論 文 の 内 容 の 要 旨

論文題目　　Pathology-Aware Generative Adversarial Networks for Medical Image Augmentation

（医用画像拡張に向けた、病変部を意識した敵対的生成ネットワーク）

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The biggest challenge in Machine Learning for Medical Imaging lies in the lack of available annotated datasets: (*i*) it is costly and laborious to collect medical images, such as Magnetic Resonance (MR) and Computed Tomography (CT) images, especially for rare disease; (*ii*) it is time-consuming and observer-dependent, even for expert physicians, to annotate them due to low signal-to-noise (i.e., pathology-to-normal) ratio. To tackle this, researchers have mainly focused on extracting as much information as possible from the available limited data. Instead, we propose to use Generative Adversarial Networks (GANs) for reliable (*i*) Data Augmentation (DA) and (*ii*) Physician Training by generating realistic/diverse pathology-aware samples—such GAN-based DA can improve Computer-Aided Diagnosis based on supervised learning, and such GAN-based Physician Training tool can train medical students/radiology trainees by showing novel pathological images despite infrastructural/legal constraints. This thesis contains five articles aiming to present GANs' such clinically-valuable novel applications in collaboration with physicians. Whereas the methods are more generally applicable, this thesis only explores a few oncological applications.

In the first article, to improve diagnostic reliability, we, for the first time, propose GAN-based medical image generation's two potential applications: (*i*) DA and (*ii*) Physician Training. Towards these, we demonstrate that GANs, especially Wasserstein GAN (WGAN), can generate diverse 128 × 128 whole brain MR images avoiding artifacts. Even an expert

physician fails to distinguish the synthetic images from the real samples in the Visual Turing Test.

The second and third articles tackle GAN-based medical image augmentation for 2D classification. Because most CNN architectures adopt around 256×256 input sizes, we use Progressive Growing of GANs (PGGANs), multi-stage generative training method, to generate realistic/diverse 256×256 whole brain MR images. For robustness, we further use Multimodal UNsupervised Image-to-image Translation (MUNIT) to refine the synthetic images' texture and shape similarly to real ones. Because it is uncertain how to achieve high sensitivity with the synthesized images, we firstly analyze how medical GAN-based DA is associated with pre-training on ImageNet and discarding weird-looking synthetic images. When combined with classic DA, our two-step GAN-based DA succeed to significantly outperform the classic DA alone, in tumor/non-tumor classification (i.e., boosting sensitivity 93.67% to 97.48%). An expert physician classifies a few synthetic images as real despite high resolution.

In the fourth article, we focus on GAN-based medical image augmentation for 2D detection. Classification cannot locate disease areas and segmentation requires expensive annotation cost. Therefore, we propose Conditional PGGANs (CPGGANs), incorporating highly-rough bounding box conditions incrementally into PGGANs to place brain metastases at desired positions/sizes on 256×256 brain MR images, for tumor detection. CPGGAN-based DA succeed to boost 10% sensitivity in diagnosis with clinically acceptable additional False Positives (FPs). Surprisingly, further tumor realism, achieved with additional normal brain MR images for CPGGAN training, does not contribute to detection performance.

Finally, we solved 3D GAN-based medical image augmentation for 2D detection. Because human body is 3D and lesions vary in position/size/attenuation, further GAN-based DA performance requires multiple 3D pathology-aware conditions. Therefore, we propose 3D Multi-Conditional GAN (MCGAN) to generate realistic/diverse $32 \times 32 \times 32$ nodules placed naturally on lung CT images to boost sensitivity in 3D object detection. We find it beneficial to train GANs without ℓ_1 loss, and to use proper augmentation ratio (i.e., 1:1). 3D MCGAN-based DA can achieve higher sensitivity under any nodule size/attenuation at fixed FP rates. Considering realism confirmed by physicians and diversity from multiple conditions, it may also perform as a Physician Training tool to display novel realistic medical images with desired abnormalities (i.e., position/size/attenuation conditions).