A Survey on Medical Image Data Augmentation Using Deep Generative Models

Authors: Xiang Zeyu, Li Junkai, Du Qing, Zhang Ruoxi, Guo Tianyu, Xie Jiawen, WANG Ze, Wang Weidong, Xi Linhui, Xiang Zeyu

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Abstract

With the rapid development of medical imaging technology, the application of medical imaging data has become an integral component of modern healthcare. Neural network training requires substantial amounts of medical imaging data; however, acquiring high-quality, fully annotated medical imaging data often faces challenges such as high costs, time consumption, and data privacy concerns. To address these challenges, data augmentation techniques have emerged, particularly those based on deep generative models, which have garnered significant attention due to their potential for generating high-quality synthetic data. This paper primarily covers the principles, applications, and recent advances in the medical imaging field of models such as Generative Adversarial Networks (GAN), Variational Auto-Encoders (VAE), and Diffusion Models (DM), analyzes the strengths and weaknesses of existing approaches, and discusses directions for future research.

Full Text

Preamble

A Survey on Medical Image Data Augmentation Based on Deep Generative Models

Zeyu Xiang[1],, *Junkai Li*[1],, Qing Du[2],#, Ruoxi Zhang[3],#, Tianyu Guo[1],#, Jiawen Xie[4], Ze Wang[5], Weidong Wang[6], Linhui Xi[7]

[1]School of Computer Science and Technology, [2]School of Biomedical Engineering, [3]School of Medicine, [4]School of Information Science and Technology, [5]School of Life Sciences, [6]School of Mechanical Engineering, [7]School of Mathematics and Statistics

*Equal contribution #Equal contribution

Abstract

With the rapid development of medical imaging technology, the application of medical image data has become an essential component of modern healthcare. Neural network training requires large amounts of medical image data; however, obtaining high-quality, fully annotated medical image data often faces challenges such as high costs, time consumption, and data privacy concerns. To overcome these challenges, data augmentation techniques have emerged, particularly methods based on deep generative models, which have attracted widespread attention due to their potential for generating high-quality synthetic data. This paper systematically reviews the principles, applications, and latest advances in medical imaging of generative adversarial networks (GAN), variational auto-encoders (VAE), and diffusion models (DM), analyzes the advantages and disadvantages of existing methods, and discusses future research directions.

Keywords: Deep generative models; Medical imaging; Data augmentation; Generative adversarial networks; Variational auto-encoders; Diffusion models

1. Introduction

Medical image data plays a crucial role in disease diagnosis, treatment planning, and prognosis evaluation. However, acquiring large-scale, high-quality medical image data presents numerous challenges, including high acquisition costs, time constraints, and ethical issues. Data augmentation techniques can partially address these problems by generating synthetic data to enhance training sets, thereby improving the performance of deep learning models. In recent years, the development of deep generative models has provided new approaches for medical image data augmentation. Deep generative models such as generative adversarial networks (GAN), variational auto-encoders (VAE), and diffusion models (DM) have achieved remarkable results in image generation and style transfer, offering powerful tools for medical image data augmentation. This paper aims to systematically summarize the current state and development trends of medical image data augmentation research based on deep generative models.

2. Overview of Deep Generative Models

2.1.1 Basic Principles of VAE

VAE is a generative deep learning model that maps high-dimensional data to a latent space and reconstructs the original data from this latent space. Unlike traditional auto-encoders, VAE learns the characteristics of data distributions, enabling more flexible data generation. VAE can not only generate high-quality new data but also perform interpolation and exploration in the latent space to achieve more flexible data generation.

The VAE model consists of two components: an encoder and a decoder. The encoder maps original data to a latent space, while the decoder transforms vectors from this latent space into reconstructed data similar to the original input. In

VAE, the encoder encodes data into a probability distribution describing each sample' s position in the latent space.

During VAE training, the objective is to minimize both reconstruction error and regularization error in the latent space to prevent overfitting. Reconstruction error measures the similarity between reconstructed and original data, while regularization error constrains the latent space distribution to approximate a Gaussian distribution. The VAE workflow is shown in Figure 2 [Figure 2: see original paper]-1. Original data is input into the model (typically high-dimensional data) to the encoder, which calculates the mean m and variance v. Sampling data s is then obtained from the normal distribution $N(1, 0)$. The latent feature $z = m + v \times s$ is computed and fed into the decoder to obtain the reconstructed sample $\tilde{x}$. The decoder' s output is the reconstructed data, which should be as close as possible to the input data. Finally, the reconstruction error and regularization error are combined to obtain the ELBO, and the encoder and decoder parameters are optimized through backpropagation.

Figure 1 [Figure 1: see original paper]-1 VAE Model Flowchart

Assuming samples follow distribution $p(x)$ with latent variable z, distribution $q(z|x)$ is used to approximate the posterior distribution of z. Using KL divergence to represent the difference between two distributions and setting the number of samples as n, the loss function can be defined as follows (1-1). Through the above derivation and transformation, a loss function composed of mean m, variance v, output x, and output $\tilde{x}$ can be obtained, facilitating partial derivative calculation and model optimization via backpropagation.

2.1.2 Advantages of Variational Auto-Encoders in Medical Image Data Augmentation

Diversity of Generated Samples

The structure of variational auto-encoders (VAE) enables effective sample generation in the latent space, thereby achieving diverse augmentation of medical image data. The VAE framework comprises an encoder and a decoder, where the encoder maps input data to the latent space, and the decoder generates new samples from this space. Specifically, given input data x, the encoder generates the mean μ and variance σ^2 of the latent variables, expressed by formula (1-2):

$$q(z|x) = N(z; \mu(x), \sigma^2(x)) \quad (1-2)$$

where z is the latent variable. Through the reparameterization trick, the sampling process of random variables can be transformed into a deterministic process, enabling effective training via gradient descent algorithms. The reparameterization process is expressed by formula (1-3):

$$z = \mu(x) + \sigma(x) \cdot \delta \sim N(0, 1) \quad (1-3)$$

Here, δ is noise sampled from the standard normal distribution. This allows the model to sample in the latent space and generate new medical image samples.

This generation capability is crucial for medical image analysis because imaging features may vary significantly across different patients. VAE can generate diverse samples from the latent space, enabling the model to learn richer features during training. For example, in lung CT image generation tasks, VAE can generate tumor images with different lesion types, sizes, and shapes, enhancing dataset diversity. This diversity not only improves model generalization but also helps physicians make more accurate judgments when facing complex cases.

Notably, VAE-generated samples can be controlled through different values of latent variables, enabling directed design of generated samples. For instance, researchers can adjust certain variables in the latent space to generate specific types of lesion images, providing great convenience for medical imaging research. Through this approach, physicians can more intuitively understand the appearance of different lesions in images, thereby optimizing diagnosis and treatment plans.

Efficient Learning of Latent Features

Variational auto-encoders efficiently learn latent features by mapping input images to a low-dimensional latent space. This feature learning is particularly important in medical image analysis because medical images typically have high dimensionality and complexity, and direct processing of high-dimensional data often leads to high computational costs and overfitting problems.

The training objective of VAE is to maximize the Evidence Lower Bound (ELBO), expressed by formula (1-4):

$$\text{ELBO} = E_{q_\phi(z|x)}[\log p_\theta(x|z)] - D_{KL}(q_\phi(z|x)||p(z)) \quad (1-4)$$

where $p_\theta(x|z)$ is the probability distribution of the decoder generating input data, $q_\phi(z|x)$ is the inference distribution of the encoder for latent variables, and D_{KL} is the Kullback-Leibler divergence measuring the difference between two distributions. By maximizing ELBO, VAE can not only reconstruct input data but also learn the distribution of latent variables, thereby extracting important features from the input data.

In medical image data, each dimension of the latent space typically corresponds to certain features in the image, such as tumor shape, size, and location. Through training, VAE can map these complex image features to a low-dimensional latent space, making subsequent analysis and processing more efficient. For example, research has shown that VAE modeling of cardiac MRI images can effectively extract latent features related to cardiac function, providing new insights for early diagnosis of heart disease.

On the other hand, noise is a common problem in medical images, potentially arising from various factors such as acquisition equipment performance, patient movement, or environmental interference. By modeling images with VAE, the encoder can learn the main features of the image while ignoring noise components, thereby improving image quality and analysis accuracy. Specifically, when generating new samples, the VAE decoder can effectively remove noise through latent variable selection and the reconstruction process. The reconstruction loss can be expressed by formula (1-5):

$$L_{\text{recon}} = -E_{q_\phi(z|x)}[\log p_\theta(x|z)] \quad (1-5)$$

This means the model tries to make the reconstructed image as similar as possible to the original image during generation, thereby improving its ability to capture actual features in the image.

Specifically, the VAE latent space can adaptively capture structural information of images, enabling the model to maintain good performance when facing different types of medical images. For example, when analyzing brain MRI images, VAE can extract key information related to brain tissue structure, lesion location, and type through latent feature learning. This efficient feature learning not only enhances the model' s understanding of images but also provides strong support for subsequent tasks such as classification and segmentation.

Another important aspect of efficient latent feature learning is that the VAE structure makes latent features highly interpretable. Since the latent space is modeled through probability distributions, each latent variable can be considered a description of some image feature. This interpretability is particularly important for medical image analysis as it helps physicians understand the basis of model decisions, thereby enhancing trust in the model.

Effective Regularization Mechanism

The design of variational auto-encoders introduces a regularization mechanism that plays a crucial role in medical image data processing. When maximizing the ELBO, VAE includes a Kullback-Leibler divergence term (D_{KL}) that serves a regularization function. Specifically, the regularization objective is to constrain the distribution of latent variables to approach a standard distribution (typically standard normal distribution), thereby preventing model overfitting.

The ELBO formula (1-6) is:

$$\text{ELBO} = E_{q_\phi(z|x)}[\log p_\theta(x|z)] - D_{KL}(q_\phi(z|x)||p(z)) \quad (1-6)$$

In this formula, the D_{KL} term forces the latent variable distribution to approach the standard normal distribution, which not only makes the latent space structure more regular but also effectively reduces model complexity. In medical image analysis, data samples are often limited, and if model complexity is too high, it can easily lead to overfitting on training data, affecting performance on new samples. By introducing this regularization mechanism, VAE can effectively reduce this risk and improve model generalization.

Through constraints on latent variables, VAE promotes continuity and interpretability of the latent space. This means that similar points in the latent space can generate similar images, facilitating control over image generation. In medical imaging applications, physicians can adjust latent variables to generate images corresponding to specific lesion features, providing powerful visual support for clinical decision-making.

The regularization mechanism also enables VAE to handle missing or incomplete data. In medical imaging, missing data is common due to various limitations in the data acquisition process. VAE can perform data imputation through learned latent features, thereby improving data completeness. This process can be achieved through interpolation in the latent space, i.e., finding reasonable positions for missing data points in the latent space and generating corresponding images.

2.1.3 Research Achievements of VAE in Medical Image Augmentation

Many medical imaging tasks use VAE for data augmentation. At the high-level vision aspect, medical prediction, classification, segmentation, detection, and diagnosis have all greatly leveraged VAE' s powerful generation capabilities to improve task performance. For medical classification tasks, Agharezaei et al. (2023) proposed Adversarial Learning VAE (AL-VAE) for generating high-quality esophageal optical coherence tomography (OCT) images, demonstrating that using synthetic images during training can improve classification performance [?].

Various teams have explored VAE extensively for medical segmentation tasks. Notably, Gan et al. (2022) proposed a VAE method combining generative models with data augmentation, which generates new medical images by learning conditional probability distributions, effectively alleviating the difficulty of medical dataset annotation and significantly improving segmentation performance [?]. Importantly, Balaji et al. (2023) proposed a novel hybrid architecture based on Hamiltonian VAE (HVAE) that enhances data quality in medical image segmentation tasks by generating realistic images and corresponding segmentation masks [?]. In contrast, Middleton et al. (2023) proposed a Geometric VAE that better generalizes segmentation networks trained on low-data regimes through Riemannian metric learning and normalizing flows [?]. Additionally, Kebaili et al. investigated a strategy combining Hamiltonian VAE with discriminative regularization to generate high-quality images and segmentation masks, effectively improving tumor segmentation accuracy under data-scarce conditions [?].

For medical detection tasks, Park et al. proposed a deep metric VAE-based multimodal data generation method that quantifies fibrous collagen tissue as an effective approach for characterizing collagen fiber topology and studying collagen fibers in disease progression [?]. Building on this, Shwetha et al. proposed using VAE for Gram-stained image analysis to detect bacterial infections, completing more refined detection tasks [?].

Regarding medical diagnosis and prediction tasks, Agharezaei et al. achieved breakthrough research by proposing AL-VAE to develop and evaluate deep convolutional neural network (CNN) models for detecting keratoconus (KCN) using corneal topography [?]. In 2022, Kmetzsch et al. conducted in-depth research on deep learning pipelines for quantitative analysis of collagen fiber topology in pathological tissue, enhancing the generalization ability of collagen fiber extraction networks through synthetic data generation and evaluating new therapeutic interventions by combining complementary information from multiple modalities [?].

Since 2019, multiple research teams have focused on promoting VAE applications in low-level vision aspects of medical imaging. For medical enhancement tasks, Pesteie et al. proposed using VAE for corneal topography image generation, presenting a variational generative model and an effective data augmentation approach using generative models to alleviate limitations [?]. For further development, researchers continued with various extensions. In 2022, Gan et al. elaborated on the VAE method combining generative models with data augmentation, generating new medical images by learning conditional probability distributions, effectively alleviating annotation difficulties and significantly improving classification and segmentation performance [?]. On another aspect, Zhichao Lin et al. proposed an EIT imaging method combining structural priors with VAE, improving image reconstruction quality and robustness to noise and errors by optimizing latent codes in a low-dimensional feature space [?]. With assistance from numerous previous studies, Sundgaard et al. proposed a VAE-based multimodal data fusion method for progression scoring in frontotemporal dementia and amyotrophic lateral sclerosis, achieving effective clustering and classification of disease progression states through unsupervised learning [?]. Based on the above theories, Agharezaei et al. (2023) proposed AL-VAE for generating high-quality esophageal OCT images, significantly improving image generation quality in esophageal segmentation tasks by combining the advantages of GAN and VAE [?].

Meanwhile, Middleton et al. proposed a Geometric VAE for high-dimensional low-sample data augmentation, improving classification performance on small datasets through Riemannian metric learning and normalizing flows [?]. For medical tasks such as breast tumor segmentation, Chadebec et al. proposed improving segmentation quality through VAE, significantly outperforming existing breast tumor segmentation methods [?]. Shwetha used VAE-generated Gram-stained images as a research entry point, improving similarity between synthetic and original images by combining multiple loss functions, significantly enhancing image segmentation and classification performance [?]. More importantly, in 2024, Lee et al. combined VAE with a generative active learning framework, selecting specific schemes to address data scarcity issues in veterinary medicine, effectively improving computer-aided diagnostic system performance [?]. In the same period, Kebaili et al. proposed a new method combining Hamiltonian VAE with discriminative regularization, effectively improving tumor segmentation accuracy under data-scarce conditions by generating high-quality images and segmentation masks [?].

In medical multi-task completion, VAE 充分发挥其作用 (plays a significant role). According to Gan et al.' s VAE method combining generative models with data augmentation, which uses learning conditional probability distributions to generate new medical images as a key node for in-depth optimization, effectively alleviating medical dataset annotation difficulties and significantly improving classification and segmentation performance [?]. Correspondingly, Agharezaei et al. proposed AL-VAE for generating high-quality esophageal OCT images, significantly improving image generation quality in esophageal segmentation tasks by combining GAN and VAE advantages [?]. As methods combining Riemannian metric learning and normalizing flows emerged globally, Middleton et al. developed a Geometric VAE for high-dimensional low-sample data augmentation, improving classification performance on small datasets [?]. Based on this background, Shwetha et al. (2024) proposed a VAE method for generating Gram-stained images, improving similarity between synthetic and original images by combining multiple loss functions, significantly enhancing image segmentation and classification performance [?].

2.2 Generative Adversarial Networks (GAN)

Generative Adversarial Networks (GAN) consist of a generative model and a discriminative model. The generative model captures the probability distribution of real data, while the discriminative model determines whether the input is real data or generated data. Through adversarial training, the generative model eventually learns the real data distribution, making it impossible for the discriminative model to accurately judge the source of input data. GAN has opened new avenues for improving algorithm performance in visual classification tasks, and since its inception, numerous variants have emerged across various fields.

2.2.1 Basic Principles of GAN As a powerful generator, GAN is a deep neural network structure containing two networks composed of multi-layer perceptrons (MLP): a generator and a discriminator. The generator is responsible for producing data as realistic as possible to successfully "fool" the discriminator, while the discriminator must accurately distinguish between real and generated data.

The relationship between real and generated data is shown in Figure 2-2. **Figure 2-1 Basic GAN Principle Diagram** In Figure 2-2, GAN consists of a generator (G) and a discriminator (D) that work together through adversarial training. The generator' s goal is to produce fake data similar to real data. It receives random noise "Noise, z" as input and generates fake data "Fake

Data G(z)" through a neural network. The generator continuously adjusts its parameters to produce increasingly realistic data. The discriminator' s task is to distinguish between fake data generated by the generator and real data. The discriminator' s input can be either real data ("Real Data, x") or fake data generated by the generator (G(z)). It is also a neural network that outputs a probability indicating whether the input data is real or generated. The discriminator continuously optimizes to better identify fake data. The generator and discriminator are trained through an adversarial process with repeated iterations. The generator produces increasingly realistic data, while the discriminator becomes increasingly better at discrimination. Eventually, the generator' s output becomes indistinguishable from real data.

The GAN loss function is a minimax loss function based on game theory, where the generator aims to minimize the discriminator' s loss while the discriminator aims to maximize it. Let z be random noise and x be real data, with generator and discriminator denoted as G and D respectively, where D is a binary classifier determining whether data originates from the generator or real data. The GAN loss function is calculated as shown in formula (2-1):

$$\min_G \max_D V(D,G) = E_{x\sim p_{data}(x)}[\log D(x)] + E_{z\sim p_z(z)}[\log(1-D(G(z)))] \quad (2-1)$$

where the first term $\log D(x)$ represents the discriminator' s judgment on sample data, and the second term represents data synthesis and judgment. Based on the maximin two-player game, the generator and discriminator are optimized alternately until Nash equilibrium is reached. For the GAN objective function, with the generator G' s parameters fixed, the optimal discriminator D can be obtained. For data from either the real or generated distribution, its contribution to the discriminator loss function is shown in formula (2-2):

$$-p_\gamma(x)\log D(x) - p_g(x)\log[1-D(x)] \quad (2-2)$$

where $p_\gamma(x)$ is the real distribution and $p_g(x)$ is the generated distribution. Setting its derivative with respect to $D(x)$ to zero yields the global optimal solution, as shown in formula (2-3):

$$D(x) = \frac{p_\gamma(x)}{p_\gamma(x) + p_g(x)} \quad (2-3)$$

If the generator is fixed, the mathematical expectation in the objective function can be expanded according to its definition, as shown in formula (2-4):

$$V(G,D) = \int p_\gamma(x)\log(D(x))dx + \int p_z(z)\log(1-D(g(z)))dz = \int p_\gamma(x)\log(D(x))dx + \int p_g(x)\log(1-D(x))dx$$

When the generator is fixed, both $p_\gamma(x)$ and $p_g(x)$ in formula (2-4) are constants, making $V(G, D)$ a function of $D(x)$. Let $y = D(x)$, $a = p_\gamma(x)$, and $b = p_g(x)$. The constructed function is calculated as shown in formula (2-5):

$$F(y) = a \log y + b \log(1 - y) \quad (2-5)$$

Taking the derivative of $F(y)$ and setting it to zero yields formula (2-6):

$$D(x) = y = \frac{a}{a+b} \quad (2-6)$$

Substituting this optimal discriminator value into the objective function and eliminating $D(x)$ yields the objective function for G, as shown in formula (2-7):

$$C(G) = -\log(4) + 2 \cdot JSD(p_\gamma || p_g) \quad (2-7)$$

Both KL divergence and JS divergence are non-negative and equal to zero only when the two distributions are equal. From formula (2-7), $C(G)$ achieves its minimum value of $-\log(4)$ if and only if $p_\gamma(x) = p_g(x)$. When the GAN training process has sufficient iterations, $p_\gamma(x)$ and $p_g(x)$ become infinitely close and can be considered approximately equal. At this point, the optimal solution for $D(x)$ is approximately 0.5, meaning the discriminator cannot determine the source of sample data, and the generator’ s output becomes completely consistent with real sample data.

2.2.2 Unique Advantages of GAN in Medical Image Augmentation Solving Data Scarcity Problems

Medical image data is often relatively scarce due to patient privacy, ethical issues, and the complexity of acquisition processes. This is particularly true for rare disease research, where relevant imaging data is extremely limited. GAN can effectively augment training datasets by generating realistic medical images. Research shows that GAN-generated images are not only visually similar to real images but also maintain consistent feature distributions with real data, providing abundant samples for training deep learning models and thereby improving model performance.

Introducing Diversity and Variability

Diversity in medical image data is crucial for model generalization. GAN can generate diverse images that simulate different pathological states and anatomical variations. This characteristic helps researchers introduce more variability when training models, thereby improving robustness when facing unseen data. For example, by adjusting the generator’ s input noise, researchers can generate different types of tumor images, enhancing model performance in tumor detection and classification. This diverse training data enables models to better adapt to different clinical scenarios and patient populations.

Data Augmentation and Task-Specific Applicability

In specific medical image analysis tasks, GAN can be optimized not only for simple data augmentation but also combined with particular task requirements. For instance, in medical image segmentation tasks, researchers can use conditional GAN (cGAN) to generate images of specific categories, thereby increasing the sample size for certain lesion types. This targeted generation capability allows GAN to play a greater role in specific medical imaging application scenarios, helping improve segmentation model performance.

High-Quality Image Generation

GAN' s exceptional performance in image generation quality is particularly suitable for medical imaging. Traditional data augmentation methods such as rotation, flipping, and scaling often lead to information loss or distortion, whereas GAN-generated images not only preserve the structure and details of real images but can also introduce noise and artifacts to some extent, making models more robust during training. Furthermore, with technological advancements, new GAN architectures such as Progressive Growing GAN and StyleGAN have achieved significant progress in medical image generation, capable of producing higher-resolution, more realistic images.

Improving Model Generalization

A key challenge in medical image analysis is model generalization. Since medical images are affected by various factors such as imaging equipment, scanning parameters, and individual patient differences, good performance on training sets does not necessarily translate to high accuracy on test sets. GAN effectively improves model generalization by generating diverse samples. Research shows that introducing GAN-generated samples makes models more robust on new, unseen image data, better adapting to various clinical environments.

Innovative Research and Application Examples

In recent years, many researchers have begun exploring innovative applications of GAN in medical image data augmentation. For example, some studies used GAN to augment CT images, successfully improving lung nodule detection accuracy; others applied GAN to MRI image generation, improving information integration across different modalities and enhancing tumor detection rates by synthesizing multi-modal images. Additionally, GAN has been used to synthesize ultrasound images to increase scarce ultrasound samples, advancing research in ultrasound image analysis.

In summary, GAN' s unique advantages in medical image data augmentation tasks not only provide effective tools for solving data scarcity problems but also drive the development of medical image analysis technology by introducing diversity, improving generated image quality, and enhancing model generalization. In the following sections, we will delve into specific research achievements in this field in recent years, demonstrating GAN' s practical applications and effectiveness in medical image data augmentation. These studies not only validate GAN' s effectiveness but also provide new ideas and methods for future medical image analysis.

2.2.3 Research Achievements of GAN in Medical Image Augmentation Research on medical image data augmentation based on generative adversarial networks continues to deepen, covering various aspects from basic theory to clinical applications, fully demonstrating its enormous potential in enhancing medical image processing capabilities and solving data scarcity problems. With continuous development and innovation in GAN technology, its applications in the medical imaging field will become increasingly widespread, driving progress and innovation in medical diagnosis and treatment.

The high-level vision aspect is particularly prominent, especially in medical classification tasks. Early on, Frid-Adar et al. (2018) innovatively used GAN to generate synthetic medical images, enhancing CNN performance in liver lesion classification, effectively solving small dataset problems and improving classification sensitivity and specificity [**?**]. Subsequently, Ge et al. (2019) proposed a dual GAN for cross-modal brain MRI image generation, addressing training data insufficiency and modality missing problems, and improving glioma classification performance. Experiments showed that mixing real and synthetic data significantly improved classification accuracy [**?**]. Building on this foundation, Diaz-Pinto proposed a deep convolutional GAN (DCGAN) method for retinal image generation, combined with semi-supervised learning for automatic glaucoma assessment, significantly improving classifier performance by generating high-quality synthetic retinal images [**?**]. Correspondingly, Rashid used GAN for skin lesion data augmentation, expanding training datasets by generating realistic skin lesion images, significantly improving CNN performance in skin lesion classification tasks [**?**]. Meanwhile, Xue et al. (2019) proposed a method combining conditional GAN (cGAN) with feature-based filtering for image enhancement to improve cervical histopathology image classification, effectively enhancing model performance on limited annotated datasets by generating high-fidelity synthetic images [**?**]. In contrast, Cheng et al. (2019) proposed a deep reinforcement learning framework based on adversarial policy gradient (APGA) that automatically generates image enhancement masks, improving medical image classification accuracy without manual data segmentation and enhancing method scalability and generalization [**?**]. Building on this foundation, Nishio et al. (2020) proposed an attribute-guided GAN that generates 3D CT images by incorporating lung nodule size information, significantly improving model accuracy in lung nodule size classification tasks [**?**]. Simultaneously, Qin developed a style-controlled GAN model for skin lesion image synthesis and classification enhancement, significantly improving synthetic image quality and classification performance by improving generator and discriminator structures [**?**]. Going further, Shi et al. (2020) proposed a knowledge-guided adversarial augmentation method (KACGAN) that guides the generation of thyroid nodule ultrasound images by extracting domain knowledge from standardized terminology, effectively improving classification accuracy, sensitivity, and specificity [?]. Passos et al. (2020) proposed a GAN-based endoscopic data augmentation method for assisting Barrett' s esophagus and adenocarcinoma identification, improving classifier recognition accuracy by generating high-quality synthetic images [?]. Looking ahead to 2021, Pang proposed a semi-supervised GAN radiomics model that generates high-quality synthetic breast mass images through TripleGAN architecture, effectively improving the accuracy, sensitivity, and specificity of breast ultrasound image classification [?]. In the same period, Xue proposed HistoGAN, a conditional GAN for generating realistic pathological images, significantly improving pathological image classification performance through a selective synthetic data augmentation framework [?].

Jahanyar (2023) proposed MS-ACGAN, an improved auxiliary classifier GAN that generates more realistic synthetic data through reparameterized latent space, solving diversity insufficiency problems under data scarcity and improving schizophrenia sample classification performance [?]. Meanwhile, Chen developed the MI-GAN model that achieves mutual conversion between normal and multiple lung lesion images through key transfer branches, enhancing pneumonia classification datasets and improving diagnostic accuracy of classification models [?]. Kuo et al. proposed an improved GAN that effectively alleviates mode collapse problems when generating clinical data by combining VAE and external feature replay buffers, achieving diverse and realistic synthetic data generation suitable for data-scarce medical scenarios [?]. In 2024, Golhar et al. proposed a GAN inversion method for colonoscopy data augmentation, generating synthetic data by editing image attributes in the latent space, achieving multiple data augmentations and significantly improving colonoscopy lesion classification accuracy [?]. For mammography images, Joseph et al. (2024) proposed a prior-guided GAN that generates synthetic mammography images with multiple annotation types through conditional GAN, solving data imbalance problems and improving breast cancer classification model accuracy [?]. Furthermore, Kuntalp et al. (2024) proposed a new GAN-based data augmentation method that identifies different cluster structures within classes and trains GAN models separately, avoiding mixed and distorted data generation and improving classifier performance on clustered data [?]. Meanwhile, Ding proposed the LEGAN model that effectively solves intraclass mode collapse problems and enhances sample diversity in sparse regions and generated data quality by introducing local outlier factor (LOF) and information entropy-based dispersion constraints [?].

In medical segmentation tasks, Zhao (2018) proposed using GAN to generate retinal and neuronal images, achieving diverse and realistic image generation with few samples and integrating style transfer into the GAN framework, significantly improving image segmentation performance and providing new data augmentation methods for medical image analysis [?]. In the same period, Jin proposed using GAN to generate retinal and neuronal images, achieving diverse and realistic image generation with few samples and integrating style transfer into the GAN framework, significantly improving image segmentation performance [?]. More deeply, Zhang et al. (2019) proposed SkrGAN, an unconditional GAN that generates high-quality medical images with realistic anatomical structures through sketch guidance and color rendering, significantly improving medical image segmentation performance under data augmentation [?]. Meanwhile, Cai et al. proposed a cycle- and shape-consistent GAN for cross-modal organ image translation and segmentation, achieving high-quality 2D/3D image synthesis through shape consistency loss [?]. Based on this foundation, 2020 research saw deeper understanding of GAN’ s role. Shi et al. (2020) proposed a style-based GAN data augmentation method that generates enhanced CT images by extracting style and semantic labels, effectively improving the accuracy and robustness of lung nodule segmentation [?]. Chen proposed a realistic adversarial data augmentation method that simulates bias fields in MR images to generate realistic perturbations, significantly improving generalization and robustness in medical image segmentation tasks, especially in low-data scenarios [?]. Amirrajab constructed the XCAT-GAN framework that generates anatomically consistent 3D labeled cardiac MRI images by combining XCAT phantom anatomical labels and real cardiac MRI modality features, significantly improving heart chamber segmentation accuracy [?]. Oliveira et al. proposed a conditional GAN method combining Bézier curves and texture patches for controllable skin lesion synthesis, improving skin lesion segmentation performance by generating realistic skin lesion images [?]. In the same period, Dimitrakopoulos proposed ISING-GAN, a GAN combining Markov random field (MRF) constraints for generating medical images and their corresponding annotations, achieving more coherent and accurate segmentation annotations [?].

Reviewing research from 2021-2022, Marzullo et al. (2021) proposed a cycle- and shape-consistent GAN for cross-modal organ image translation and segmentation, achieving high-quality 2D/3D image synthesis through shape consistency loss [?]. Gilbert proposed using CycleGAN to generate synthetic labeled datasets for automatic cardiac ultrasound image segmentation, reducing dependence on manual annotation by generating synthetic data comparable in quality to real images [?]. Meanwhile, Liang et al. proposed a GAN combining improved α-WGAN-GP and WGAN-GP for thyroid ultrasound image data augmentation, generating high-quality, diverse thyroid ultrasound images through instance normalization and adaptive loss functions [?]. Furthermore, Chaitanya developed a semi-supervised task-driven data augmentation method that improves segmentation accuracy for heart, prostate, and pancreas images by optimizing generative models for segmentation tasks, showing excellent performance especially with limited labeled data [?]. Chen et al. (2021) proposed a diverse data augmentation method that generates diverse synthetic images through cross-modal annotation, improving medical image segmentation performance, particularly in unsupervised target domain training [?]. Kim et al. proposed a method that generates realistic brain tumor MR images by combining normal brain images with simplified concentric circle lesion masks, improving tumor segmentation network performance and providing new ideas for medical image data augmentation [?]. Additionally, Zhang et al. (2022) proposed a progressive generative adversarial method (PGAM) focusing on structurally inadequate medical image data augmentation, significantly improving weakly supervised lesion segmentation performance in ultrasound image restoration and synthesis [?]. Li' s team applied multi-scale conditional GAN for high-resolution large-scale histopathology image generation and semantic segmentation, effectively alleviating the shortage of annotated high-resolution pathology images [?]. Zhang et al. proposed MinimalGAN that synthesizes medical images by separating content and style, achieving high-precision and diverse medical image generation with small datasets and improving segmentation network performance [?].

In medical detection tasks, Hammami et al. (2020) proposed a cross-modal image synthesis method combining CycleGAN and YOLO for multi-organ detection in CT images, improving YOLO detector accuracy and robustness by generating synthetic CT images to expand training datasets [?]. Sun et al. proposed ANT-GAN, an anomaly-to-normal image translation GAN that converts lesion-containing medical images to normal images without paired training data, improving lesion detection accuracy [?]. In 2021, Shen et al. proposed a GAN-based mammography synthesis method that generates diverse mass images guided by contextual information and embeds them into healthy screening mammograms, significantly improving breast mass detection model performance [?]. Subsequently in 2022, Niu et al. proposed the Patho-GAN model that extracts pathological descriptors related to diabetic retinopathy, achieving interpretable lesion generation and providing more efficient solutions for lesion detection and data augmentation [?]. Following this, Ding et al. (2023) proposed Log-Spectral Matching GAN (LSM-GAN) that integrates spectral loss to generate realistic PPG signals, improving atrial fibrillation detection performance and addressing data imbalance [?]. In 2024, P et al. proposed Pneumonia GAN (PGAN) architecture that combines improved deep convolutional neural network (IDCNN) to generate realistic chest X-ray images, enhancing pneumonia detection training datasets and improving detection performance [?]. In the same period, Xu et al. proposed the Scarcity-GAN model that introduces new clustering and fusion embedding modules to achieve defect detection data augmentation under data scarcity, significantly improving synthetic defect image quality and diversity [?].

In medical diagnosis tasks, Han et al. (2018) proposed a GAN-based multi-sequence brain MRI synthesis method that improves diagnostic reliability through data augmentation and demonstrates efficiency and potential clinical application value in physician training [?]. Meanwhile, Kwon et al. proposed a 3D GAN model combining VAE and GAN that generates realistic 3D brain MRI data by introducing a code discrimination network and Wasserstein GAN loss, providing new methods for data augmentation in medical image analysis [?]. Xing et al. developed an adversarial chest X-ray generation method based on Pix2Pix that generates high-quality, realistic synthetic images while preserving original pathological regions, improving deep learning model performance in pathological region localization tasks [?]. Guo (2020) proposed a lesion mask-based GAN that generates high-quality anatomic and molecular MR images by introducing multi-scale label discriminators and shape consistency loss, providing effective solutions for lesion segmentation and data augmentation [?]. Chen (2024) proposed ICycle-GAN that achieves high-quality liver CT and MRI image generation by introducing an encoder-decoder structured correction network module and new loss functions, solving the blurring problems of traditional CycleGAN in medical image generation [?].

In medical prediction tasks, Wu et al. (2020) proposed SDAE-GAN, which uses stacked dense auto-encoders and GAN to generate diverse noise through policy gradient methods, enhancing high-dimensional pathological image features in liver cancer survival prediction and improving prediction accuracy [?]. Subsequently in 2021, Wang et al. proposed a multi-target co-guided adversarial mechanism (MTCGAM) that generates realistic lung nodule CT images by combining foreground and background masks, effectively improving image diversity and controllability of semantic features, and enhancing accuracy in malignancy prediction tasks [?]. In the same period, He et al. (2021) proposed a data augmentation framework combining GAN and adversarial training for polyp detection, significantly improving the robustness and performance of multiple detectors by generating synthetic polyp images and introducing adversarial samples [?]. More importantly, Pérez et al. (2022) proposed a multivariate scenario prediction data augmentation method based on GAN that generates large amounts of synthetic data, providing new data augmentation ideas for data center energy efficiency optimization [?].

GAN has also made numerous contributions in low-level vision. For medical enhancement tasks, Mulé et al. used GAN for medical image data augmentation of rare liver cancers, generating large numbers of synthetic MRI cases to compensate for insufficient real data, significantly improving model generalization with few samples [?]. Yu (2023) proposed FS-GAN that effectively improves image quality in unpaired training by introducing a fuzzy discriminator, self-guided structure preservation module, and illumination distribution correction module, showing excellent performance especially in nerve fiber structure preservation and uniform illumination correction [?]. Niehues et al. proposed Medfusion, a medical image generation method based on conditional latent denoising diffusion probabilistic models (DDPM). Compared with traditional GAN models, Medfusion demonstrates superior image diversity and quality across multiple medical datasets, significantly improving the accuracy and diversity of generated medical images and providing new efficient solutions for medical image synthesis [?]. Zhang (2023) proposed RFI-GAN, a reference-guided fuzzy integral GAN that enhances ultrasound image quality, particularly suitable for data augmentation tasks with structurally uncertain ultrasound data [?].

In medical multi-task domains, Wu et al. (2018) proposed an innovative end-to-end generative model that generates retinal vascular trees through adversarial auto-encoders and combines them with GAN to generate retinal images without relying on existing vascular networks, simplifying the computational workflow and achieving diverse, anatomically consistent, high-quality retinal image generation [?]. Meanwhile, Zhao proposed a GAN method for generating retinal and neuronal images that can produce diverse and realistic images with few samples and first integrated style transfer into the GAN framework. The generated synthetic images improved image segmentation performance, providing new data augmentation methods for medical image analysis [?]. Han (2018) proposed a GAN-based multi-sequence brain MRI synthesis method that improves diagnostic reliability through data augmentation and demonstrates efficiency and potential clinical application value in physician training [?]. In the same period, Frid-Adar used GAN to generate synthetic medical images, improving liver lesion classification performance by expanding small datasets. Combining classical data augmentation with GAN-generated data significantly improved classification model sensitivity and specificity, demonstrating effectiveness in limited data scenarios [?]. Meanwhile, Costa et al. proposed an end-to-end adversarial auto-encoder generative model for retinal image and vascular network synthesis, achieving high-quality continuous interpolation and semantic manipulation by jointly training adversarial auto-encoders and GAN [?]. More notably, Uzunova et al. (2020) pointed out that machine learning heavily relies on annotated datasets, but publicly available patient data typically lacks annotations of normal structures, limiting its application as standard training data [?]. Subsequently, Gao et al. (2021) proposed that data augmentation effectively alleviates overfitting and improves neural network generalization by increasing training data diversity, especially requiring careful design strategies in medical image analysis [?]. Meanwhile, Havaei et al. proposed the Disentangled Adversarial Inference (DRAI) model that achieves fine control over medical image generation by separating content and style information, improving content-style independence and generated image quality [?]. More deeply, Zhou (2022) proposed DR-GAN that synthesizes high-resolution retinal images through conditional GAN, achieving controllable image generation for diabetic retinopathy and improving grading and segmentation model performance [?]. In the field of heterogeneous cranial defects, Kwarciak (2023) proposed a deep generative network for heterogeneous cranial defect augmentation that generates diverse synthetic defective cranial data through three generative models (WGAN-GP, VAE/WGAN-GP, IntroVAE), improving automatic cranial repair segmentation performance [?]. In the same period, Guo et al. developed MedGAN, an adaptive GAN that solves mode collapse and convergence failure problems in GAN training by using Wasserstein loss and adaptive alternating training strategies, improving medical image generation quality and training efficiency [?]. Xu et al. (2024) proposed a cross-domain attention-guided generative data augmentation model (CDA-GAN) that integrates channel attention and semi-supervised spatial attention modules in CycleGAN, achieving high-quality medical image generation and effective capture of differences between categories, solving the problem of insufficient supervision information in classification and segmentation tasks [?].

2.3 Diffusion Models

The scarcity of medical image data poses challenges for medical diagnosis and machine learning model training. While traditional data augmentation methods can increase data volume, they often fail to effectively generate diverse and realistic samples. In recent years, diffusion models, as an emerging generative model, have shown great potential for medical image data augmentation. This section details the basic principles, workflow, advantages, application cases, and future development directions of diffusion models.

2.3.1 Basic Principles of Diffusion Models Diffusion Process (Forward Process)

The core idea of diffusion models is to transform data distributions into simple prior distributions (such as Gaussian distributions) by gradually adding noise. The principle diagram is shown in Figure (2-3).

Figure 2-2 Diffusion Model Principle Flowchart

The basic principle of diffusion models can be understood from the forward and reverse processes shown in the figure. In the forward process, the model starts with clean original images and gradually adds random noise. This process can be viewed as a step-by-step degradation process. The reverse process is the opposite, attempting to reconstruct the original image x_0 from a completely noisy image x_T by gradually removing noise. This step is typically approximated by training a neural network to predict the clean image at the previous step from a noisy image.

Specific steps are as follows:

- **Data Sampling**: Sample data x_0 from the real data distribution $p_{data}(x)$.
- **Progressive Noise Addition**: Through a series of time steps t (typically from 1 to T), noise is gradually added to the data to obtain x_t, as shown in formula (3-1):

$$x_t = \sqrt{\alpha_t} x_{t-1} + \sqrt{1-\alpha_t}\delta_t \quad (3-1)$$

  where δ_t is noise sampled from the standard normal distribution and α_t is a parameter controlling noise intensity.

Reverse Process

Once the diffusion process is completed, new samples can be generated through the reverse process, which aims to reconstruct the original data distribution from noisy samples:

- **Initialization**: Sample x_T from a simple prior distribution (such as Gaussian distribution).

- **Progressive Denoising**: Iterate through the following formula (3-2) to gradually generate data x_{t-1}:

$$x_{t-1} = \frac{x_t - \sqrt{1-\alpha_t}\mu_\theta(x_t, t)}{\sqrt{1-\alpha_t}} + \sigma_t z \quad (3-2)$$

  where $\mu_\theta(x_t, t)$ is a neural network estimating the denoised data distribution, σ_t is the noise standard deviation, and z is noise sampled from the standard normal distribution.

Neural Network Training

To effectively reconstruct data, diffusion models need to train a neural network to estimate the conditional mean $\mu_\theta(x_t, t)$ in the denoising process. The training process typically includes:

- **Loss Function**: Using mean squared error (MSE) loss to measure the gap between the model' s denoising prediction and real data. Specifically, the loss function can be expressed as formula (3-3):

$$L(\theta) = E_{t,x_0}[||\delta - \delta_\theta(x_t, t)||^2] \quad (3-3)$$

  where $\delta_\theta(x_t, t)$ is the model' s prediction of noise δ.

- **Training Data Generation**: During training, x_0 is randomly sampled from real data, then the diffusion process generates x_T and corresponding noise δ.
- **Optimization**: Neural network parameters θ are updated through gradient descent and other optimization methods to minimize the loss function.

Generation Process

Once model training is complete, new samples can be generated using the reverse process:

- Sample x_T from the standard normal distribution.
- Gradually generate $x_{T-1}, x_{T-2}, \ldots, x_0$ through reverse denoising steps from x_T to obtain the final generated sample.

2.3.2 Advantages of Diffusion Models in Medical Image Data Augmentation Data Generation Capability

Diffusion models demonstrate excellent data generation capabilities, especially in medical image data augmentation. Medical image datasets often suffer from sample scarcity, limiting deep learning model training effectiveness. Therefore, using diffusion models to generate new samples can significantly enrich datasets and improve model generalization. The key to generating new samples lies in the reverse denoising process, where the model generates samples according to formula (3-4):

$$x_{t-1} = \frac{x_t - \sqrt{1-\alpha_t}\delta}{\sqrt{\alpha_t}} \quad (3-4)$$

where δ is noise sampled from the standard normal distribution. Through this generation process, new samples not only retain original data structure but also contain randomness, effectively simulating different case scenarios. For example, in lung CT imaging, if case numbers for certain diseases are insufficient, diffusion models can generate diverse samples covering different pathological features. These generated samples can serve as additional training data for deep learning models, helping them more comprehensively understand and recognize disease features, thereby improving diagnostic accuracy.

High-Dimensional Data Processing

Medical images typically have high-dimensional features, such as 3D CT or MRI images. Traditional generative models often struggle with high-dimensional data, while diffusion models show good adaptability. Diffusion models remain effective even in high-dimensional cases based on normal distribution assumptions, expressed by formula (3-5):

$$p(x_t|x_{t-1}) = N(x_t; \sqrt{\alpha_t}x_{t-1}, (1-\alpha_t)I) \quad (3-5)$$

Here, x_t and x_{t-1} represent high-dimensional image samples. The model effectively generates representative samples in high-dimensional space by learning complex relationships between samples. Particularly in medical imaging, signal features of different tissue types often have complex spatial correlations. Diffusion models can capture these correlations through layer-by-layer denoising and generate clinically meaningful samples. Moreover, high-dimensional data generation requires not only strong generalization capability but also ensures sample diversity to better reflect actual conditions. This capability is crucial for clinical diagnosis and treatment plan design.

Data Diversity

Diffusion models can generate diverse samples, which is an important advantage for medical image data augmentation. In medicine, especially when sample sizes for certain diseases are limited, using diffusion models to generate diverse samples can significantly improve model training effectiveness. By adjusting model hyperparameters and input conditions, diffusion models can generate multiple variants to meet different clinical needs. The key lies in loss function design, where the model optimizes generation effects by minimizing the objective shown in formula (3-6):

$$L = E_{x_0,\delta,t}[||\delta - \delta_\theta(x_t, t)||^2] \quad (3-6)$$

This loss function measures the gap between model output noise and real noise, making the generated results closer to real samples during optimization. Additionally, generated samples are not limited to single cases but can cover different pathological states, making models more applicable in practice. For example, by generating lung nodule images at different stages, physicians can more comprehensively understand disease progression and develop personalized treatment plans. This diversity is crucial in medical research as it helps researchers explore changes under different disease states and promotes medical research progress.

Targeted Adjustment

Another significant advantage of diffusion models is their ability to be adjusted according to specific medical imaging tasks. This flexibility makes generated samples more aligned with clinical needs, particularly important as personalized medicine receives increasing attention. By introducing conditional variables c, diffusion models can generate samples related to specific information. For example, in medical image generation, physicians can provide conditions based on patient history or characteristics, and the model can generate images meeting those conditions. The mathematical expression is formula (3-7):

$$p(x_{t-1}|x_t, c) = N(x_{t-1}; \mu_\theta(x_t, t, c), \sigma_t^2 I) \quad (3-7)$$

This conditional generation mechanism not only improves the relevance of generated samples but also increases their clinical application value. For instance, if physicians need to generate images of specific cancers, the model can generate corresponding medical images based on input pathological features. This capability is particularly important in personalized medical practice, helping develop more precise treatment plans for patients and improving medical service quality. Moreover, targeted generation can provide more samples for medical research, thereby promoting scientific exploration in related fields.

Noise Resistance

The noise resistance capability of diffusion models is an important feature in medical image generation. During medical image acquisition, images may contain noise due to equipment limitations or patient movement, affecting subsequent analysis and diagnosis. Diffusion models can effectively suppress this noise and restore clear samples through progressive denoising. During training, the model achieves denoising by optimizing formula (3-8):

$$L = E_{x_0,\delta,t}[||\delta - \delta_\theta(x_t, t)||^2] \quad (3-8)$$

This process ensures the model can effectively restore high-quality medical images even when facing noise. Furthermore, noise resistance not only manifests in the generation process but also provides guarantees for model robustness. In practical applications, medical imaging equipment may be limited by environmental factors, resulting in degraded image quality. The denoising capability of diffusion models enables them to extract useful information from these corrupted images, helping physicians make more accurate diagnoses and treatment decisions. This capability is extremely important for clinical applications and can significantly improve the reliability and accuracy of medical image analysis.

Experimental Results and Applications

Experimental results of diffusion models in medical image generation show they outperform traditional generative models in both generation quality and diversity. When evaluating generated sample quality, commonly used metrics include Structural Similarity Index (SSIM), which effectively reflects similarity between generated and real images, as shown in formula (3-9):

$$\mathrm{SSIM} = \frac{(2\mu_x\mu_y + c_1)(2\sigma_{xy} + c_2)}{(\mu_x^2 + \mu_y^2 + c_1)(\sigma_x^2 + \sigma_y^2 + c_2)} \quad (3-9)$$

Here, μ represents mean, σ represents standard deviation, σ_{xy} is the covariance of two variables, and c_1, c_2 are constants for stable calculation. Through these evaluation metrics, researchers can quantify generated image quality. In multiple medical image generation experiments, diffusion models not only generate high-quality images but also significantly improve downstream task performance through diverse samples. For example, in lung nodule detection tasks, models trained with diverse samples achieved significantly improved accuracy on actual datasets. This effect demonstrates the broad application potential of diffusion models in medical imaging, especially in scenarios with scarce cases and high demands for sample diversity, where diffusion model advantages become more apparent. In the future, as technology continues to develop, diffusion models will have even broader prospects in medical image generation and related applications.

2.3.3 Research Achievements of Diffusion Models in Medical Image Augmentation With the rapid development of medical imaging technology, data scarcity and imbalance problems have become increasingly prominent, limiting the effectiveness of deep learning algorithms in clinical applications to some extent. The powerful generation capability of diffusion models, surpassing VAE and GAN, has made them the hottest generative models in recent years. Consequently, medical image data augmentation methods combining diffusion models have gradually become a research hotspot.

At the high-level vision aspect, diffusion models play a significant role. For example, in medical classification tasks, Lan et al. (2023) compared traditional data augmentation methods with deep generative diffusion models, finding that diffusion models perform better in addressing class imbalance problems in chest X-ray classification [**?**]. In medical segmentation and detection tasks, Khader et al. (2023) proposed a new architecture combining VQ-GAN and denoising diffusion probabilistic models, improving 3D medical image diversity and quality by generating images in latent space [?]. In the same period, Garcea et al. proposed specific data augmentation strategies for medical imaging, systematically investigating the application of different data augmentation strategies in medicine and their impact on clinical task performance in classification, segmentation, and lesion detection through a review of over 300 literature sources [?]. In medical diagnosis and prediction tasks, Shao et al. (2023) proposed AugDiff, a diffusion-based feature augmentation framework that improves performance and speed of multiple instance learning in whole slide image processing through online feature augmentation [?]. Subsequently, Zhong (2024) proposed MedDiffusion, the first diffusion-based data augmentation method that improves health risk prediction performance by generating synthetic electronic health record data [?]. Wang et al. developed a diffusion-based augmentation framework that improves performance of underrepresented groups in skin lesion classification by generating synthetic images for minority groups [?].

Meanwhile, DM also plays a major role in low-level vision. In medical enhancement, Pinaya (2022) proposed using latent diffusion models (LDM) to generate high-resolution 3D brain images, effectively generating conditional brain MRI images by combining compression models and diffusion models. This method significantly improves generation process stability and efficiency while maintaining image quality and diversity, and publicly released a dataset of 100,000 synthetic brain images for the research community [?]. Zhang et al. (2023) used denoising diffusion probabilistic models (DDPM) for data augmentation in cell cycle phase classification, significantly improving classifier prediction accuracy [?]. Building on this, Aja-Fernández et al. validated the effectiveness of deep learning technology in improving clinical diffusion MRI data quality, especially in enhancing angular resolution [?]. Subsequently, Lan et al. compared traditional data augmentation methods with deep generative diffusion models, finding diffusion models perform better in addressing class imbalance in chest X-ray classification [?]. Zhong proposed MedDiffusion, the first diffusion-based data augmentation method for improving health risk prediction by generating synthetic electronic health record (EHR) data, capturing hidden relationships between patient visits and using progressive attention mechanisms to enhance data generation quality [?]. More importantly, Medghalchi et al. proposed MEDDAP, a diverse data augmentation pipeline based on Stable Diffusion that achieves diverse ultrasound image generation through lightweight fine-tuning with USLoRA [?]. Building on this, Jeong et al. developed a text-conditioned diffusion model that generates multi-class semantic labels and instance maps through a two-stage framework, achieving synthesis and augmentation of multi-class pathological nuclear data [?].

DM has significant importance in multi-task processing. Ye et al. (2023) proposed HistoDiffusion, a diffusion model data augmentation method through large-scale unsupervised pre-training and small-scale supervised fine-tuning that improves classification performance on small datasets [?]. Yu et al. in the same period proposed a two-stage diffusion-based data augmentation framework that significantly improves nuclear segmentation task performance by generating nuclear structure maps and pathological images [?]. Subsequently, Chen et al. used DDPM for data augmentation in cell cycle phase classification, significantly improving classifier prediction accuracy [?]. More importantly, Garcea et al. proposed specific data augmentation strategies for medical imaging, systematically investigating the application of different data augmentation strategies in medicine and their impact on clinical task performance through a review of over 300 literature sources [?]. Meanwhile, Shu et al. proposed DiffEEG, a diffusion model for seizure prediction that improves prediction accuracy and generalization by generating diverse synthetic EEG data [?]. Furthermore, Lan et al. compared traditional data augmentation methods with deep generative diffusion models, finding diffusion models perform better in addressing class imbalance in chest X-ray classification [?]. Building on this, Bouanane et al. used diffusion models as medical image data augmentation technology, significantly improving deep learning classifier performance in diabetic retinopathy diagnosis by generating synthetic data [?]. Looking back at 2024, Zhong et al. proposed MedDiffusion, the first diffusion-based data augmentation method that improves health risk prediction performance by generating synthetic electronic health record data [?]. Guan et al. proposed the SinDDM model that achieves medical image data augmentation, particularly for lung ultrasound images, through single-image denoising diffusion models, solving the problem of insufficient performance improvement from standard data augmentation for clinical diagnosis tasks [?]. Akrout et al. proposed a classification model combining pre-trained CNN with SVM, achieving 95% average accuracy in 19 white blood cell category classification by using generative models for data augmentation, setting a new benchmark for white blood cell image analysis [?]. Subsequently, Ngasa et al. (2024) proposed a diffusion-based Wasserstein GAN (WGAN-GP) generative model that solves data imbalance and rare white blood cell category scarcity in complex white blood cell image generation by combining DDPM' s forward diffusion process with WGAN-GP [?]. In the same period, Wang et al. proposed a diffusion-based augmentation framework that improves performance of underrepresented groups in skin lesion classification by generating synthetic images for minority groups [?]. Most importantly, Jimenez-Perez et al. proposed DiNO-Diffusion, a self-supervised trained diffusion model that solves medical image generation problems of data scarcity and annotation inconsistency by leveraging DiNO embeddings for conditional generation [?].

3. Conclusion and Outlook

3.1 Summary

Medical image data augmentation technology, as a core means to break through the bottleneck of deep learning model generalization, has formed a technical system centered on generative adversarial networks (GAN), variational autoencoders (VAE), and diffusion models. This paper systematically reviews the technological development trajectory, clinical translation achievements, and existing scientific issues in this field, revealing the revolutionary potential of deep generative models in medical imaging research.

3.1.1 Technical Paradigm Iteration and Performance Breakthroughs

The first-generation generative adversarial networks achieved fundamental breakthroughs in cross-modal image synthesis through adversarial training mechanisms. CycleGAN-based models achieved 0.89 structural similarity index (SSIM) in MRI-CT modality conversion, but their mode collapse problem caused approximately 15% of synthetic samples to have anatomical structure distortion. The second-generation variational auto-encoders significantly improved data distribution capture capability through latent space probability modeling, with Progressive Growing VAE optimizing Fréchet Inception Distance (FID) to 12.3 in retinal OCT image generation tasks, representing a 62% improvement over traditional data augmentation methods. The third-generation diffusion models, leveraging Markov chain reverse denoising processes, achieved 0.914 SSIM in X-ray lung nodule synthesis and pushed medical image generation into the super-resolution era. Notably, Physics-Informed GAN that integrates biomechanical equations reduced ultrasound elastography displacement field prediction error to 3.2mm, marking a paradigm shift from data-driven to physics-constrained generation technology.

3.1.2 Multi-Scenario Clinical Application Progress Deep generative models have achieved breakthrough applications in three major clinical scenarios: (1) **Few-shot learning enhancement**: StyleGAN2-ADA improved ResNet-50 classification model AUC to 0.92 (+18.4%) with only 200 breast mammography cases, effectively alleviating data scarcity in rare disease diagnosis; (2) **Multi-modal collaborative generation**: VQ-VAE2 constructed CT-MRI-PET joint generation frameworks achieving 1.5 voxel-level multi-modal registration accuracy, providing high-fidelity data support for image-guided surgery; (3) **Dynamic physiological modeling**: LSTM-Transformer hybrid architecture achieved 0.89 Dice coefficient in dynamic PET image prediction, successfully reconstructing myocardial perfusion spatiotemporal dynamics. In privacy protection, federated generation framework (FedMed-GAN) improved model generalization by 11.6% while meeting GDPR compliance requirements through distributed training protocols across multiple medical institutions for brain tumor data.

3.1.3 Technical Evolution Trend Summary Current research shows three major integration trends: cross-scale generation (from cellular-level pathology to organ-level CT), multi-disciplinary coupling (biomechanical equations fused with neural networks), and closed-loop evaluation (generation-diagnosis-prognosis joint optimization). Generative models have evolved from simple data replacement tools to digital twin engines supporting lesion intervention simulation and treatment plan optimization. However, achieving routine clinical application still requires solving fundamental problems such as generation stability under few-shot conditions and cross-modal semantic alignment, as well as establishing internationally unified standards for generated data certification. Future research must advance collaboratively in algorithm innovation, clinical validation, and ethical regulation to push medical image analysis toward a new era of computable and explainable medicine.

3.2 Outlook

Medical image data augmentation technology is undergoing a paradigm shift from "data-driven"to "knowledge-guided."Future research needs to break through the following core directions to build an intelligent generation system with clinical credibility:

3.2.1 Few-Shot Adaptive Generation Architecture Current generative models still face mode collapse risks in extremely low sample size scenarios (<50 cases). Transformer-based meta-learning frameworks (such as MedGAN-Transformer) can achieve cross-organ knowledge transfer through parameter sharing mechanisms. Prototype studies show that 2,000 high-quality samples (FID<15) can be generated from 50 pancreatic CT cases. The combination of federated generative learning and zero-shot generation is expected to break rare disease data barriers. For example, prompt-tuning-based diffusion models have achieved 88% pathological feature fidelity in Alzheimer' s disease PET synthesis. Future work needs to develop latent space mapping algorithms constrained by organ anatomical topology to ensure anatomical rationality under few-shot conditions.

3.2.2 Multi-Physics Field Coupled Generation Models Functional imaging (such as fMRI, DWI) generation requires integration of biophysical laws. The latest PDE-Guided GAN (partial differential equation-guided generative adversarial network) embeds hemodynamic equations into the generator, reducing mean relative error to 4.7% in brain perfusion image synthesis. The next step requires constructing cross-scale generation frameworks that simultaneously model molecular diffusion (DTI), electrophysiological signals (EEG), and macroscopic anatomical structures. Neuroscience-driven Neural ODE generators may provide breakthroughs. The "digital heart twin" reported in Science Robotics 2023 has preliminarily validated this approach' s feasibility.

3.2.3 Closed-Loop Evaluation and Causal Inference System Existing evaluation metrics (such as SSIM, FID) have semantic gaps with clinical needs. Evaluation matrices based on radiomics feature mapping (Radiomics Quality Score, RQS$ $18) and causal generative models (CausalGAN) will become key tools. Experiments show that introducing clinical prognosis data as supervision signals can improve diagnostic consistency of lung cancer CT-generated samples by 32%. A generation-diagnosis-prognosis closed-loop validation platform needs to be established, using counterfactual reasoning to locate generation defects, such as quantifying lesion feature credibility through Shapley values.

3.2.4 Lightweight and Privacy Security Collaborative Optimization Clinical deployment requires both generation speed (<100ms/sample) and privacy protection. Neural Architecture Search (NAS)-driven micro diffusion models (such as LiteDiffusion) compress model parameters to 1/40 of the prototype while maintaining PSNR>38dB. The fusion scheme of differential privacy (DP) and homomorphic encryption (DP-HE GAN) has achieved privacy protection strength of =1.5 in federated training of breast ultrasound data. Future research needs to explore new privacy protection mechanisms such as quantum noise injection and deep integration with edge computing frameworks.

3.2.5 Generative Ethics and Regulatory Constraints The WHO 2024 "AI Medical Device Ethics Guidelines" emphasize that generated data must meet "traceability and irreversible anonymization" requirements. Blockchain-enabled distributed generation protocols (such as BlockMed-GAN) achieve data lineage tracking through smart contracts, with synthetic data traceability accuracy reaching 99.3%. There is an urgent need to establish internationally unified standards for generated data certification (such as ISO/TR 23497-2025) and develop adversarial sample detection tools to prevent malicious data injection.

3.3 Conclusion

Medical image generation technology is experiencing a paradigm shift from "data replacement" to "knowledge creation." With deep integration of interdisciplinary technologies such as Physics-Informed Neural Networks (PINN) and Neural Radiance Fields (NeRF), full-organ digital twin construction is expected to be achieved within the next five years. However, we must be vigilant against technology abuse risks and establish strict standards for generated data certification and clinical access regulations. Only by balancing technological innovation with ethical constraints can we ensure healthy development in this field and ultimately advance precision medicine toward the era of computable medicine.

4. References

[1] Agharezaei, Zhila; Firouzi, Reza; Hassanzadeh, Samira; Zarei-Ghanavati, Siamak; Bahaadinbeigy, Kambiz; Golabpour, Amin; Akbarzadeh, Reyhaneh; Agharezaei, Laleh; Bakhshali, Mohamad Amin; Sedaghat, Mohammad Reza; Eslami, Saeid. Computer-aided diagnosis of keratoconus through VAE-augmented images using deep learning. In Scientific Reports, 2023.

[2] Gan, Meng; Wang, Cong. Esophageal optical coherence tomography image synthesis using an adversarially learned variational autoencoder. In Biomedical Optics Express, Vol. 13, Issue 3, pp. 1188-1201, 2022.

[3] Balaji, K.. Image Augmentation based on Variational Autoencoder for Breast Tumor Segmentation. In Academic Radiology, 2023.

[4] Middleton, Jon; Bauer, Marko; Johansen, Jacob; Nielsen, Mads; Sommer, Stefan; Pai, Akshay. Instance-Specific Augmentation of Brain MRIs with Variational Autoencoders. In Springer, 2023.

[5] Kebaili, Aghiles; Lapuyade-Lahorgue, Jérôme; Vera, Pierre; Ruan, Su. Discriminative Hamiltonian Variational Autoencoder for Accurate Tumor Segmentation in Data-Scarce Regimes. In arXiv, 2024.

[6] Park, Hyojoon; Li, Bin; Liu, Yuming; Nelson, Michael S.; Wilson, Helen M.; Sifakis, Eftychios; Eliceiri, Kevin W. Collagen fiber centerline tracking in fibrotic tissue via deep neural networks with variational autoencoder-based synthetic training data generation. In Medical Image Analysis, 2023.

[7] V, Shwetha; Prasad, Keerthana; Mukhopadhyay, Chiranjay; Banerjee, Barnini. Data augmentation for Gram-stain images based on Vector Quantized Variational AutoEncoder. In Neurocomputing, 2024.

[8] Agharezaei, Zhila; Firouzi, Reza; Hassanzadeh, Samira; Zarei-Ghanavati, Siamak; Bahaadinbeigy, Kambiz; Golabpour, Amin; Akbarzadeh, Reyhaneh; Agharezaei, Laleh; Bakhshali, Mohamad Amin; Sedaghat, Mohammad Reza; Eslami, Saeid. Computer-aided diagnosis of keratoconus through VAE-augmented images using deep learning. In Scientific Reports, 2023.

[9] Kmetzsch, Virgilio; Becker, Emmanuelle; Saracino, Dario; Anquetil, Vincent; Rinaldi, Daisy; Camuzat, Agnès; Gareau, Thomas; Ber, Isabelle Le; Colliot, Olivier. A multimodal variational autoencoder for estimating progression scores from imaging and microRNA data in rare neurodegenerative diseases. In ResearchGate, 2022.

[10] Pesteie, Mehran; Abolmaesumi, Purang; Rohling, Robert N.. Adaptive Augmentation of Medical Data Using Independently Conditional Variational Auto-Encoders. In IEEE Transactions on Medical Imaging, 2019.

[11] Gan, Meng; Wang, Cong. Esophageal optical coherence tomography image synthesis using an adversarially learned variational autoencoder. In Biomedical Optics Express, Vol. 13, Issue 3, pp. 1188-1201, 2022.

[12] Zhichao Lin; Rui Guo; Ke Zhang; Maokun Li; Fan Yang; Shenheng Xu. Feature-Based Inversion Using Variational Autoencoder for Electrical Impedance Tomography. In IEEE Xplore, 2022.

[13] Sundgaard, Josefine Vilsbøll; Hannemose, Morten Rieger; Laugesen, Søren; Bray, Peter; Harte, James; Kamide, Yosuke; Tanaka, Chiemi; Paulsen, Rasmus R.; Christensen, Anders Nymark. Multi-modal data generation with a deep metric variational autoencoder. In Digital Bibliography & Library Project, 2022.

[14] Agharezaei, Zhila; Firouzi, Reza; Hassanzadeh, Samira; Zarei-Ghanavati, Siamak; Bahaadinbeigy, Kambiz; Golabpour, Amin; Akbarzadeh, Reyhaneh;

Agharezaei, Laleh; Bakhshali, Mohamad Amin; Sedaghat, Mohammad Reza; Eslami, Saeid. Computer-aided diagnosis of keratoconus through VAE-augmented images using deep learning. In Scientific Reports, 2023.

[15] Middleton, Jon; Bauer, Marko; Johansen, Jacob; Nielsen, Mads; Sommer, Stefan; Pai, Akshay. Instance-Specific Augmentation of Brain MRIs with Variational Autoencoders. In Springer, 2023.

[16] Chadebec, Clément; Thibeau-Sutre, Elina; Burgos, Ninon; Allassonnière, Stéphanie. Data Augmentation in High Dimensional Low Sample Size Setting Using a Geometry-Based Variational Autoencoder. In IEEE Transactions on Pattern Analysis and Machine Intelligence, 2023.

[17] V, Shwetha; Prasad, Keerthana; Mukhopadhyay, Chiranjay; Banerjee, Barnini. Data augmentation for Gram-stain images based on Vector Quantized Variational AutoEncoder. In Neurocomputing, 2024.

[18] Lee, In-Gyu; Oh, Jun-Young; Yu, Hee-Jung; Kim, Jae-Hwan; Eom, Ki-Dong; Jeong, Ji-Hoon. Generative Active Learning with Variational Autoencoder for Radiology Data Generation in Veterinary Medicine. In 2024 IEEE Conference on Artificial Intelligence (CAI), 2024.

[19] Kebaili, Aghiles; Lapuyade-Lahorgue, Jérôme; Vera, Pierre; Ruan, Su. Discriminative Hamiltonian Variational Autoencoder for Accurate Tumor Segmentation in Data-Scarce Regimes. In arXiv, 2024.

[20] Gan, Meng; Wang, Cong. Esophageal optical coherence tomography image synthesis using an adversarially learned variational autoencoder. In Biomedical Optics Express, Vol. 13, Issue 3, pp. 1188-1201, 2022.

[21] Agharezaei, Zhila; Firouzi, Reza; Hassanzadeh, Samira; Zarei-Ghanavati, Siamak; Bahaadinbeigy, Kambiz; Golabpour, Amin; Akbarzadeh, Reyhaneh; Agharezaei, Laleh; Bakhshali, Mohamad Amin; Sedaghat, Mohammad Reza; Eslami, Saeid. Computer-aided diagnosis of keratoconus through VAE-augmented images using deep learning. In Scientific Reports, 2023.

[22] Middleton, Jon; Bauer, Marko; Johansen, Jacob; Nielsen, Mads; Sommer, Stefan; Pai, Akshay. Instance-Specific Augmentation of Brain MRIs with Variational Autoencoders. In Springer, 2023.

[23] V, Shwetha; Prasad, Keerthana; Mukhopadhyay, Chiranjay; Banerjee, Barnini. Data augmentation for Gram-stain images based on Vector Quantized Variational AutoEncoder. In Neurocomputing, 2024.

[24] Frid-Adar, Maayan; Diamant, Idit; Klang, Eyal; Amitai, Michal; Goldberger, Jacob; Greenspan, Hayit. GAN-based synthetic medical image augmentation for increased CNN performance in liver lesion classification. In Neurocomputing, 2018.

[25] Ge, Chenjie; Gu, Irene Yu-Hua; Store Jakola, Asgeir; Yang, Jie. Cross-Modality Augmentation of Brain Mr Images Using a Novel Pairwise Generative

Adversarial Network for Enhanced Glioma Classification. In 2019 IEEE International Conference on Image Processing, 2019.

[26] Diaz-Pinto, Andres; Colomer, Adrián; Naranjo, Valery; Morales, Sandra; Xu, Yanwu; Frangi, Alejandro F. Retinal Image Synthesis and Semi-Supervised Learning for Glaucoma Assessment. In IEEE Transactions on Medical Imaging, 2019.

[27] Rashid, Haroon; Tanveer, M. Asjid; Aqeel Khan, Hassan. Skin Lesion Classification Using GAN based Data Augmentation. In 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2019.

[28] Xue, Yuan; Zhou, Qianying; Ye, Jiarong; Long, L. Rodney; Antani, Sameer; Cornwell, Carl; Xue, Zhiyun; Huang, Xiaolei. Synthetic Augmentation and Feature-Based Filtering for Improved Cervical Histopathology Image Classification. In MICCAI, 2019.

[29] Cheng, Kaiyang; Iriondo, Claudia; Calivá, Francesco; Krogue, Justin; Majumdar, Sharmila; Pedoia, Valentina. Adversarial Policy Gradient for Deep Learning Image Augmentation. In MICCAI, 2019.

[30] Nishio, Mizuho; Muramatsu, Chisako; Noguchi, Shunjiro; Nakai, Hirotsugu; Fujimoto, Koji; Sakamoto, Ryo; Fujita, Hiroshi. Attribute-guided image generation of three-dimensional computed tomography images of lung nodules using a generative adversarial network. In Computers in Biology and Medicine, 2020.

[31] Qin, Zhiwei; Liu, Zhao; Zhu, Ping; Xue, Yongbo. A GAN-based image synthesis method for skin lesion classification. In Computer Methods and Programs in Biomedicine, 2020.

[32] Shi, Guohua; Wang, Jiawen; Qiang, Yan; Yang, Xiaotang; Zhao, Juanjuan; Hao, Rui; Yang, Wenkai; Du, Qianqian; Kazihise, Ntikurako Guy-Fernand. Knowledge-guided synthetic medical image adversarial augmentation for ultrasonography thyroid nodule classification. In Computer Methods and Programs in Biomedicine, 2020.

[33] Luis A. de Souza, Jr., Leandro A. Passos, Robert Mendel, Alanna Ebigbo, Andreas Probst, Helmut Messmann, Christoph Palm, João P. PapaAuthors Info & Claims. Assisting Barrett’ s esophagus identification using endoscopic data augmentation based on Generative Adversarial Networks. In ACM Digital Library, 2020.

[34] Pang, Ting; Wong, Jeannie Hsiu Ding; Ng, Wei Lin; Chan, Chee Seng. Semi-supervised GAN-based Radiomics Model for Data Augmentation in Breast Ultrasound Mass Classification. In Computer Methods and Programs in Biomedicine, 2021.

[35] Xue, Yuan; Ye, Jiarong; Zhou, Qianying; Long, L. Rodney; Antani, Sameer; Xue, Zhiyun; Cornwell, Carl; Zaino, Richard; Cheng, Keith C.; Huang, Xiaolei.

Selective synthetic augmentation with HistoGAN for improved histopathology image classification. In Medical Image Analysis, 2021.

[36] Jahanyar, Bahareh; Tabatabaee, Hamid; Rowhanimanesh, Alireza. MS-ACGAN: A modified auxiliary classifier generative adversarial network for schizophrenia' s samples augmentation based on microarray gene expression data. In Computers in Biology and Medicine, 2023.

[37] Chen, Yunfeng; Lin, Yalan; Xu, Xiaodie; Ding, Jinzhen; Li, Chuzhao; Zeng, Yiming; Xie, Weifang; Huang, Jianlong. Multi-domain medical image translation generation for lung image classification based on generative adversarial networks. In Computer Methods and Programs in Biomedicine, 2023.

[38] Kuo, Nicholas I-Hsien; Garcia, Federico; Sönnerborg, Anders; Böhm, Michael; Kaiser, Rolf; Zazzi, Maurizio; Polizzotto, Mark; Jorm, Louisa; Barbieri, Sebastiano. Generating synthetic clinical data that capture class imbalanced distributions with generative adversarial networks: Example using antiretroviral therapy for HIV. In Journal of Biomedical Informatics, 2023.

[39] Golhar, Mayank V.; Bobrow, Taylor L.; Ngamruengphong, Saowanee; Durr, Nicholas J. GAN Inversion for Data Augmentation to Improve Colonoscopy Lesion Classification. In IEEE Journal of Biomedical and Health Informatics, 2024.

[40] Joseph, Annie Julie; Dwivedi, Priyansh; Joseph, Jiffy; Francis, Seenia; P. n., Pournami; P.b., Jayaraj; Shamsu, Ashna V.; Sankaran, Praveen. Prior-guided generative adversarial network for mammogram synthesis. In Biomedical Signal Processing and Control, 2024.

[41] Kuntalp, Mehmet; Düzyel, Okan. A new method for GAN-based data augmentation for classes with distinct clusters. In Expert Systems with Applications, 2024.

[42] Ding, Hongwei; Huang, Nana; Wu, Yaoxin; Cui, Xiaohui. LEGAN: Addressing Intraclass Imbalance in GAN-Based Medical Image Augmentation for Improved Imbalanced Data Classification. In IEEE Transactions on Instrumentation and Measurement, 2024.

[43] Zhao, He; Li, Huiqi; Maurer-Stroh, Sebastian; Cheng, Li. Synthesizing retinal and neuronal images with generative adversarial nets. In Medical Image Analysis, 2018.

[44] Jin, Dakai; Xu, Ziyue; Tang, Youbao; Harrison, Adam P.; Mollura, Daniel J. CT-Realistic Lung Nodule Simulation from 3D Conditional Generative Adversarial Networks for Robust Lung Segmentation. In MICCAI, 2018.

[45] Zhang, Tianyang; Fu, Huazhu; Zhao, Yitian; Cheng, Jun; Guo, Mengjie; Gu, Zaiwang; Yang, Bing; Xiao, Yuting; Gao, Shenghua; Liu, Jiang. SkrGAN: Sketching-Rendering Unconditional Generative Adversarial Networks for Medical Image Synthesis. In MICCAI, 2019.

[46] Cai, Jinzheng; Zhang, Zizhao; Cui, Lei; Zheng, Yefeng; Yang, Lin. Towards cross-modal organ translation and segmentation: A cycle- and shape-consistent generative adversarial network. In Medical Image Analysis, 2019.

[47] Shi, Haoqi; Lu, Junguo; Zhou, Qianjun. A Novel Data Augmentation Method Using Style-Based GAN for Robust Pulmonary Nodule Segmentation. In 2020 Chinese Control And Decision Conference, 2020.

[48] Chen, Chen; Qin, Chen; Qiu, Huaqi; Ouyang, Cheng; Wang, Shuo; Chen, Liang; Tarroni, Giacomo; Bai, Wenjia; Rueckert, Daniel. Realistic Adversarial Data Augmentation for MR Image Segmentation. In MICCAI, 2020.

[49] Amirrajab, Sina; Abbasi-Sureshjani, Samaneh; Al Khalil, Yasmina; Lorenz, Cristian; Weese, Jürgen; Pluim, Josien; Breeuwer, Marcel. XCAT-GAN for Synthesizing 3D Consistent Labeled Cardiac MR Images on Anatomically Variable XCAT Phantoms. In MICCAI, 2020.

[50] Oliveira, Dario Augusto Borges. Controllable Skin Lesion Synthesis Using Texture Patches, Bézier Curves and Conditional GANs. In 2020 IEEE 17th International Symposium on Biomedical Imaging, 2020.

[51] Dimitrakopoulos, P.; Sfikas, G.; Nikou, C. ISING-GAN: Annotated Data Augmentation with a Spatially Constrained Generative Adversarial Network. In 2020 IEEE 17th International Symposium on Biomedical Imaging, 2020.

[52] Marzullo, Aldo; Moccia, Sara; Catellani, Michele; Calimeri, Francesco; Momi, Elena De. Towards realistic laparoscopic image generation using image-domain translation. In Computer Methods and Programs in Biomedicine, 2021.

[53] Gilbert, Andrew; Marciniak, Maciej; Rodero, Cristobal; Lamata, Pablo; Samset, Eigil; Mcleod, Kristin. Generating Synthetic Labeled Data From Existing Anatomical Models: An Example With Echocardiography Segmentation. In IEEE Transactions on Medical Imaging, 2021.

[54] Liang, Junzhao; Chen, Junying. Data Augmentation of Thyroid Ultrasound Images Using Generative Adversarial Network. In 2021 IEEE International Ultrasonics Symposium, 2021.

[55] Chaitanya, Krishna; Karani, Neerav; Baumgartner, Christian F.; Erdil, Ertunc; Becker, Anton; Donati, Olivio; Konukoglu, Ender. Semi-supervised task-driven data augmentation for medical image segmentation. In Medical Image Analysis, 2021.

[56] Chen, Xu; Lian, Chunfeng; Wang, Li; Deng, Hannah; Kuang, Tianshu; Fung, Steve H.; Gateno, Jaime; Shen, Dinggang; Xia, James J.; Yap, Pew-Thian. Diverse data augmentation for learning image segmentation with cross-modality annotations. In Medical Image Analysis, 2021.

[57] Kim, Sunho; Kim, Byungjai; Park, HyunWook. Synthesis of Brain Tumor MR Images for Learning Data Augmentation. In Medical Physics, 2021.

[58] Zhang, Ruixuan; Lu, Wenhuan; Wei, Xi; Zhu, Jialin; Jiang, Han; Liu, Zhiqiang; Gao, Jie; Li, Xuewei; Yu, Jian; Yu, Mei; Yu, Ruiguo. A Progressive Generative Adversarial Method for Structurally Inadequate Medical Image Data Augmentation. In IEEE Journal of Biomedical and Health Informatics, 2022.

[59] Li, Wenyuan; Li, Jiayun; Polson, Jennifer; Wang, Zichen; Speier, William; Arnold, Corey. High resolution histopathology image generation and segmentation through adversarial training. In Medical Image Analysis, 2022.

[60] Zhang, Yipeng; Wang, Quan; Hu, Bingliang. MinimalGAN: diverse medical image synthesis for data augmentation using minimal training data. In Applied Intelligence, 2022.

[61] Hammami, Maryam; Friboulet, Denis; Kechichian, Razmig. Cycle GAN-Based Data Augmentation For Multi-Organ Detection In CT Images Via Yolo. In 2020 IEEE International Conference on Image Processing, 2020.

[62] Sun; Wang, Jiexiang; Huang, Yue; Ding, Xinghao; Greenspan, Hayit; Paisley, John. An Adversarial Learning Approach to Medical Image Synthesis for Lesion Detection. In IEEE Journal of Biomedical and Health Informatics, 2020.

[63] Shen, Tianyu; Hao, Kunkun; Gou, Chao; Wang, Fei-Yue. Mass Image Synthesis in Mammogram with Contextual Information Based on GANs. In Computer Methods and Programs in Biomedicine, 2021.

[64] Niu, Yuhao; Gu, Lin; Zhao, Yitian; Lu, Feng. Explainable Diabetic Retinopathy Detection and Retinal Image Generation. In IEEE Journal of Biomedical and Health Informatics, 2022.

[65] Ding, Cheng; Xiao, Ran; Do, Duc H.; Lee, David Scott; Lee, Randall J.; Kalantarian, Shadi; Hu, Xiao. Log-Spectral Matching GAN: PPG-Based Atrial Fibrillation Detection can be Enhanced by GAN-Based Data Augmentation With Integration of Spectral Loss. In IEEE Journal of Biomedical and Health Informatics, 2023.

[66] P, Porkodi S.; V, Sarada. Data Augmentation using Generative Adversarial Network with Enhanced Deep Convolutional Neural Network for Pneumonia Chest X-ray Images. In IEEE Xplore, 2024.

[67] Xu, Chaobin; Li, Wei; Cui, Xiaohui; Wang, Zhenyu; Zheng, Fengling; Zhang, Xiaowu; Chen, Bin. Scarcity-GAN: Scarce data augmentation for defect detection via generative adversarial nets. In Neurocomputing, 2024.

[68] Han, Changhee; Hayashi, Hideaki; Rundo, Leonardo; Araki, Ryosuke; Shimoda, Wataru; Muramatsu, Shinichi; Furukawa, Yujiro; Mauri, Giancarlo; Nakayama, Hideki. GAN-based synthetic brain MR image generation. In 2018 IEEE 15th International Symposium on Biomedical Imaging, 2018.

[69] Kwon, Gihyun; Han, Chihye; Kim, Dae-shik. Generation of 3D Brain MRI Using Auto-Encoding Generative Adversarial Networks. In 2019 41st Annual

International Conference of the IEEE Engineering in Medicine and Biology Society, 2019.

[70] Xing, Yunyan; Ge, Zongyuan; Zeng, Rui; Mahapatra, Dwarikanath; Seah, Jarrel; Law, Meng; Drummond, Tom. Adversarial Pulmonary Pathology Translation for Pairwise Chest X-Ray Data Augmentation. In MICCAI, 2019.

[71] Guo, Pengfei; Wang, Puyang; Zhou, Jinyuan; Patel, Vishal M.; Jiang, Shanshan. Lesion Mask-Based Simultaneous Synthesis of Anatomic and Molecular MR Images Using a GAN. In MICCAI, 2020.

[72] Chen, Ying; Lin, Hongping; Zhang, Wei; Chen, Wang; Zhou, Zonglai; Heidari, Ali Asghar; Chen, Huiling; Xu, Guohui. ICycle-GAN: Improved cycle generative adversarial networks for liver medical image generation. In Biomedical Signal Processing and Control, 2024.

[73] Wu, Hejun; Gao, Rong; Sheng, Yeong Poh; Chen, Bo; Li, Shuo. SDAE-GAN: Enable high-dimensional pathological images in liver cancer survival prediction with a policy gradient based data augmentation method. In Medical Image Analysis, 2020.

[74] Wang, Qiuli; Zhang, Xiaohong; Zhang, Wei; Gao, Mingchen; Huang, Sheng; Wang, Jian; Zhang, Jiuquan; Yang, Dan; Liu, Chen. Realistic Lung Nodule Synthesis With Multi-Target Co-Guided Adversarial Mechanism. In IEEE Transactions on Medical Imaging, 2021.

[75] He, Fan; Chen, Sizhe; Li, Shuaiyi; Zhou, Lu; Zhang, Haiqin; Peng, Haixia; Huang, Xiaolin. Colonoscopic Image Synthesis For Polyp Detector Enhancement Via Gan And Adversarial Training. In 2021 IEEE 18th International Symposium on Biomedical Imaging, 2021.

[76] Pérez, Jaime; Arroba, Patricia; Moya, José M.. Data augmentation through multivariate scenario forecasting in Data Centers using Generative Adversarial Networks. In Applied Intelligence, 2022.

[77] Mulé, Sébastien; Lawrance, Littisha; Belkouchi, Younes; Vilgrain, Valérie; Lewin, Maité; Trillaud, Hervé; Hoeffel, Christine; Laurent, Valérie; Ammari, Samy; Morand, Eric; Faucoz, Orphée; Tenenhaus, Arthur; Cotten, Anne; Meder, Jean-François; Talbot, Hugues; Luciani, Alain; Lassau, Nathalie. Generative adversarial networks (GAN)-based data augmentation of rare liver cancers: The SFR 2021 Artificial Intelligence Data Challenge. In Diagnostic and Interventional Imaging, 2023.

[78] Yu, Yu-Feng; Zhong, Guojin; Zhou, Yi; Chen, Long. FS-GAN: Fuzzy Self-guided structure retention generative adversarial network for medical image enhancement. In Information Sciences, 2023.

[79] Müller-Franzes, Gustav; Niehues, Jan Moritz; Khader, Firas; Arasteh, Soroosh Tayebi; Haarburger, Christoph; Kuhl, Christiane; Wang, Tianci; Han, Tianyu; Nolte, Teresa; Nebelung, Sven; Kather, Jakob Nikolas; Truhn, Daniel. A multimodal comparison of latent denoising diffusion probabilistic models and

generative adversarial networks for medical image synthesis. In Scientific Reports, 2023.

[80] Zhang, Ruixuan; Lu, Wenhuan; Gao, Jie; Tian, Yuan; Wei, Xi; Wang, Chenhan; Li, Xuewei; Yu, Mei. RFI-GAN: A reference-guided fuzzy integral network for ultrasound image augmentation. In Information Sciences, 2023.

[81] Wu, Yirui; Yue, Yisheng; Tan, Xiao; Wang, Wei; Lu, Tong. End-To-End Chromosome Karyotyping with Data Augmentation Using GAN. In 2018 25th IEEE International Conference on Image Processing, 2018.

[82] Zhao, He; Li, Huiqi; Maurer-Stroh, Sebastian; Cheng, Li. Synthesizing retinal and neuronal images with generative adversarial nets. In Medical Image Analysis, 2018.

[83] Han, Changhee; Hayashi, Hideaki; Rundo, Leonardo; Araki, Ryosuke; Shimoda, Wataru; Muramatsu, Shinichi; Furukawa, Yujiro; Mauri, Giancarlo; Nakayama, Hideki. GAN-based synthetic brain MR image generation. In 2018 IEEE 15th International Symposium on Biomedical Imaging, 2018.

[84] Frid-Adar, Maayan; Klang, Eyal; Amitai, Michal; Goldberger, Jacob; Greenspan, Hayit. Synthetic data augmentation using GAN for improved liver lesion classification. In 2018 IEEE 15th International Symposium on Biomedical Imaging, 2018.

[85] Costa, Pedro; Galdran, Adrian; Meyer, Maria Ines; Niemeijer, Meindert; Abràmoff, Michael; Mendonça, Ana Maria; Campilho, Aurélio. End-to-End Adversarial Retinal Image Synthesis. In IEEE Transactions on Medical Imaging, 2018.

[86] Uzunova, Hristina; Ehrhardt, Jan; Handels, Heinz. In Generation of Annotated Brain Tumor MRIs with Tumor-induced Tissue Deformations for Training and Assessment of Neural Networks. In MICCAI, 2020.

[87] Gao, Yunhe; Tang, Zhiqiang; Zhou, Mu; Metaxas, Dimitris. Enabling Data Diversity: Efficient Automatic Augmentation via Regularized Adversarial Training. In arXiv, 2021.

[88] Havaei, Mohammad; Mao, Ximeng; Wang, Yiping; Lao, Qicheng. Conditional generation of medical images via disentangled adversarial inference. In Medical Image Analysis, 2021.

[89] Zhou, Yi; Wang, Boyang; He, Xiaodong; Cui, Shanshan; Shao, Ling. DR-GAN: Conditional Generative Adversarial Network for Fine-Grained Lesion Synthesis on Diabetic Retinopathy Images. In IEEE Journal of Biomedical and Health Informatics, 2022.

[90] Kwarciak, Kamil; Wodziński, Marek. Deep Generative Networks for Heterogeneous Augmentation of Cranial Defects. In ICCV, 2023.

[91] Guo, Kehua; Chen, Jie; Qiu, Tian; Guo, Shaojun; Luo, Tao; Chen, Tianyu; Ren, Sheng. MedGAN: An adaptive GAN approach for medical image genera-

tion. In Computers in Biology and Medicine, 2023.

[92] Xu, Zhenghua; Tang, Jiaqi; Qi, Chang; Yao, Dan; Liu, Caihua; Zhan, Yuefu; Lukasiewicz, Thomas. Cross-domain attention-guided generative data augmentation for medical image analysis with limited data. In Computers in Biology and Medicine, 2024.

[93] Lan, Xinhao Lan. Traditional Augmentation Versus Deep Generative Diffusion Augmentation for Addressing Class Imbalance in Chest X-ray Classification. In IEEE Xplore, 2023.

[94] Khader, Firas; Müller-Franzes, Gustav; Tayebi Arasteh, Soroosh; Han, Tianyu; Haarburger, Christoph; Schulze-Hagen, Maximilian; Schad, Philipp; Engelhardt, Sandy; Baeßler, Bettina; Foersch, Sebastian; Stegmaier, Johannes; Kuhl, Christiane; Nebelung, Sven; Kather, Jakob Nikolas; Truhn, Daniel. Denoising diffusion probabilistic models for 3D medical image generation. In Scientific Reports, 2023.

[95] Garcea, Fabio; Serra, Alessio; Lamberti, Fabrizio; Morra, Lia. Data augmentation for medical imaging: A systematic literature review. In Computers in Biology and Medicine, 2023.

[96] Shao, Zhuchen; Dai, Liuxi; Wang, Yifeng; Wang, Haoqian; Zhang, Yongbing. AugDiff: Diffusion based Feature Augmentation for Multiple Instance Learning in Whole Slide Image. In IEEE Xplore, 2023.

[97] Zhong, Yuan; Cui, Suhan; Wang, Jiaqi; Wang, Xiaochen; Yin, Ziyi; Wang, Yaqing; Xiao, Houping; Huai, Mengdi; Wang, Ting; Ma, Fenglong. MedDiffusion: Boosting Health Risk Prediction via Diffusion-based Data Augmentation. In Proceedings of the 2024 SIAM International Conference on Data Mining (SDM), 2024.

[98] Wang, Janet; Chung, Yunsung; Ding, Zhengming; Hamm, Jihun. From Majority to Minority: A Diffusion-based Augmentation for Underrepresented Groups in Skin Lesion Analysis. In arXiv, 2024.

[99] Pinaya, Walter H. L.; Tudosiu, Petru-Daniel; Dafflon, Jessica; Da Costa, Pedro F.; Fernandez, Virginia; Nachev, Parashkev; Ourselin, Sebastien; Cardoso, M. Jorge. Brain Imaging Generation with Latent Diffusion Models. In arXiv, 2022.

[100] Zhang, Xiaohui; Gangopadhyay, Ahana; Chang, Hsi-Ming; Soni, Ravi. Diffusion Model-Based Data Augmentation for Lung Ultrasound Classification with Limited Data. In Proceedings of Machine Learning Research, 2023.

[101] Aja-Fernández, Santiago; Martín-Martín, Carmen; Planchuelo-Gómez, Álvaro; Faiyaz, Abrar; Uddin, Md Nasir; Schifitto, Giovanni; Tiwari, Abhishek; Shigwan, Saurabh J.; Kumar Singh, Rajeev; Zheng, Tianshu; Cao, Zuozhen; Wu, Dan; Blumberg, Stefano B.; Sen, Snigdha; Goodwin-Allcock, Tobias; Slator, Paddy J.; Yigit Avci, Mehmet; Li, Zihan; Bilgic, Berkin; Tian, Qiyuan; Wang, Xinyi; Tang, Zihao; Cabezas, Mariano; Rauland, Amelie; Merhof, Dorit;

Manzano Maria, Renata; Campos, Vinícius Paraníba; Santini, Tales; da Costa Vieira, Marcelo Andrade; HashemizadehKolowri, SeyyedKazem; DiBella, Edward; Peng, Chenxu; Shen, Zhimin; Chen, Zan; Ullah, Irfan; Mani, Merry; Abdolmotalleby, Hesam; Eckstrom, Samuel; Baete, Steven H.; Filipiak, Patryk; Dong, Tanxin; Fan, Qiuyun; de Luis-García, Rodrigo; Tristán-Vega, Antonio; Pieciak, Tomasz. Validation of deep learning techniques for quality augmentation in diffusion MRI for clinical studies. In NeuroImage: Clinical, 2023.

[102] Lan, Xinhao Lan. Traditional Augmentation Versus Deep Generative Diffusion Augmentation for Addressing Class Imbalance in Chest X-ray Classification. In IEEE Xplore, 2023.

[103] Zhong, Yuan; Cui, Suhan; Wang, Jiaqi; Wang, Xiaochen; Yin, Ziyi; Wang, Yaqing; Xiao, Houping; Huai, Mengdi; Wang, Ting; Ma, Fenglong. MedDiffusion: Boosting Health Risk Prediction via Diffusion-based Data Augmentation. In Proceedings of the 2024 SIAM International Conference on Data Mining (SDM), 2024.

[104] Medghalchi, Yasamin; Zakariaei, Niloufar; Rahmim, Arman; Hacihaliloglu, Ilker. MEDDAP: Medical Dataset Enhancement via Diversified Augmentation Pipeline. In Digital Bibliography & Library Project, 2024.

[105] Oh, Hyun-Jic; Jeong, Won-Ki. Controllable and Efficient Multi-Class Pathology Nuclei Data Augmentation using Text-Conditioned Diffusion Models. 2024.

[106] Ye, Jiarong; Ni, Haomiao; Jin, Peng; Huang, Sharon X.; Xue, Yuan. Synthetic Augmentation with Large-Scale Unconditional Pre-training. In Springer, 2023.

[107] Yu, Xinyi; Li, Guanbin; Lou, Wei; Liu, Siqi; Wan, Xiang; Chen, Yan; Li, Haofeng. Diffusion-Based Data Augmentation for Nuclei Image Segmentation. In arXiv, 2023.

[108] Chen, Zirui. Diffusion Models-based Data Augmentation for the Cell Cycle Phase Classification. In Journal of Physics: Conference Series, 2023.

[109] Garcea, Fabio; Serra, Alessio; Lamberti, Fabrizio; Morra, Lia. Data augmentation for medical imaging: A systematic literature review. In Computers in Biology and Medicine, 2023.

[110] Shu, Kai; Zhao, Yuchang; Wu, Le; Liu, Aiping; Qian, Ruobing; Chen, Xun. Data Augmentation for Seizure Prediction with Generative Diffusion Model. In arXiv, 2023.

[111] Lan, Xinhao Lan. Traditional Augmentation Versus Deep Generative Diffusion Augmentation for Addressing Class Imbalance in Chest X-ray Classification. In IEEE Xplore, 2023.

[112] Bouanane, Khadra; Berdjouh, Chemousse; Lakas, Badia Ouissam. DIFFUSION MODELS FOR DATA AUGMENTATION OF MEDICAL IMAGES.

In arXiv, 2023.

[113] Zhong, Yuan; Cui, Suhan; Wang, Jiaqi; Wang, Xiaochen; Yin, Ziyi; Wang, Yaqing; Xiao, Houping; Huai, Mengdi; Wang, Ting; Ma, Fenglong. MedDiffusion: Boosting Health Risk Prediction via Diffusion-based Data Augmentation. In Proceedings of the 2024 SIAM International Conference on Data Mining (SDM), 2024.

[114] Guan, Xianchao; Wang, Yifeng; Lin, Yiyang; Zhang, Yongbing. Data Augmentation Based on DiscrimDiff for Histopathology Image Classification. In MICCAI, 2024.

[115] Akrout, Mohamed; Gyepesi, Bálint; Holló, Péter; Poór, Adrienn; Kincső, Blága; Solis, Stephen; Cirone, Katrina; Kawahara, Jeremy; Slade, Dekker; Abid, Latif; Kovács, Máté; Fazekas, István. Diffusion-Based Data Augmentation for Skin Disease Classification: Impact Across Original Medical Datasets to Fully Synthetic Images. In MICCAI, 2024.

[116] Ngasa, Emmanuel Edward; Jang, Mi-Ae; Tarimo, Servas Adolph; Woo, Jiyoung; Shin, Hee Bong. Diffusion-based Wasserstein generative adversarial network for blood cell image augmentation. In Engineering Applications of Artificial Intelligence, 2024.

[117] Wang, Janet; Chung, Yunsung; Ding, Zhengming; Hamm, Jihun. From Majority to Minority: A Diffusion-based Augmentation for Underrepresented Groups in Skin Lesion Analysis. In arXiv, 2024.

[118] Jimenez-Perez, Guillermo; Osorio, Pedro; Cersovsky, Josef; Montalt-Tordera, Javier; Hooge, Jens; Vogler, Steffen; Mohammadi, Sadegh. DiNO-Diffusion. Scaling Medical Diffusion via Self-Supervised Pre-Training. In arXiv, 2024.

Note: Figure translations are in progress. See original paper for figures.