, there has been a growing demand for biomedical imaging computing to be a component of clinical trials and device improvement.

Currently, Generative adversarial networks (GANs) [2] have been attached growing interests in the computer vision community due to their capability of data generation or translation. GAN-based models are able to learn from a set of training data and generate new data with the same characteristics as the training ones, which have also proven to be the state of the art for generating sharp and realistic images [3]. More importantly, GAN has been rapidly applied to many traditional and novel applications in the medical domain [4]–[7], such as image reconstruction, segmentation, diagnosis, synthesis, and so on. Despite GAN substantial progress in these areas, their application to medical image computing still faces challenges and unsolved problems remain. For example, how to synthesize realistic or physically-plausible imagery from small datasets? What are the best GAN architectures and loss functions for specific image computing tasks? When is possible to conduct unsupervised/weak versus supervised deep learning? How to deal with noisy and incomplete data? How to deal with data that is only partially labelled or annotated? How to ensure that learning from GAN-synthesized data generalizes to real-world data? How to develop GAN architectures that integrate biomedical imaging with other biomedical data like omics, radiological text reports, electronic health records, etc.?

This special issue is meant to provide the state-of-the-art algorithms that progress the field of research and applications into advanced GANs in biomedical imaging. This Special Issues seek contributions include (1) GAN-based algorithms for medical image synthesis, segmentation, registration, and reconstruction; (2) un/semi/weakly-supervised learning with GANs in biomedical image computing; (3) novel GAN architectures, loss functions, and theoretical developments; (4) GAN under limited, sparse, incomplete, and noisy data inputs, and datasets with incomplete or limited annotations; (5) new datasets and benchmarks, and evaluation protocols suitable for GANs in biomedical imaging. In the Call-For-Papers, researchers were encouraged to submit high quality unpublished original work that are related to GAN and Adversarial learning for biomedical medical computing.

The first paper by Zhang *et al.* [A1] proposes a progressive generative adversarial method for structurally inadequate medical image data augmentation framework. In this method, the progressive texture generative adversarial network alleviates the adverse effect of completely truncating the reconstruction of structure and texture during the generation process and enhances the implicit association between structure and texture. Besides, an image data augmentation strategy based on mask-reconstruction is proposed to overcome data imbalance issue.

Due to the limitations of time consuming and expensive cost, some image sequences of patients may be lost or corrupted, thus medical image synthesis has caused increasing attention to alleviate the issues. In this special issue, there are three papers on multi-modality medical image synthesis presented. Zhan *et al.* [A2] propose a multi-scale gate mergence based generative adversarial network model to synthesize one MR modality from other ones. This method introduces a gate mergence strategy to automatically learn the weights of different modalities across locations, resulting in enhancing the task-related information while suppressing the irrelative information. Peng *et al.* [A3] propose a novel confidence-guided aggregation and cross-modality refinement network for multi-modality MR image synthesis, which effectively utilizes complementary and correlative information of multiple modalities to synthesize high-quality target-modality images. Gao *et al.* [A4] propose a task-induced pyramid and attention generative adversarial network to generate the missing PET data with their MRI and achieve disease classification task.

Two papers on diabetic retinopathy image synthesis are presented. Niu *et al.* [A5] propose a novel strategy to encode pathological descriptors from the activated neurons directly related to the prediction, and a Patho-GAN is proposed to visualize the pathological descriptor into a pathology retinal image from an

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unseen binary vessel segmentation. Zhou *et al.* [A6] propose a diabetic retinopathy generative adversarial framework to synthesize high-resolution fundus images, which can be manipulated with arbitrary grading and lesion information. In this case, a large-scale generated data can be obtained and used for more meaningful augmentation to train a DR grading and lesion segmentation model.

Besides, adversarial learning has been widely applied to medical segmentation tasks. In this special issue, three papers focus on unsupervised domain adaptation segmentation and another one focuses on unbalanced targets. Du *et al.* [A7] propose a constraint-based unsupervised domain adaptation network for multi-modality cardiac image segmentation, which consists of image synthesis and reconstruction module, and two different modality segmentation modules. The image synthesis and reconstruction module utilizes the mutual translation between the source domain and the target domain to align the source domain and the target domain, and then the translated data is used for the training of the subsequent segmentation module. Li *et al.* [A8] propose an unsupervised domain adaptation segmentation framework for pancreatic cancer based on GCN and meta-learning strategy, which conducts encoders incorporating adversarial learning to separate domain-invariant features from domain-specific ones for achieving visual appearance translation. Lei *et al.* [A9] propose an unsupervised domain adaptation method based on image synthesis and feature alignment method to segment optic disc and cup on fundus images. In this method, the content and style feature alignment strategy is utilized to ensure the feature consistency among source domain images, target-like query images and target domain images, and the adversarial learning is used to extract domain-invariant features for output-level feature alignment. Chen *et al.* [A10] propose an inter-cascade generative adversarial network to segment the unbalanced atrial targets from LGE CMR images automatically and accurately in an end-to-end way.

Moreover, in this special issue, there are disease detection and landmark detection works presented. Zhang *et al.* [A11] propose a novel model by jointly optimize the cycle generative adversarial network (CycleGAN) and the convolutional neural network (CNN) to detect retinal diseases and localize lesion areas with limited training data, in which the CycleGAN with cycle consistency can generate more reliable and realistic images. Shara *et al.* [A12] propose a multi-stage framework to mutually improve the performance of unpaired image-to-image translation and suture detection task. In this framework, a fixed suture detection network integrated with a CycleGAN network to first produce more physically plausible image translation. Then, a new suture detection network is trained from scratch with a combined dataset consisting of the generated, more-consistent, fake intra-operative images, and the real intra-operative data.

Last but not least, adversarial learning has also been applied in denoising, surface reconstruction, and acoustic simulation. Three papers are presented on these topics. Zhou *et al.* [A13] propose a new denoising method to suppress speckle noise in retinal OCT images and achieves superb performances in retinal structure preservation and contrast enhancement. Tian *et al.* [A14] design a new two-stage generative adversarial network to reconstruct a dental crown surface in the data-driven perspective. In the first stage, a conditional GAN is designed to learn the inherent relationship between the defective tooth and the target crown. In the second stage, an improved CGAN is further devised by considering an occlusal groove parsing network and an occlusal fingerprint constraint to enforce the generator to enrich the functional characteristics of the occlusal surface. Koh *et al.* [A15] propose to generate synthetic CT from T1-weighted magnetic resonance imaging (MRI) and investigate its applicability to transcranial focused ultrasound (tFUS) acoustic simulation.

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APPENDIX: RELATED ARTICLES

[A1] R. Zhang *et al.*, "A progressive generative adversarial method for structurally inadequate medical image data augmentation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3101551.

[A2] B. Zhan, D. Li, X. Wu, J. Zhou, and Y. Wang, "Multi-modal MRI image synthesis via GAN with multi-scale gate mergence," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3088866.

[A3] B. Peng, B. Liu, Y. Bin, L. Shen, and J. Lei, "Multi-modality MR image synthesis via confidence-guided aggregation and cross-modality refinement," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3082541.

[A4] X. Gao, F. Shi, D. Shen, and M. Liu, "Task-induced pyramid and attention GAN for multimodal brain image imputation and classification in Alzheimer's disease," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3097721.

[A5] Y. Niu, L. Gu, Y. Zhao, and F. Lu, "Explainable diabetic retinopathy detection and retinal image generation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3110593.

[A6] Y. Zhou, B. Wang, X. He, S. Cui, and L. Shao, "DR-GAN: Conditional generative adversarial network for fine-grained lesion synthesis on diabetic retinopathy images," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2020.3045475.

[A7] X. Du and Y. Liu, "Constraint-based unsupervised domain adaptation network for multi-modality cardiac image segmentation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3126874.

[A8] J. Li, C. Feng, X. Lin, and X. Qian, "Utilizing GCN and meta-learning strategy in unsupervised domain adaptation for pancreatic cancer segmentation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3085092.

[A9] H. Lei, W. Liu, H. Xie, B. Zhao, G. Yue, and B. Lei, "Unsupervised domain adaptation based image synthesis and feature alignment for joint optic disc and cup segmentation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3085770.

[A10] J. Chen *et al.*, "JAS-GAN: Generative adversarial network based joint atrium and scar segmentation on unbalanced atrial targets," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3077469.

[A11] Z. Zhang, Z. Ji, Q. Chen, W. Fan, and S. Yuan, "Joint optimization of CycleGAN and CNN classifier for detection and localization of retinal pathologies on color fundus photographs," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3092339.

[A12] L. Shara *et al.*, "Mutually improved endoscopic image synthesis and landmark detection in unpaired image-to-image translation," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3099858.

[A13] Y. Zhou *et al.*, "Speckle noise reduction for OCT images based on image style transfer and conditional GAN," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3074852.

[A14] S. Tian *et al.*, "DCPR-GAN: Dental crown prosthesis restoration using two-stage generative adversarial networks," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3119394.

[A15] H. Koh, T. Y. Park, Y. A. Chung, J.-H. Lee, and H. Kim, "Acoustic simulation for transcranial focused ultrasound using GAN-based synthetic CT," *IEEE J. Biomed. Health Informat.*, vol. 26, no. 1, Jan. 2022, doi: 10.1109/JBHI.2021.3103387.

References

[1] C. Tempany *et al.*, "Advances in biomedical imaging," *JAMA*, vol. 285, no. 5, pp. 562–567, 2001.

[2] I. Goodfellow *et al.*, "Generative adversarial nets," in *Proc. Adv. Neural Inf. Process. Syst.*, 2014, pp. 2672–2680.

[3] Z. Yi *et al.*, "Dualgan: Unsupervised dual learning for image-to-image translation," in *Proc. IEEE Int. Conf. Comput. Vis.*, 2017, pp. 2849–2857.

[4] P. Zhang *et al.*, "Multi-channel generative adversarial network for parallel magnetic resonance image reconstruction in K-space," in *Proc. Int. Conf. Med. Image Comput. Comput.-Assist. Interven.*, 2018, pp. 180–188.

[5] X. Dong *et al.*, "Automatic multiorgan segmentation in thorax CT images using U-Net-GAN," *Med. Phys.*, vol. 46, no. 5, pp. 2157–2168, 2019.

[6] D. Kiyasseh *et al.*, "Plethaugment: Gan-based PPG augmentation for medical diagnosis in low-resource settings," *IEEE J. Biomed. Health Informat.*, vol. 24, no. 11, pp. 3226–3235, Nov. 2020.

[7] T. Zhou, H. Fu, G. Chen, J. Shen, and L. Shao, "Hi-net: Hybrid-fusion network for multi-modal MR image synthesis," *IEEE Trans. Med. Imag.*, vol. 39, no. 9, pp. 2772–2781, Sep. 2020.