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Generative Adversarial Networks in Brain Imaging: A Decade-Long Review of Progress and Future Directions

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ABSTRACT

Due to the increasing demand for effective and objective analysis to address complex challenges such as brain medical image reconstruction, segmentation, and classification, medical image analysis for brain tumor research has gained significant attention. The ability of Generative Adversarial Networks (GANs) to increase the probability density over data distributions by estimating density ratios, along with their capacity to uncover high-dimensional latent distributions, has led to substantial performance improvements in visual feature extraction. Furthermore, the adversarial loss incurred by the discriminator offers a subtle method of incorporating unlabeled samples into training, thereby improving accuracy at higher orders. These characteristics of GANs have proven valuable in various applications, including enhancing medical images and translating images across different modalities. Additionally, the ability of GANs to generate images with remarkable realism offers hope that, through these generative models, the ongoing challenge of limited labelled data in the medical field may be overcome. The aim of this review is to provide a comprehensive overview, starting with a concise summary of the range of available GAN architectures and datasets. This study then highlights the research conducted in processing and interpreting GAN-based brain images. Finally, the limitations of GAN-based methods for brain image analysis are discussed, identifying unresolved research issues and suggesting avenues for further exploration in this emerging field.

الشبكات التوليدية التنافسية في تحليل تصوير الدماغ: استعراض شامل لعقد من التقدم والتوجهات المستقبلية

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الكلمات المفتاحية:
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الرؤية الحاسوبية.

الملخص

وتقسيمها وتصنيفها، فقد اكتسب تحليل الصور الطبية لأبحاث أورام الدماغ اهتمامًا كبيرًا باستمرار. إن قدرة الشبكات التوليدية التنافسية (GANs) على زيادة كثافة الاحتمال على توزيع إنتاج البيانات باستخدام تقدير نسبة الكثافة وقدرتها على الكشف عن التوزيع الكامن عالي الأبعاد للبيانات، مما يؤدي إلى تحسينات كبيرة في الأداء في استخراج السمات المرئية. بالإضافة إلى ذلك، فإن الخسارة السلبية التي يتكبدها المميز توفر وسيلة خفية لدمج العينات غير المميزة في التحضير وفرض دقة أعلى مرتبة. وقد أثبتت خصائص الشبكات التوليدية التنافسية أنها قيمة في مجموعة متنوعة من الظروف، بما في ذلك تحسين الصور الطبية وترجمة الصور من نمط إلى آخر. وعلاوة على ذلك، فإن قدرة الشبكات التوليدية التنافسية على بناء الصور بواقعية توفر أيضًا الأمل في أنه باستخدام هذه النماذج التوليدية، يمكن التغلب على الافتقار المستمر للبيانات المصنفة في المجال الطبي. الهدف من هذه المقالة الاستعراضية هو تقديم نظرة عامة شاملة من خلال تقديم ملخص موجز للمجموعة المتعددة من بنيات GAN المتاحة أولاً. ولتسليط الضوء على الأبحاث التي تم إجراؤها، تقدم هذه الدراسة ملخصًا للمساهمات العلمية في مجال معالجة وتفسير صور الدماغ القائمة على GAN. وأخيرًا، تمت مناقشة قصور الطرق القائمة على GAN لتحليل صور الدماغ من أجل تحديد قضايا البحث غير المحلولة والاقتراحات لمزيد من الدراسة في هذا المجال الناشئ.

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1. Introduction

Medical imaging plays a crucial role in enhancing public health for all demographic groups, utilizing a variety of imaging modalities and procedures to capture images of the human body, including the brain, heart, and soft tissues, for diagnostic and therapeutic purposes. Numerous imaging techniques, such as computed tomography (CT), positron emission tomography (PET), magnetic resonance imaging (MRI), X-rays, and ultrasound, each use different image capturing methods, which significantly influence patient diagnosis and treatment. However, the fundamental principles behind these modalities differ, especially in terms of image capture, data processing, and complexity [1]. The complexity and dimensionality of CT, PET, and MRI images are tailored to incorporate modality-specific information, which improves the accuracy of image diagnosis. Brain tumors arise when abnormal cell growth occurs inside or around the brain, disturbing normal brain function and impacting a patient's health [2]. Recently, researchers, radiologists, and clinicians have focused on brain imaging analysis, diagnosis, and therapy using approved medical imaging techniques [3]. Brain tumors, being fatal, account for a significant proportion of mortality in low-income countries, making brain image processing vital. The latest advancements in soft tissue and non-invasive imaging techniques have resulted in vast amounts of high-resolution data. Radiologists use these high-resolution soft tissue images to diagnose various diseases, including viral infections, traumatic brain injury, aneurysms, and brain cancer. Additionally, soft tissue scans provide abundant data that help differentiate between diseased and healthy tissue. Unfortunately, no single imaging method can serve as a universal diagnostic tool, requiring a combination of imaging techniques to detect specific brain disorders [4]. Each type of soft tissue exhibits a distinct signature, which is formed by integrating image sets from different modalities [5], leading to a large number of features that drive deep learning applications.

In many of these supervised applications, convolutional neural networks (CNNs) are trained to provide accurate predictions based on input images. CNNs are highly effective in distinguishing between images or image voxels belonging to different classes, making them invaluable for segmentation, classification, and predicting patient survival times for brain cancer.

For a long time, medical image analysis focused primarily on supervised learning. However, this paradigm shifted with the advent of Generative Adversarial Networks (GANs) [6], which introduced a new wave of interest in generative modeling and understanding data distributions. The central idea behind generative models is to learn the underlying structure of data and the processes that generate it. This enables researchers to better understand the data and generate new data by sampling from the model. GANs have been particularly groundbreaking due to their ability to combine supervised learning with image generation. Their success largely stems from their capacity to fine-tune the probability density of data generation, using techniques such as density ratio estimation [7]. Furthermore, GANs excel at uncovering hidden, complex patterns in data, leading to significant advances in feature extraction and analysis.

This study aims to provide a comprehensive and up-to-date overview of GAN-based techniques used in brain image processing, focusing on tasks such as image synthesis, segmentation, and reconstruction. We reviewed various databases, including PubMed, arXiv, and proceedings from esteemed conferences like the International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI), SPIE Medical Imaging, the IEEE International Symposium on Biomedical Imaging (ISBI), and the International Conference on Medical Imaging with Deep Learning (MIDL), to ensure a thorough review of GANs in medical imaging. Additionally, we examined key references and citations to uncover further relevant research. Given that GANs are a relatively new field and many studies are still in the publication pipeline, we also included preprints to capture the latest advancements and trends in this rapidly evolving area.

Although several previous reviews have explored GANs in medical image analysis, most of them focus on general surveys introducing the progress of GANs, their architectural variants, and various medical imaging applications [8][9][10][11][12], or delve into specific applications such as image synthesis, classification, and segmentation [13][14][15][16][17]. Additionally, some surveys only cover one type of imaging technology [18][19].

To the best of our knowledge, this paper is the first comprehensive survey on the application of GAN-based methods in brain image analysis. Motivated by the rapid development of GANs in this field, this review covers the latest advancements across all areas of brain imaging, including synthesis, segmentation, reconstruction, detection, denoising, registration, and classification. By including a broad array of recent studies, we present a wide variety of GAN-based methods used for brain tumor analysis, highlighting key contributions, methodologies, techniques, frameworks, architectures, and evaluations in brain tumor analysis.

The structure of the remainder of the paper is as follows. Section 2 provides a brief overview of GAN basics and structural variants, followed by a discussion on available brain imaging datasets. Section 3 presents a comprehensive analysis of medical image processing tasks using GANs, organized around core tasks such as detection, registration, classification, segmentation, reconstruction, image synthesis, and more. Finally, Section 4 concludes the review, discussing potential applications and suggesting future research directions.

2. Background

In order to provide an inclusive perspective into the use of brain medical image analysis and applications, this background section will provide the basic GANs architecture concepts behind these applications as well as accessible datasets for medical brain images.

2.1 Variance of GANs architectures

Generally, there are three categories of generative models: Generative Adversarial Networks (GANs) [6], Variational Autoencoder (VAE) [20], and AutoRegressive Networks [21]. With no clear aim function and difficult training, GANs may create remarkably realistic images. However, their extremely limited diversity may cause mode collapse when the generator is unable to learn. The other most popular deep generative models, Variational Autoencoders (VAEs), have an objective function to optimize, which may result in fuzzier samples because of noise and insufficient sample reconstruction [22].

In 2014, Ian Goodfellow and colleagues published an article [6] titled "Generative Adversarial Networks," which was the first demonstration of the generative adversarial network architecture technique. In the study, a generator model with fully linked layers (MLPs) and ReLU activations is described. This model uses a latent space as input points and generates an image. In addition, a discriminator model that uses fully connected layers (MLPs) with maxout activations to distinguish between actual and fake images is used. Using typical image datasets like MNIST and CIFAR-10, this model was implemented.

In the literature, there are many forms of GANs architecture variants are introduced. Architecture variant of GANs have recently seen substantial advances in numerous applications such as image-to-image translation, image resolution enhancements, image reconstruction. Many medical imaging researchers have therefore started using GANs in many fields, such as image resolution enhancement, identification of anomalies and estimate of CT images from the corresponding MR images. To acquire images with the desired characteristics, fully convolutional layers and conditional image constraints were later used instead of the GAN, which was first deployed with fully connected layers and no data generation limits. They typically use conditional GANs to generate desired images since GANs allow for the application of conditioning on class labels and images, making learning robust latent spaces hard.

To meet the desired performance, several different versions of the GAN model were suggested. The main purpose of this paper, however, is to only address base GAN models for the application of brain medical imaging, which are generally: GAN, cGAN, DCGAN, LAPGAN, pix2pix, CycleGAN, WGAN, WGAN-GP, VAEGAN (BiGAN), StyleGAN and StyleGAN2. Table (1) summarizes the basic GAN models employed in brain medical imaging applications according to the literature.

2.2 Available Datasets.

Large and balanced dataset generation might be seen as a major barrier to the creation of high-quality AI systems for image processing in radiology. This is due to the expensive cost of creating these datasets as well as the restricted availability of pre-existing datasets. The sharing of such information is expected to be hindered by privacy concerns about patient data interchange and the competitive advantage of medical AI companies from their own private databases. In recent years, a number of significant ongoing initiatives worldwide have made a substantial number of early releases from public databases available to academics in an effort to solve these problems. Table (2) compiled the brain imaging datasets that are publicly available for brain tumor analysis training and evaluation.

2.3 GANs Potential over ML Approaches

Generative Adversarial Networks (GANs) have carved a niche in brain image analysis by overcoming limitations inherent to traditional machine learning (ML) approaches, particularly in scenarios requiring data generation, cross-modal synthesis, and anomaly detection. Classical ML methods, such as Support Vector Machines (SVMs) and Random Forests, rely heavily on handcrafted features and static datasets, which struggle to capture the complex, high-dimensional patterns in brain imaging data. These methods are inherently limited by their inability to generate new data, forcing reliance on small, often imbalanced datasets. For instance, conventional data augmentation (e.g., rotation, flipping) only creates superficial variations, failing to address the need for anatomically diverse synthetic samples. In contrast, GANs learn underlying data distributions, enabling synthesis of realistic brain images that enhance model robustness. Frid-Adar et al. [23] demonstrated this in medical imaging by augmenting scarce lesion datasets with GAN-generated samples, improving classification accuracy, a strategy directly applicable to brain pathology detection where data scarcity is acute.

Non-generative deep learning approaches, such as standard CNNs and autoencoders, also face critical limitations in tasks like cross-modal image synthesis (e.g., MRI-to-CT translation). Traditional CNNs, optimized for pixel-wise losses (e.g., mean squared error), often produce blurry or anatomically implausible outputs due to their inability to model global structural coherence. Autoencoders, while capable of dimensionality reduction, lack the adversarial feedback loop of GANs, resulting in less realistic reconstructions. For example, Nie et al. [24] showed that GANs outperform autoencoders in synthesizing high-fidelity brain MRIs, as adversarial training enforces realism by penalizing "unnatural" features. Similarly, CycleGAN [25] addressed unpaired image translation—common in clinical settings where paired datasets are rare, while classical methods like sparse coding or patch-based regression fail to generalize across such heterogeneous data. These limitations underscore GANs' superiority in preserving fine-grained anatomical details critical for applications like radiotherapy planning.

In anomaly detection, traditional ML approaches like One-Class SVMs or isolation forests require explicit assumptions about data distributions, which are often violated in neuroimaging due to the high variability of brain anatomy. Supervised CNNs, meanwhile, demand large labeled datasets of pathologies—a practical barrier given the rarity of conditions like rare brain tumors. GANs circumvent these issues by learning the distribution of healthy brain scans and flagging deviations without requiring labeled anomalies. AnoGAN [26], for instance, identifies subtle pathologies in retinal OCT images by reconstructing inputs and quantifying residuals, a framework adaptable to brain MRI. Similarly, U-Net, a gold standard for segmentation, relies on pixel-wise losses (e.g., Dice loss) that may overlook structural context, leading to fragmented or over-smoothed tumor boundaries. Adversarial frameworks like SegAN [27] mitigate this by incorporating a discriminator to penalize anatomically implausible segmentations, enhancing precision in tasks like glioblastoma delineation.

However, GANs are not without trade-offs. Their computational complexity and training instability—issues less prevalent in simpler ML models like SVMs—can hinder deployment in resource-constrained clinical environments. Additionally, GANs' "black-box" nature complicates interpretability compared to decision-tree-based methods, raising concerns in clinical validation. Yet, their ability to synthesize data, refine image quality, and detect anomalies without heavy reliance on labeled data positions GANs as uniquely transformative. While traditional ML remains valuable for interpretable, low-dimensional tasks, GANs address foundational gaps in neuroimaging, pushing boundaries in personalized medicine and multimodal diagnostics. Ongoing advancements in stable training (e.g., Wasserstein GANs) and hybrid models (e.g., GANs combined with transformers) aim to further solidify their role in brain image analysis.

3. GANs Medical Application for Brain Imaging Analysis

For clinical diagnosis and medical treatment, medical imaging is necessary because it offers valuable information into certain diseases whose structures can be concealed by the skin or bones. A variety of different medical imaging modalities, such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT), X-Ray, ultrasound and Positron Emission Tomography (PET), have been applied to GAN-based approaches. This diversity of image modalities has led to a variety of adversarial image applications used to detect, classify and predict a brain disease and disorder. As a result, GANs and adversarial techniques have been used in recent years to address a wide range of medical image processing problems. The most common uses of the adversarial technique in medical image processing have focused on segmentation, image synthesis, and quality improvement as illustrated in Figure 1. This section discusses only the GANs applications that are related to brain image analysis of these applications.

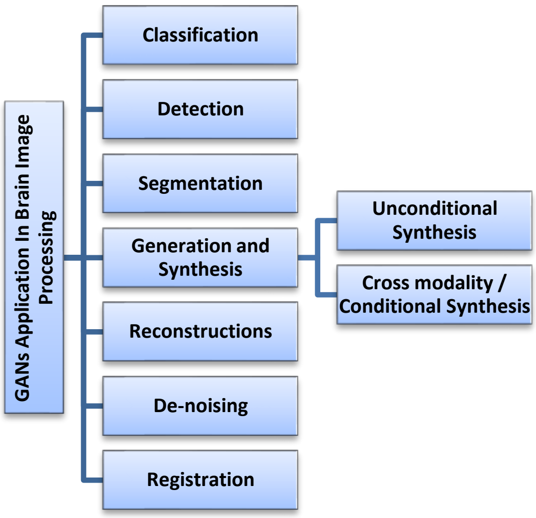

Figure 1: GANs Medical Application for Brain Imaging Analysis

3.1 Brain Image Generation and Synthesis

GANs have been used to generate samples from a latent distribution of medical images. These samples may be used to synthesis data for training human experts or to expand training sets for discriminatory models. While there may be some tolerance for faults in generated samples in some areas, such natural images, this might be a challenging task since errors could have serious detrimental consequences on medical imaging. Improvements in medical image analysis [28], including brain imaging classification and segmentation, have recently been shown by deep neural networks, especially convolutional neural networks (CNNs). CNN training, however, requires comprehensive medical datasets that is time consuming to acquire [29]. Furthermore, one of the key barriers to the inadequate number of positive cases of each pathology is patient privacy concerns related to disclosing or releasing their medical images to the public research domain. The absence of experts who can annotate medical images is another obstacle to the use of supervised learning methods. However, as Table. 2 summarizes, a number of cooperative efforts are being carried out by various healthcare institutions to provide extensive open access data sets.

In response to these challenges, data augmentation techniques are common for better performance by reconstructing original images. Scaling, rotation, flipping, translation, and elastic deformation are common methods of augmenting the training sample [30]. These advancements do not, however, take into consideration variances in the size, shape, location, and appearance of individual pathologies, as

Table 1: Basic GAN models employed in brain medical imaging applications

GAN Architectures	Authors	Basic Concept	Loss Function Mathematical Formula	Pros / Cons
GAN (Vanilla GAN)	Goodfellow et al., 2014 [1]	Generative (G): a fully connected layers (MLPs) with ReLU activations and discriminative (D): fully connected layers (MLPs) with maxout activations.	$\min_G \max_D V(D, G) = E_{x\sim p_{data}(x)}[\log(D(x))] + E_{z\sim p_z(z)}[1 - \log(D(G(z)))]$	Hard to train. Convergence is heavily dependent on hyper-parameter. Vanishing or exploding gradients issues. Prone to mode collapse.
cGAN	Mirza and Osindero, 2014 [2]	The generator is given random noise z along with some preexisting information c. The discriminator is then supplied the relevant true or false data together with the prior knowledge c.	$\min_G \max_D V(D, G) = E_{x\sim p_{data}(x)}[\log(D(x\|c))] + E_{z\sim p_z(z)}[1 - \log(D(G(z\|c)))]$	Improves the generation of detailed features. Helps training stability.
DCGAN	Radford et al., 2015 [3]	The generator (G) and discriminator (D) both follow a deep convolutional network architecture.	Constraints CNN architectures: Removing fully-connected hidden layers. Replacing the pooling layers with strided convolutions on the discriminator. Replacing pooling layers with fractional strided convolutions on the generator. Using batchnormalization on both the generator and the discriminator. Using ReLU activations in every layer of the generator except the last layer. LeakyReLU activations in all layers of the discriminator.	Helps training stability. Mode collapse was not entirely resolved.
LAPGAN	Denton et al., 2015 [4]	layers of conditional GAN model with Laplacian pyramid representation. Each of layers adds higher frequency into a generated image.	$h_k = L_k(I) = G_k(I) - U(G_{k+1}(I)) = I_k - U(I_{k+1})$ $I_k = U(I_{k+1}) + h_k = U(I_{k+1}) + G_k(Z_k, U(I_{k+1}))$	To obtain a maximum resolution image, a sequential sampling procedure is used. Take advantage of the cGAN model by applying to both the generator and the discriminator a low-pass image I_k.
CycleGAN	Zhu et al., 2017 [5]	It combines two GANs to determine a mapping from domain X to domain Y and vice versa. Generators G: X → Y, trained by discriminator DY, and F: Y → X, taught by discriminator DX, make up these.	$L(G, F, D_X, D_Y) = L_{GAN}(G, D_Y, X, Y) + L_{GAN}(F, D_X, Y, X) + \lambda L_{cyc}(G, F)$ $L_{cyc}(G, F) = E_{x\sim P_{data}(x)}[\\|F(G(x)) - x\\|_1] + E_{y\sim P_{data}(y)}[\\|G(F(y)) - y\\|_1]$	Unpaired data is used to do higher-resolution image-to-image translation. Could not construct geometric reverse transformation.
pix2pix	Isola et al., 2017 [6]	is a cGAN design using an encoder-decoder structure instead of a generator. The class information combines the L1 regularizer loss and the cGAN loss, as does the comparable image from the second domain.	$L_{CGAN}(G, D) = E_{x,y}[\log D(x, y)] + E_{x,z}[\log(1 - D(x, G(x, z)))]$ $L_{L1}(G) = E_{x,y\sim P_{data}(x,y), z\sim P(z)}[\\|y - G(x, z)\\|_1]$ $G^*, D^* = \arg\min_G \max_D L_{CGAN}(G, D) + \lambda L_{L1}(G)$	Earned approval for image synthesis across the domain users. Surpasses CycleGAN for high quality medical image synthesis.
WGAN	Arjovsky et al., 2017 [7]	prevents gradients from disappearing by using a more effective divergence measure, such as the Earth Mover (ME) or Wasserstein-1 distance.	$W(P_r, P_\theta) = \sup_{\\|f\\|_L \leq 1} E_{x\sim P_r}[f(x)] - E_{x\sim P_\theta}[f(x)]$ $\max_{w\in W} E_{x\sim P_r}[f_w(x)] - E_{z\sim p(z)}[f_w(g_\theta(z))]$ $\nabla_\theta W(P_r, P_\theta) = -E_{z\sim p(z)}[\nabla_\theta f(g_\theta(z))]$	Able to minimize the vanishing gradient and mode collapse problem. Improve the stability of learning. Proven to be much more robust. Easy to implement. Slow optimization. The constant c for weight clipping may cause a vanishing gradient problem.
WGAN-GP	Gulrajani et al., 2017 [8]	Utilizing a gradient penalty to enforce the 1-Lipshitz constraint on the discriminator.	$G = -E_{z\sim P(z)}[D(G(z))]$ $D = E_{x\sim P_{data}(x), z\sim P_z(z)}[D(\tilde{x}) - D(x) + \lambda(\\|\nabla_{\hat{x}} D(\hat{x})\\|_2 - 1)^2]$ where $e \sim U[0, 1]$, $\tilde{x} = G(z)$, $\hat{x} = ex + (1 - e)\tilde{x}$	Converges more quickly than WGAN. Learn complicated functions. Reduces the vanishing gradient. Cannot use batch normalization because gradient. Penalization is done for each sample in the batch.
PGGAN	Karras et al., 2017 [9]	Starting with low-quality images, this GAN training process gradually raises the resolution by adding layers to the networks for the discriminator and generator.	WGAN-GP loss was used alternately on a per-minibatch basis between optimizing the generator and the discriminator. A fourth term with an extremely small weight, to prevent the discriminator output from shifting far away from zero, was inserted into the discriminator loss.	High image quality. Training is stable in large resolutions. Semantic sensibility Understanding dataset dependent constraints.
VAEGAN (BiGAN)	Donahue et	The discriminator (D), generator (G), and encoder	Min Max V(D, E, G) =	Capable of projecting data back into latent space (learning

	al., 2017 [10]	(E) make up the architecture in general. Actual sample data is encoded into E(x) by E and decoded into G(z) by G. Finding the difference between each pair's (E(x); x) and (G(z); z) is the aim of D. G never sees E(x), and E never sees G(z), indicating that E and G do not directly interact.	G,E D,E,G *Where* $V(D, E, G) := \underbrace{E_{x\sim p}X \; [\; E_{z\sim p}E(\cdot\|x)\,[\log D(x, z)]}_{\log D(x, E(x))}\;] \; +$ $E_{z\sim p}Z\;[\; \underbrace{E_{x\sim p}G(\cdot\|z)\,[\log(1 - D(x, z))]}_{\log(1-D(G(z),z))}]$	the inverse mapping).
StyleGAN	Karras et al., 2019 [11]	It makes several important suggestions for improving the generator model, such as using a mapping network to link latent space points to intermediate latent space, using intermediate latent space to control the generator model's style at each point, and adding noise as a source of variance at each point.	A progressive growing GAN architecture with five modifications: Tuning addition and bilinear up sampling. Mapping Network Extension and AdaIN (styles). Removing the generator's latent vector input. Adding noise to each block. Adding mixed Regularization.	Introduces control at various levels over the style of generated images. When used to generate synthetic human faces, remarkable results are obtained. It makes it possible for the intermediate latent space W to be much less entangled than the latent space Z input. The applied bias and noise allowing their relative effect to be inversely proportional to the present style's magnitudes.
StyleGAN2	Karras et al., 2020 [12]	With many shifts, it expands on StyleGAN. Next, the normalization of adaptive instances is redesigned and replaced by a method of normalization called weight demodulation. Furthermore, new forms of regularization such as lazy regularization and path length regularization are introduced, and an expanded training method is implemented upon progressively growing.	Modifications to StyleGAN: Eliminate some initial, pointless processes Adjust the bias and noise to operate outside of a style's active region. Only change the standard deviation for each feature map. In place of instance normalization, use a "demodulation" operation on the weights assigned to each convolution layer.	Because W is the pertinent latent space from the perspective of the synthesis network, this approach concentrates all study on it. Putting these operations (noise and bias) outside the style block, where they work on data that has been normalized. enhancement of perceived image quality and current distribution quality measures.

Table 2: Available brain image datasets

Dataset	***Name***	***Modalities***	***Description***	***Related Active Links***
BraTS	*Multimodal Brain Tumor Segmentation Challenge (BraTS2012 to BraTS2023)*	*Magnetic resonance imaging (MRI) utilizes multi-institutional pre-operative MRI scans.*	*A large dataset of MR scans of brain tumors in which the required tumor structures were defined. Focuses on: the segmentation of brain tumors which are fundamentally heterogeneous, namely gliomas. Also, the prediction of overall survival and the experimentally evaluate the uncertainty in the segmentation of tumors.*	*https://www.med.upenn.edu/cbica/brats/*
BrainWeb	*BrainWeb is a Simulated Brain Database (SBD).*	*Magnetic resonance imaging (MRI)*	*It comprises a collection of realistic volumes of MRI data produced by an MRI simulator, a normal brain database and MS lesion brain database. To evaluate the performance of various image analysis methods in a setting where the truth is known.*	*https://brainweb.bic.mni.mcgill.ca/brainweb/*
ISLES2015 & ISLES2016)	*Ischemic Stroke Lesion segmentation.*	*Multi-spectral MRI images.*	*A public dataset of diverse ischemic stroke cases for Segmentation. Provides stroke lesion/clinical outcome prediction from acute MRI scans.*	*http://www.isles-challenge.org/ISLES2015/* *http://www.isles-challenge.org/ISLES2016/*
ISLES2017	*Ischemic Stroke Lesion segmentation.*	*Multi-spectral MRI images.*	*Stroke lesions segmentation dataset includes acute stroke imaging scans and manually outlined lesions on follow-up scans.*	*http://www.isles-challenge.org/ISLES2017/*
ISLES2018	*Ischemic Stroke Lesion segmentation.*	*CT perfusion data.*	*Stroke lesions segmentation provides Segmentation of stroke lesions based on acute CT perfusion data that includes new dataset of stroke patients and matching expert segmentations.*	*http://www.isles-challenge.org/*
IBSR	*The Internet Brain Segmentation Repository.*	*Magnetic resonance imaging (MRI)*	*Evaluation and development of brain segmentation methods. It provides manually-guided expert segmentation results along with magnetic resonance brain image data.*	*https://www.nitrc.org/projects/ibsr/*
ABIDE I & ABIDE II	*Autism Brain Imaging Data Exchange.*	*Functional magnetic resonance imaging (R-fMRI)*	*Promote discovery science on the brain connectome in ASD. It is a multi-international site, sharing previously collected resting*	*http://fcon_1000.projects.nitrc.org/indi/abide/abide_I.html*

			state functional magnetic resonance imaging (R-fMRI), anatomical and phenotypic characterization, particularly in regard to measures of core ASD and associated symptoms.	*http://fcon_1000.projects.nitrc.org/indi/abide/abide_II.html*
OASIS	*Open Access Series of Imaging Studies.*	*OASIS-1: Cross-sectional MRI Data in Young, Middle Aged, Nondemented and Demented Older Adults.* *OASIS-2: Longitudinal MRI Data in Nondemented and Demented Older Adults.* *OASIS-3: Longitudinal Neuroimaging, Clinical, and Cognitive Dataset for Normal Aging and Alzheimer's Disease (MRI & PET).*	*The goal of OASIS is to make neuroimaging databases publicly accessible to the scientific community. This multi-modal dataset created by the Knight ADRC and its related studies is compiled and freely distributed.*	*https://www.oasis-brains.org/*
HCP	*The Lifespan Human Connectome Project Development.*	*Namely structural MRI, resting state fMRI, task fMRI, and diffusion MRI.*	*The goal of the Human Connectome Project is to provide an unparalleled compilation of neural data, an interface to access this data graphically and the ability to reach unprecedented conclusions about the living human brain.*	*http://www.humanconnectomeproject.org/*
ADNI	*Alzheimer's Disease Neuroimaging Initiative.*	*Dataset (ADNI1, ADNI-GO, ADNI2 and ADNI3) includes MRI and PET images, genetics, cognitive tests, CSF and blood biomarkers as predictors of Alzheimer's disease.*	*The goal of ANDI is to discover, improve, standardize, and verify the biomarkers and clinical trial interventions used in AD clinical studies.*	*http://adni.loni.usc.edu/*
iSeg-2017 and iSeg-2019	*Challenge data 6-month Infant brain MRI Segmentation.*	*Magnetic resonance imaging (MRI) for data 6-month Infant brain.*	*These challenges aim to promote automatic segmentation algorithms on 6-month infant brain MRI from multiple sites.*	*http://iseg2017.web.unc.edu/* *http://iseg2019.web.unc.edu/*
IXI	*Information eXtraction from Images dataset.*	*Magnetic resonance imaging (MRI) from normal, healthy subjects.*	*To facilitate the computational study of brain development.*	*https://brain-development.org/ixi-dataset/*
MIDAS	*Designed Database of MR Brain Images of Healthy Volunteers.*	*Magnetic resonance imaging (MRI) from normal, healthy subjects.*	*Analyze illness through empirical review of the awareness of the variety of shapes identified by magnetic resonance (MR) images of the brain of healthy anatomical structures.*	*http://insight-journal.org/midas/community/view/21*
BALSA	*The Brain Analysis Library of Spatial maps and Atlases database.*	*Magnetic resonance imaging (MRI).*	*BALSA is a structured archive of reference data precisely mapped to surfaces and volumes of the brain atlas, including different forms of spatial maps extracted anatomically and functionally, as well as brain connectivity.*	*https://balsa.wustl.edu/study/show/WG33*
TCIA	*The Cancer Imaging Archive.*	*Magnetic resonance imaging (MRI).*	*Glioblastoma that has been recently identified and treated with surgery and standard concurrent chemotherapy and radiation treatment (CRT) with adjuvant chemotherapy is included in TCIA.*	*https://wiki.cancerimagingarchive.net/display/Public/Brain-Tumor-Progression*
PBTA	*Pediatric Brain Tumor Atlas.*	*Magnetic resonance imaging (MRI)*	*Full genomic data (WGS), RNAseq, proteomics, longitudinal clinical data, imaging data (including MRIs and radiology records), histology slides, pathology reports, and matching tumor/normal are all included in PBTA.*	*https://cbttc.org/pediatric-brain-tumor-atlas/*
PING	*Pediatric Imaging, Neurocognition, and Genetics*	*Magnetic resonance imaging (MRI).*	*The aim is to create a broad MRI and genetics data resource that can be shared freely with the science community. The data resource provides information on the development of children's mental and emotional functions.*	*https://www.nitrc.org/projects/ping/*
CoRR	*The consortium for Reliability and Reproducibility.*	*Magnetic resonance imaging (MRI). resting state fMRI (R-fMRI) and diffusion imaging data.*	*Aims to promote the evaluation of reliability and reproducibility of the test-retest for functional and structural connectomics. By concentrating on fundamental phenotypic tests, which are generally common in the field of neuroimaging, as well as important for interpretation and sample characterization.*	*http://fcon_1000.projects.nitrc.org/indi/CoRR/html/index.html*

well as changes resulting from different imaging techniques or sequences. In this regard, GANs-based data augmentation has shown impressive performance in broad computer vision tasks. The capacity of GAN to fit the generated distribution of noise variables with a
sharp value function to the real one is attributed to its excellent generalization capabilities. Specifically, Shrivastava et al. (SimGAN) beat the state-of-the-art with a relative 21 percent gain in eye-gaze prediction [31]. Typically, the most direct application of GANs is data generation, as a kind of generative model. This is to benefit from the distribution of actual samples and to generate samples compliant with distribution. The majority of current GAN research focuses on improving the effectiveness and utility of imagine synthesis and generating capabilities. As a result, GANs are increasingly widely employed and have been used to augment training medical images in a number of studies with promising outcomes. For medical image synthesis, applied GAN research may be broadly categorized into two groups: unconditional image synthesis and conditional image synthesis. Here, we concentrate on GAN-based synthesis techniques, which are divided into two categories: conditional (cross modality) as an example shown in **Fig. 2**, Conditional synthesis of a reconstructed two-dimensional super resolution MR image by using different GAN-based algorithms [32], and unconditional medical image synthesis, as **Fig. 3** shows visual results by CycleGAN and switchable CycleGAN on the ABCD Study Dataset, T1w to T2w image synthesis [33].

3.1.1 Unconditional Brain Image Synthesis

Unconditional synthesis involves the generation of random noise images with no other conditional information. A vast amount of work has recently surfaced in the field of unsupervised medical image generation using GANs, enabling the resolution of issues like class imbalance and data scarcity [34], encouraging data simulation [35], and contributing to a better understanding of the existence of data distributions and their latent structure. The medical imaging sector uses DCGAN, WGAN, and PGGAN extensively because of their exceptional training stability. Table 3 lists all of the unconditional brain image synthesis research that are currently accessible. Preliminary studies have shown that the DCGAN can be used for realistic synthesizing. Using DCGAN, Bermudez et al. [45] were able to generate high-fidelity images that closely mimic acquired images.

The promising results obtained are presumably due to a sufficiently homogeneous training set to solve a basic problem in terms of acquisition parameters and demographics. Previous quality control research by Kazuhiro et al. [46] indicates that DCGAN may help satisfy the requirement to provide large data sets with high-quality MR images, such that even seasoned neuroradiologists can be misled. Islam J and Zhang Y. [47] suggested a model based on the DCGAN model that can be extended using PET images in disease diagnosis systems and can help complement the training dataset. The suggested model's qualitative and quantitative assessment shows that the synthesized images are similar to actual brain PET images of multiple phases of Alzheimer's disease. Lee et al. [48] used CycleGAN to suggest a more stable model to synthesize brain tumor-segmented MR images due to its significant success in medical imaging.

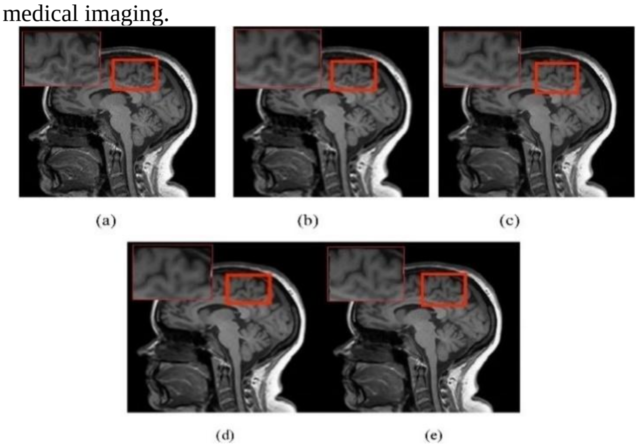

Figure2: Visual results of reconstructed two-dimensional super resolution MR image by using different GAN-based algorithms [32]

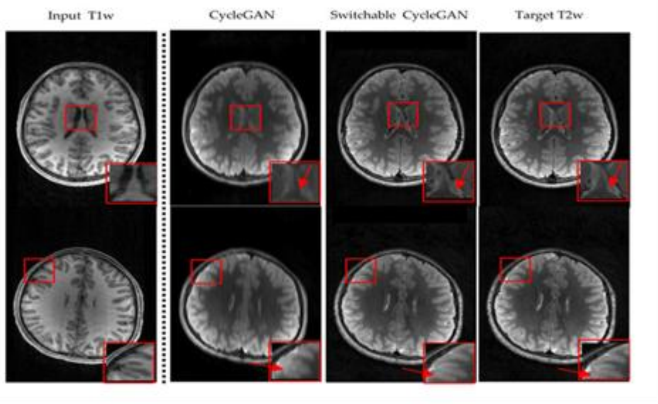

Figure3. Visual results by CycleGAN and switchable CycleGAN on the ABCD Study Dataset, T1w to T2w image synthesis. Different rows display two individual brain MRI images [33].

In their research, the proposed generative networks demonstrated the capacity to synthesize not only brain tumor-segmented images, but also other medical images, such as lung and heart segmentation. Finally, Chang et al. [49] demonstrated that GANs are capable of producing pediatrics wbMRIs required to allow automatic anomaly detection. In this study, samples generated using the StyleGAN2 architecture, in particular, had high visual quality, which the radiologist considered to be true. In order to identify tumor lesions, the role of anomaly detection using GAN trained on normal images was shown, that could minimize the need for limited examples of wbMRI tumors.

3.1.2 Cross modality / Conditional Brain Image Synthesis

In clinical practice, data from many medical imaging modalities is often combined. However, information obtained in one imaging modality may already be available in another, depending on the application. Accurate image conversion from one imaging modality to another may reduce the number of acquisitions required, which would reduce expenses and patient discomfort. As a result, conditional synthesis and cross modality (such as creating CT-like images from MR images) are thought to be highly beneficial. Table 4. summarized available cross modality / conditional brain image synthesis studies.

An early study by Nie et al. [24], which was motivated by the possibility of cell damage and cancer due to radiation exposure induced by CT imaging, used a cascades 3D FCNN to synthesize CT images from MR acquisitions. In addition to the adversarial training, the model is trained with a pixel-wise reconstruction loss and an image gradient loss to increase the realism of the synthetic CT images. The definition of using a generator cascade derives from an Auto-Context Model (ACM). In ACMs, a network contributes its output to a successful network as additional input to provide contextual information and facilitate adjustments.

In cross modality synthesis, however, many studies have used the CycleGAN-based approach because it uses unpaired data to achieve higher-resolution image-to-image translation. Jin et al. [63] proposed a dual CycleGAN-based solution called MR-GAN, which uses paired and unpaired data together to address the problem of unpaired training context-misalignment and to remove rigid registration operations and blurred effects of paired training. The results suggest that structures inside the complex 2D brain slices can be effectively measured by the synthetic method and MR-GAN can also be used in CT-based radiotherapy planning by further removing image registration uncertainties while integrating MRI with CT and reducing clinical workload. Moreover, Welander et al. [69] evaluates two unsupervised GAN models (CycleGAN and UNIT) by comparing synthetic MR images generated to ground truth images for image-to-image conversion of T1 and T2-weighted MR images. The results indicated that the GAN models that have been applied can synthesize visually realistic MR images. and that, relative to ground-truth results, models generating more visually accurate synthetic representations do not inherently have better quantitative error measurements.

Another well-accepted model architecture used for conditional image synthesis is the cGAN-based method, a two-stage deep learning framework is proposed by Pan et al. [68] to use all available MRI and PET for the diagnosis of Alzheimer's disease.

The missing PET images are assigned, in the first stage, by 3D-cGAN by learning bi-directional mappings between MRI and PET. While in the second stage, they create a landmark multi-modal multi-instance learning method for the diagnosis of Alzheimer's disease, based on the full MRI and PET, by automatically learning MRI and PET features in a data-driven way. The results demonstrate that their proposed two-stage deep learning framework beats traditional multi-modal approaches for classification of Alzheimer's disease and the synthetic PET images generated by their method are acceptable. By using a GAN model with a ResNet architecture as the generator, Emami et al. [62] present a cGAN-based approach to generating synCTs from T1-weighted post-Gadolinium MRI datasets. Their strategy presented strong potential to facilitate near-real-time MR-only brain treatment planning. Additionally, a new end-to-end framework for medical image translation activities, introduced by Armanious et al. [65], is MedGAN. It integrates the conditional adversarial framework with a modern mix of non-adversarial losses and a CasNET generator architecture to increase the accuracy of global outcomes and high frequency details. With no task-specific changes, MedGAN was introduced to three difficult medical imaging tasks: PET-CT translation, MR motion correction and PET denoising. MedGAN has quantitatively and qualitatively outperformed most related translation methods through the various proposed activities. Furthermore, Yu et al. [70] is exploring how to synthesize T1 FLAIR images to facilitate single modality brain tumor segmentation based on T1. Via the suggested 3D cGAN and the local adaptive fusion scheme, their structure produces the synthesized FLAIR images. The synthesized FLAIR images effectively improve the segmentation of entire tumors and tumor from the T1 modality with the two-way 3D CNN segmentation model.

3.2 Brain Image Segmentation

For many applications, such as detection and classification, segmentation of objects and organs in medical images is an important prerequisite. A significant role for cancer diagnosis, treatment, and assessment of treatment results is the segmentation of the tumor area. Using MRI, CT, PET, and multimodal segmentation techniques, such as PET/CT and PET/MRI, a large range of semi-automatic and automatic segmentation methods and techniques are used for tumor segmentation. In medical image processing, the tedious and time-consuming nature of manual segmentation made automated methods the most active area in Deep-Learning research.

Numerous GAN-based brain segmentation techniques have been suggested, including semi-automatic techniques and fully automatic techniques. The primary goal of image segmentation is to divide an image into homogeneous regions that are mutually exclusive and exhaustive with respect to a predefined criterion. In brain tumors, segmentation includes the isolation of various. tumor tissues such as solid or active tumor, edema, and necrosis, from the normal brain tissues such as gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF).

Segmentation of brain tumors requires an objective measure that can be used to define the homogeneity of each tissue. There are two approaches to accomplish an analytical measure, namely unsupervised and supervised segmentation processes **Fig. 4** illustrate the visual segmented patch resulted from 3DAdGanSeg model for different types of brain tissue. In brain tumor segmentation studies that involve image textures [127], local histograms [128], and structure tensor eigenvalues [129], MRIs have different features that are adopted. MRI comprises multi-sequence approaches that include T1-weighted (TI)

Table 3: Unconditional brain image synthesis studies

Paper Authors	GAN-based Methods	Modality	Dataset/s
Calimeri et al. (2017) [13]	LAPGAN	3D-T1-weighted MRI	Self-acquired
Bowles et al. (2018) [14]	PGGAN	CT(CSF) + MRI(FLAIR)	2 unknown Datasets
Han et al. (2018) [15]	WGAN	T1, T1c, T2-weighted and FLAIR MRI	BRATS2016
Beers et al. (2018) [16]	PGGAN	T1, T1 post-gadolinium, T2, and T2 FLAIR weighted MRI	BRATS2017
Bermudez et al. (2018) [17]	DCGAN	T1-weighted MRI	BLSA
Kazuhiro et al. (2018) [18]	DCGAN	T1-weighted MRI	Self-acquired
Mondal et al. (2018) [19]	GAN (3D U-Net)	T1, T1IR, FLAIR + T1, T2 -weighted	MRBrains-2013 + iSeg2017
Lee et al. (2020) [20]	cycleGAN	MRI	Self-acquired
Chang et al. (2020) [21]	StyleGAN2	wbMRIs	Self-acquired
Islam J, and Zhang Y (2020) [22]	DCGAN	PET	ADNI
Wang S et al. (2022) [23]	UTC-GAN	CT	ISLES 2018
Sun L et al. (2022) [24]	HA-GAN	CT, MRI	COPDGen + GSP
Mourad D etal.(2024) [25]	CDGAN	MRI	OpenNeuro websire
Xin B et al. (2024) [26]	DA-GAN	T1, T2	BraTS2018

Table 4: Cross modality / Conditional brain image synthesis

Paper Authors	GAN-based Methods	Modality	Dataset/s
Nie et al. (2017) [27]	(3D) FCN + ACM(GAN)	MRI To CT	ADNI
Wolterink et al. (2017) [28]	synthesisGAN (CNNs)	MRI To CT / CT To MRI	Self-acquired
Nie et al. (2018) [29]	(3D) FCN + ACM(GAN)	MRI To CT/ 3T MRI to 7T MRI	ADNI
Emami et al. (2018) [30]	cGAN (GAN + ResNet)	MRI To CT	IRB approved study dataset
Jin et al. (2018) [31]	MR-GAN (cycleGAN)	CT To MRI	Self-acquired
Yang et al. (2018) [32]	cycleGAN	CT To MRI	Self-acquired
Armanious et al. (2018) [33]	cGAN (U-block (U-nets) + CasNet (cascades residual blocks)	PET To CT	Self-acquired
Wei et al. (2018) [34]	cGANs	MR To PET	Self-acquired
Yang et al. (2018) [35]	cGAN	T1 To/From T2 MRI	BRATS2015
Pan et al. (2018) [36]	3D CycleGAN	MR To PET	ADNI
Welander et al. (2018) [37]	cycleGAN + UNIT	T1 To/From T2 MRI	HCP
Yu et al. (2018) [38]	(3D) cGAN	T1 To FLAIR MR	BRATS2015
Chen et al. (2018) [39]	PTGAN (U-Net + CNN)	T2-weighted To PD-weighted	IXI
Olut et al. (2018) [40]	sGAN (PatchGAN)	T1, T2 To MRA	IXI
Ge et al. (2019) [41]	pairwise GAN (U-Net + Markovian)	Enhanced-T1-MRI and T2-MRI	TCGA
Dar et al. (2019) [42]	cycleGAN (pGAN + cGAN)	T1 To/From T2 MRI	MIDAS + IXI + BRATS2015
Kwon et al. (2019) [43]	3D GAN (VAE + α-GAN + WGAN-GP)	T1, T2, FLAIR and T1-weighted	ADNI + BRATS2018 + ATLAS
Han et al. (2019) [44]	CPGGAN	T1-weighted (T1c) brain axial MRI	Self-acquired (National Center for Global Health and Medicine, Tokyo, Japan)
Ali et al. (2019) [45]	CAE + DCGAN	T1ce, T2 and FLAIR	BRATS2017
Yu et al. (2019) [46]	Ea-GANs (U-Net + CNN)	T1 To T2 and FLAIR	BRATS2015 + IXI
Huang et al. (2019) [47]	CoCa-GAN	T1 MRI	BRATS2015
Armanious et al. (2019) [48]	MedGAN (cGAN)	Fluorine-18-FDG PET To CT	Self-acquired

Anders Eklund (2019) [49]	3D PGAN	T1-weighted To T1-weighted MRI	HCP
Yurt et al. (2019) [50]	mustGAN	T1, T2, PD-weighted and FLAIR images	IXI + ISLES
Carver et al. (2019) [51]	U-Net	T1, T2, and FLAIR MRI	BRATS2018
Lei et al. (2020) [52]	unified GAN	T1-weighted, T1c Flair and T2-weighted MRI	
Kearney et al (2020) [53]	A-CycleGAN + VAE	MR To CT	
Xin et al. (2020) [54]	TC-MGAN	T2 To T1, T1ce and FLAIR	BRATS2018
Emami et al. (2020) [55]	attention-GAN (encoder decoder + 3 CNN)	T1-weighted to CT/synCT	Self-acquired
Hagiwara et al. (2020) [56]	GAN (pixel-wise translation network + multiresolution classification)	MRI To FLAIR	Self-acquired
Dikici et al. (2020) [57]	cGANe (DCGAN + FD)	T1-weighted to 3D MRI	Self-acquired
Koike et al. (2020) [58]	cGAN (U-Net + PatchGAN)	MRI To sCT / T1w, T2w and FLAIR	TCIA
Hamghalam et al. (2020) [59]	GAN (Enh-Seg-GAN)	FLAIR to FLAIR, T1c, and T2	BRATS2013
Dar et al. (2020) [60]	sGAN + jGAN + rGAN + sr-sGAN	T1-weighted, T2-weighted, PDweighted and FLAIR	MIDAS + IXI + BRATS2015
Li et al. (2020) [61]	cycleGAN	MRI To CT	
Bourbonne V et al. (2021) [62]	cGAN based on the pix2pix architecture	planning CT and MRI-T1	Self-acquired
Gao X et al. (2021) [63]	TPA-GAN + PT-DCN	MRI to PET	ADNI-1 & ADNI-2
Liu X et al. (2021) [64]	cGAN (GAN + ResNet)	MRI to CT	Generated synCT images
Abu-Srhan A et al. (2021) [65]	uagGAN	Bidirectional MR-CT	Self-acquired
Matsui T et al. (2022) [66]	Modified StarGAN	fMRI	HCP
Mehmood M et al. (2022) [67]	Pix2pix (cGAN)	T1-CE	T1-CE MRI
Hu S et al. (2022) [68]	BMGAN	MRI to PET	ADNI
Mukherkjee D et al. (2022) [69]	AGGrGAN	T1ce, T1, T2, T2-FLAIR	Brain tumor dataset + BraTS 2020
Zhan B et al. (2022) [70]	D2FE-GAN	T1, T2, T1c, FLAIR	BraTS2015 + IXI
Zhao X et al. (2022) [71]	sTBI-GAN	T1	Self-acquired + ADNI
Zhang H et al. (2022) [72]	switchable CycleGAN	T1w to/from T2w	ABCD
Wang J et al. (2022) [73]	FedMed-ATL	T1, T2, PD	IXI + BraTS2021
Huang P et al. (2022) [74]	eCoCa-GAN and iCoCa-GAN Frameworks	T1, T1c, T2, and T2-F	BraTS19
Luo Y et al. (2022) [75]	AR-GAN	LPET to HPET	Self-acquired
Qin Z et al. (2022) [76]	ST-cGAN	MRI	IXI
Bai X et al. (2022) [77]	dual-generator GAN	T1w to T2w	Self-acquired
Alrashedy et al. (2022) [78]	Vanilla GAN and DCGAN	T1, T2, PD	Brain Tumor Classification-Kaggle
Aljohani A et al. (2022) [79]	Pix2Pix GAN	T1, T2, PD	IXI
Finck T et al. (2022) [80]	Extended pix2pix	T1w, FLAIR to DIR	Self-acquired
Zhang J et al. (2022) [81]	BPGAN	MRI to PET	ADNI
Wang J et al. (2023) [82]	FedMed-GAN	T1, T2, PD-weighted images (PD)	IXI + BraTS2021
Gu X et al. (2023) [83]	perceptual supervised GAN	MRI to CT	Self-acquired
Li Y et al. (2023) [84]	3D StyleGAN	T1	ADNI + OASIS
Zhang X et al. (2023) [85]	BCGAN	CBCT to CT	Self-acquired
Jin Y et al. (2023) [86]	3D Contrastive Learning GAN	T1w, FLAIR to PET-Aβ	ADNI
Wang B et al. (2023) [87]	feature-consistency GAN & three-dimensional encoder-decoder network with mean absolute error loss	synthesizing CBV maps using T1-weighted images, contrast-enhanced T1-weighted images, and apparent diffusion coefficient (ADC) maps	Self-acquired SCALE-PWI
Cao B et al. (2023) [88]	ACA-GAN	T1, T1GD, T2, FLAIR	BraTS2020
Hamghalam M et al. (2024) [89]	ESGAN + EnhGAN	FLAIR, T1, T1c, T2	BraTS 2013 + BraTS 2018
You S et al. (2024) [90]	FA-GAN	MRI to PET	ADNI
Huang Y et al. (2024) [91]	BrainGAN	T1, T2, T1c, FLAIR	MIDAS + IXI + BraTS 2018
Zhang Y et al. (2024) [92]	Unified Framework based on GAN	T1+T2+T1Gd→FLAIR and T1+PD→T2	BraTS2019 + IXI
Jiang M et al. (2024) [93]	cGAN based on the pix2pix architecture	T1WI, T2WI, FLAIR, and DWI from CT	Self-acquired
Fard AS et al. (2024) [94]	Pix2pix (cGAN)	SPECT from PET and MRI	Self-acquired
Tabassum M et al (2024) [95]	pix2pix WGAN	T1, T2, and FLAIR to T1c	BraTs2023

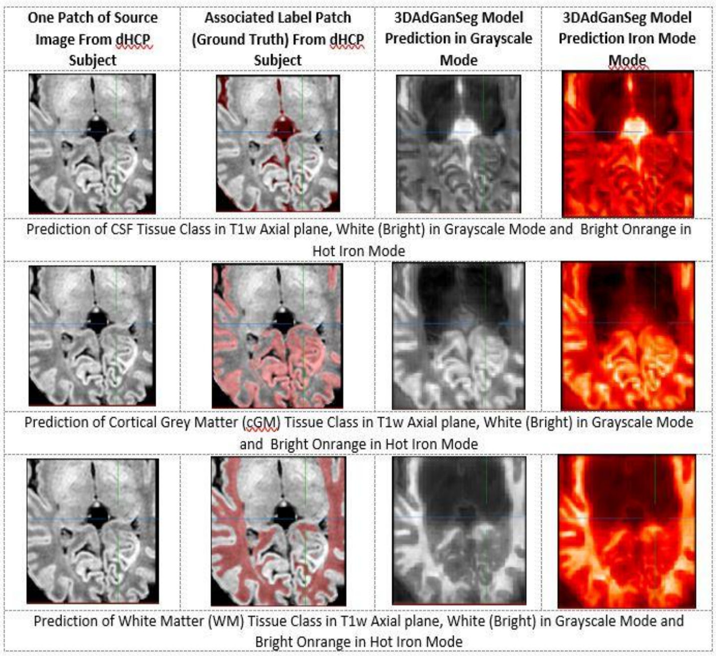

Figure4. The Visual Segmented Patch Resulted From 3DAdGanSeg model for Different Types of Brain Tissue from Source Domain (dHCP Dataset) [127]

and T1-weighted contrast-enhanced (T1c), T2-weighted and T2-weighted fluid attenuated inversion recovery (FLAIR) techniques that are used for brain tumor segmentation.

In brain tumor segmentation studies, deep-learning-based techniques are becoming common, as their success is superior in fields, such as object detection [130], image classification [131] and semantic segmentation [132]. An important method for image recognition and prediction is the Convolutional Neural Network (CNN). However, CNN is mainly used for patient segmentation, assessment, and recovery time estimation of brain tumors [133]. In brain tumor segmentation, there are a variety of unsolved issues. As an example, the goal of brain tissue segmentation or anatomical segmentation of the brain is to mark each voxel or pixel into a distinct class of brain tissue. This segmentation presumption is that no tumor tissue or other abnormalities are included in the brain image [134][135]. Besides that, some research methods return the single label segmentation mask or the tumor core center as the point of interest without further reasoning and segmentation being done.

Segmentation techniques can be roughly divided into four categories: threshold-based techniques, region-based techniques, model-based techniques, and pixel/voxel classification techniques [136]. Researchers have typically used pixel-wise or voxel-wise loss for segmentation, such as cross entropy. In automatically obtained segmentations, where a voxel-wise unstructured loss is usually used to train them, this can lead to holes and fragments. In addition, in deep networks, the pixel-wise assessment and optimization mechanism is not adequate to remove notions of anatomical structures. To resolve these downside, additional corrections for the CNNs architecture required, such as Conditional Random Fields (CRFs) and Statistical Shape Models (SSMs) [137][138]. These additional methods are usually hard to optimize. A potential solution to these issues is the GANs, which offer a different learning flow. As outlined in Table (6), only GAN-based segmentation approaches to brain medical imaging research are discussed in this section.

Numerous GAN-based brain segmentation techniques have been suggested, including semi-automatic techniques and fully automatic techniques. The primary goal of image segmentation is to divide an image into homogeneous regions that are mutually exclusive and exhaustive with respect to a predefined criterion. In brain tumors, segmentation includes the isolation of various tumor tissues such as solid or active tumor, edema, and necrosis, from the normal brain tissues such as gray matter (GM), white matter (WM) and cerebrospinal fluid (CSF). Segmentation of brain tumors requires an objective measure that can be used to define the homogeneity of each tissue. There are two approaches to accomplish an analytical measure, namely unsupervised and supervised segmentation processes. Early research by Moeskops et al. [139] indicates that the use of the GAN training strategy in CNNs not only increases the reliability of methods of semantic segmentation, but also puts non-semantic segmentation methods closer to semantic methods. A superior efficiency of GANs in the segmentation of normalized patches of brain tumors is also highlighted by Li et al. [140]. Through preserving the premise that the distribution of tumor image pixels is partially different from that of a healthy reconstruction image, tumor segmentation can be done easily by comparing the input image with the healthy image reconstructed. The adversarial loss can also be used as an adaptively trained indicator of similarities between the segmented outputs and the input image annotated. Instead of computing the similarity in the pixel domain, the discriminatory network then projections the input to a low-dimensional manifold and evaluates the similarity there. The adversarial loss is then determined from a network trained adaptively during the generator's progress. Xue et al. [27] suggest the SegAN structure that uses the U-Net as the GAN generator architecture. This was shown to be successful in applying multi-scale spatial constraints on segmentation maps and achieved state-of-the-art results. In addition to adversarial and pixel-wise losses, they demonstrate that pixel-dependencies are learned best when using a multiscale loss function. Output loss on unseen images is one of the recognized difficulties of most supervised segmentation approaches. Yang et al. [148] employed an end-to-end training adversarial network composed of a segmentor and a discriminator in a pixel-wise classification way. Their segmentor is a 3D residual U-Net designed to be conscious of contours by applying contour constraints to the training process. In order to provide auxiliary supervision, the discriminator network is trained alongside the segmentation network. They demonstrated that the neural network was able to generate predictions that closely resemble reality and fine-tune predictions due to subtle anomalies by adding additional constraints by contours and adversarial training to the model. In addition, a 3D image segmentation using 3D Pix2Pix GAN, named Vox2Vox, was introduced by Cirillo et al. [189] to segment brain gliomas. Their group of numerous Vox2Vox models re-transform high-quality segmentation outputs. Besides that, not only for image segmentation, but also for further image augmentation, their Vox2Vox model can be used as they stated. Moreover, Weninger et al. [152] have suggested an unsupervised method of semantic segmentation for gliomas in brain MRI, which can classify the three distinct types of tumor tissue. Differently, Rezaei et al. [190] suggested end-to-end trainable architecture for semantic brain tumor segmentation by conditional adversarial training for the multi-class classification of brain tumors. They utilized cGAN and trained a CNN semantic segmentation along with an adversarial network that discriminates against segmentation maps from the real images or the segmentation network. These networks learn a loss adapted to the task and data at hand, which makes it applicable in unseen data. Yu et al. [70], however, used an 11-layer, two-pathway 3D CNN segmentation model to efficiently segment brain tumors with the synthesized FLAIR-like, created from their proposed 3D cGAN and T1 MR images, achieving high performance on multimodal segmentation of brain tumors. The synthesized FLAIR images only improve the segmentation of entire tumors and tumor core components efficiently from the T1 modality.

Yet, due to the distinct image characteristics of multiple modalities, multimodal segmentation using a single model remains very difficult. The extraction of modality-invariant functionality is a critical issue. Previous methods of multimodal segmentation needed paired images of n-modality. A two-stream unified attentional generative adversarial network (UAGAN) is proposed by Yuan et al. [149] to overcome the constraint of having paired multimodal images. They incorporate the features of all streams of segmentation and translation and recalibration of features is carried out with attentional blocks to highlight valuable features. Brain tumor segmentation studies show that, in most cases, their UAGAN framework achieved better efficiency.

Moreover, the issue of paired multimodal medical image shortage can be alleviated. Even while GANs-based approaches have allowed a major advance in brain image segmentation. In general, experimental findings suggest that rivalry is closed between segmentors that use and do not use adversarial training.

3.3 Brain Image Reconstructions

The diagnostic accuracy of obtained medical images can be restricted by noise and artifacts because of restrictions of clinical environments, such as radiation dosage and patient comfort. In brain medical diagnostics, Magnetic Resonance Imaging (MRI) is commonly used. A key challenge in medical imaging is fast MR regeneration without losing data. Any kind of motion artifact is directly decreased by rapid acquisition and restoration and is thus highly desirable. In order to recreate images, classic compressed sensing-based solutions specifically use k-space information [191]. In images with quick inference, the potential to foster realism makes GANs an obvious candidate for solving the problem of MR reconstruction. GAN-based MR reconstruction analysis focuses on the alteration and combination of well-known architectures with suitable loss functions. In the following, Table (7) above, summarized available brain reconstruction GAN-based medical images studies.

Yang G et al., [192] presented an early study on GAN-based MR reconstruction concentrating on the DAGAN architecture. A perceptual loss is applied to adversarial and pixel-wise losses in this approach to compare deep derived features in real and generated data, which also improves the model's stability. Also, by modifying loss functions to retain frequency information, they refine the DAGAN architecture. Quan et al. [195], who added a refinement network to distinguish pixel-wise and perceptual information-based training, has revised the DAGAN architecture. Centered on the reconstruction of data in the missing frequencies, they suggest a cyclic training strategy. Moreover, they suggest using a generator chain to resolve the uncertainties that have been generated in previous generators. In addition to ensuring fidelity of image domain data, frequency domain data fidelity is often enforced when raw K-space data is usable in MR reconstruction.

Otherwise, Pix2pix-based is a well-accepted model used to maintain data fidelity in situations where multiple image modality data can be co-registered. For MRI reconstruction, the simple pix2pix structure has been used in several studies includes [193][197][198]. In order to cope with volumetric details and boost the reliability of the proposed GAN model, researches in [222] are adapting the SRGAN with 3D convolutional layers. To overcome the blurring effect in the reconstructions, their loss function blends a pixel-wise loss with a Gradient-Based Loss (GDL).

GAN-based methods of reconstruction usually apply alternative loss functions to the initial structure. A software-only architecture for high-quality MRI reconstruction using only 52 percent of the initial k-space data was suggested by Shitrit and Raviv [193]. The main concept is to use an adversarial loss in addition to the loss of L2. Also, Zhang et al. [200] suggested a multi-channel GAN model for parallel MRI reconstruction that uses multi-channel complex-valued k-space data directly. By introducing a new loss function to merge adversarial and perceptual loss in image reconstruction for better artifact reduction. Recently the proposed framework of Shaul et al. [206] uses the capabilities of the U-Net and GAN architectures for high-quality MRI reconstruction. They provided up to 20% of k-space data with a deep learning model for MRI reconstruction and demonstrated its usefulness as a real-time software-only approach for MRI acceleration. A two-stage GAN process for estimating the missing k-space samples and fixing aliasing artifacts in the image-space is the basis of the proposed method. This is achieved by an end-to-end optimization mechanism involving image-space, k-space, and adverse loss functions.

Differently, A multi-level Densely Connected Super-Resolution Network (mDCSRN), which is a hybrid of the WGAN model and a revised version of DenseNet, was proposed by Chen et al. [197]. To overcome the substantial memory footprint of the problem of 3D convolution. In addition, in other study, Chen et al. [205] applied a 3D U-Net deep convolutional neural network approach to enhancing dipole inversion problems in the reconstruction of QSM (Quantitative susceptibility mapping). The proposed QSMGAN model is based on a 3D U-Net architecture with an improved input phase receptive field relative to the output. Further refinement to the network was then accomplished by the use of the WGAN-GP with gradient penalty training strategy. Their approach effectively produces reliable QSM maps from single orientation step maps and performs substantially better than conventional dipole inversion algorithms that are non-learning-based. Their findings indicate that their suggested approach

Table 6: Brain segmentation medical images studies

Paper Authors	GAN-based Methods	Modality	Dataset/s
Moeskops et al. (2017) [96]	GAN (FCN + DN)	T1-weighted MRI	Self-acquired
Li et al. (2017) [97]	CNN + GAN	T1, T1c, T2-weighted and FLAIR MRI	BRATS 2017
Kamnitsas et al. (2017) [98]	GAN ((3D) CNN)	MPRAGE, FLAIR, T2 and PD MRI (for TBI)	2 unknown Datasets
Rezaei et al. (2017) [99]	cGAN (U-Net + Markovian GAN)	T1, T2 -weighted MRI	BRATS 2017
Rezaei et al. (2018) [100]	cGAN (U-Net+ LSTM)	T1, T1c, T2-weighted and FLAIR MRI	BRATS 2017
Xue et al. (2018) [101]	SegAN (GAN + novel multi-scale loss function)	T1c, T2-weighted and FLAIR MRI Segmentation	BRATS 2013 + BRATS 2015
Mondal et al. (2018) [102]	DCGAN	T1, T1IR, FLAIR + T1, T2 -weighted	MRBrains-2013 + iSeg2017
Bowles et al. (2018) [14]	PGGAN	CT(CSF) + MRI(FLAIR)	2 unknown Datasets
Yang et al. (2018a) [35]	cGAN	T1 To/From T2 MRI	BRATS2015
Rezaei et al. (2018) [103]	3D voxel-GAN (S (U-Net) + D (FC Markovian PatchGAN))	T1, T2, T1ce, and Flair + 4DPWI, CBF, CBV, MTT, Tmax	BRATS2018 + ISLES2018
Yu et al. (2018) [38]	(3D) cGAN	T1 To FLAIR MR	BRATS2015
Baur et al. (2018) [104]	AnoVAEGAN (VAE + AnoGAN)	FLAIR and T1 images	Self-acquired
Zhu et al. (2018) [105]	GAN (SR (LFSR))	T1-weighted (T1Gd) MRI	BRATS2018
Yang et al. (2018b) [106]	GAN (S (3D Residual U-Net) + D (auxiliary discriminator))	T1, T1ce, T2, and FLAIR MRI	BRATS2018
Yuan et al. (2019) [107]	UAGAN (U-net)	T1Gd, T2 and FLAIR	Medical Segmentation Decathlon dataset
Rezaei et al. (2019) [108]	3DJoinGANs	MRI + CT	ISLES2018
Liu et al. (2019) [109]	3D U-Net		
Weninger et al. (2019) [110]	VAEs + GANs	FLAIR and T1CE MRI	BRATS2018
Cui et al. (2019) [111]	DGAN		
Tokuoka et al. (2019) [112]	3D U-Net + Cycle-GAN based UDA	T1w, T2w, T1ce and FLAIR	BRATS2015 + BRATS2017 + ADNI
Shi et al. (2019) [113]	UG-net (U-Net) + GAN	3D T1-weighted and T2-weighted brain MRI	CIND Center in San Francisco + ADNI
Hamghalam et al. (2020) [114]	GAN (2D-U-net + 2D FCN)	FLAIR MRI	BRATS2019
Sun et al. (2020) [115]	Parasitic GAN (S (3D U-Net) + G (3D GAN) + D (PatchGAN))	T1, T1ce, T2, and FLAIR MRI	BRATS2015 + BRATS2017
Li et al. (2020) [116]	TumorGAN (CycleGAN)	T1, T1ce, T2, and FLAIR MRI	BRATS2017
Nema et al. (2020) [117]	RescueWNe	T1, T1c, T2, and FLAIR MRI	BRATS2015 + BRATS2017
Yuan et al. (2020) [118]	UAGAN	T1, T1Gd, T2 and T2 FLAIR	3 collected datasets from other studies
Cirillo et al. (2020) [119]	Vox2Vox (3D U-Net)	T1, T1-weighted (T1Gd), T2-weighted, and T2 FLAIR	BRATS2018
Giacomello et al. (2020) [120]	SegAN-CAT (SegAN)	T1, T1c, T2-weighted and FLAIR MRI	BRATS2015 + BRATS2019
Hamghalam et al. (2020) [59]	GAN (Enh-Seg-GAN)	FLAIR to FLAIR, T1c, and T2	BRATS2013
Wang S et al. (2021) [121]	CPGAN	3D T1w	ATLAS
Cui S et al. (2022) [122]	GAN-segNet	T1, T1w, T1c, T2, T2w, FLAIR	BarTS2018
Zhao X et al. (2022) [123]	TBI-GAN	T1	Self-acquired + ADNI
Wang S et al. (2022) [23]	UTC-GAN	CT	ISLES 2018
Khaled A et al. (2022) [124]	GAN Transfer Model	T1, T1w, T2, T2w, FLAIR	iSEG2017 + MRBrains
Zhu L et al. (2022) [125]	GMMS(DualMMP-GAN+CACNN-Wnet)	T1, T1w, T1c, T2, T2w, FLAIR	BarTS2018
Neelima G et al. (2022) [126]	DeepMRSeg + Optimizer (SPO)	T1, T1w, T1c, T2, T2w, FLAIR	BarTS2018

Khaled A et al. (2022) [127]	multi-stage GAN	T1, T1w, T2, T2w, FLAIR	iSEG2017 + MRBrains
Zoghbi A et al. (2022) [128]	CADe system	T1c	Figshare
De Asis-Cruz J et al. (2022) [129]	FetalGAN	rs-fMRI	Self-acquired
Prajapati R et al. (2022) [130]	cGAN + patchGAN	T1-w	OASIS 1
Niu K et al. (2022) [131]	QBrain	T1-w	SLANT-27 + Self acquired
Huang L et al. (2022) [132]	transformer-based GAN	T1, T1GD, T2, FLAIR	BraTS2015+BraTS2018+BraTS2020
Dong D et al. (2022) [133]	AMD-DAS	MRI + CT	RSNA 2019 + MSD challenge
Kiani Kalejahi B et al. (2023) [134]	AC-GAN	T1, T1GD, T2w, T2FLAIR	BraTS 2019
Narayanan SJ et al. (2023) [135]	DCGAN+pix2pix GAN	T1, T2, PD	BraTS 2021
Sille R et al. (2023) [136]	DCGAN	T1, T1GD, T2, FLAIR	BarTS2015
Güven et al. (2023) [137]	SSimDCL		
Xie B et al. (2023) [138]	MLP-GAN	Brain Vessel	DeepVesselNe
Fan C et al. (2023) [139]	U-Patch GAN	SPECT, TI, MRT1, MRT2, PET, FDG	The whole Brain Atlas
Tao C et al. (2023) [140]	VAE-GAN	T1w, T1c	Self-acquired
Datta P et al. (2024) [141]	ViT+ GAN	T1w	BraTS 2020 + Masoud2021 + SARTAJ + Figshare + BR35H
Raut P et al. (2024) [142]	Pix2PixNIfTI	T1w, T2w, T1ce, FLAIR	BraTS2021
Usman Akbar M et al. (2024) [143]	progressive GAN30+StyleGAN	T1, T1wGD, T2w, T2FLAIR	BraTS2020+BraTS2021
Asadi F et al. (2024) [144]	StyleGAN2-ada	T1, T2, FLAIR	TCIA
Hamghalam M et al. (2024) [89]	ESGAN + EnhGAN	T1, T2, T1c, FLAIR	BraTS2013+BraTS2018
Shaari et al. (2024) [145]	3DAdGanSeg	T1w, T2w	dHCP + Schizophrenia Bulletin 2008
Paramarthalingam A et al. (2024) [146]	Keras GAN models	Brain tumor	CE-MRI

Table 1: Brain reconstructions medical images studies

Paper Authors	**GAN-based Methods**	**Modality**	**Dataset/s**
Yu et al. (2017) [147]	cGAN	T1-weighted MRI	IXI
Yang G, et al. (2017)[148]	dubbed DAGAN	T1-weighted	MICCAI 2013 grand challenge
Shitrit and Raviv (2017) [149]	GAN	MRI	Self-acquired
Armanious et al. (2018) [150]	cGAN (Cascade U-Net + Markovian GAN (PatchGAN)	CT + (FLAIR) MRI	Self-acquired
Quan et al. (2018) [151]	cycleGAN	MRI	IXI
Sanchez and Vilaplana (2018) [152]	SRGAN	(3D) T1-weighted MRI	ADNI
Chen et al. (2018) [153]	3D mDCSRN-GAN (WGAN-GP)	(3D) T1-weighted MRI	HCP
Dar et al. (2018) [154]	GAN (rsGAN)	T1-weighted, T2-weighted and PD-weighted	MIDAS + IXI + BRATS2015
Ran et al. (2018) [155]	WGAN	T1, T2, PD-weighted MRI	IXI + BrainWeb
Zhang et al. (2018) [156]	GANCS	T1, T2 weighted MRI	Self-acquired
Armanious et al. (2018) [157]	MedGAN (cGAN)	T1 weighted MRI	Self-acquired
Wang et al. (2018) [158]	3D c-GANs (3D U-net-like generator)	3D PET	Self-acquired
Armanious et al. (2018) [159]	CasNet (cascades residual blocks)	T1 weighted MRI / PET (2D axial slices)	Self-acquired
Latif et al. (2018) [160]	U-Net	MRI	BRATS2015
Chen et al. (2020) [161]	SMGAN (U-Net +WGAN-GP)	QSM	Self-acquired
Shaul et al. (2020) [162]	DCE-MRI sequences	T1, T2, PD, and FLAIR	IXI + DCE-MRI + MS-lesion
Usman et al. (2020) [163]	CG-SENSE + GAN(U-Net)	T2 FLAIR	BRATS2018
Dar et al. (2020) [60]	sGAN + jGAN + rGAN + sr-sGAN	T1-weighted, T2-weighted, PD weighted and FLAIR	MIDAS + IXI + BRATS2015
Li G et al. (2021) [164]	RSCA-GAN	CS-MRI	Calgary Campinas brain MR
Lv J et al. (2021) [165]	PI-GAN	T1w, T1SAG, FLAIR	Calgary-Campinas brain MR + Self acquired
Han C et al. (2021) [166]	MADGAN	T1w, T1c	OASIS-3 + Self acquired
Zhao Y et al. (2021) [167]	mi-GAN	sMRI	ADNI
Sandhiya B et al. (2021) [168]	DCGAN+ Faster R-CNN	MRI	Self-acquired
Fei Y et al. (2022) [169]	BiC-GAN	LPET to SPET	Self-acquired
Pan J et al. (2022) [170]	CT-GAN	DTI, rs-fMRI	ADNI
Lui X et al. (2023) [171]	BTMF-GAN	T1WI, CE-T1WI, T2WI, FLAIR	BraTS2019
Li X et al. (2023) [172]	DR-CAM-GAN	CS-MRI	MPRAGE + diencephalon challenge + OASIS
Cong S et al. (2024) [173]	DDASR	T1w	ADNI-1
Tudosiu PD et al. (2024) [174]	3D generative model	T1w	ADNI + UKB
Zhou X et al. (2024) [175]	GAN-NOV + GAN-VAN	T1w	ADNI + NACC
Zuo Q et al. (2024) [176]	UCT-GAN	fMRI	ADNI
Wang Y et al. (2024) [177]	MEaTransGAN	LPET to SPET	Self-acquired

Table 8: Brain detection medical images studies

Paper Authors	**GAN-based Methods**	**Modality**	**Dataset/s**
Alex et al. (2017) [178]	GAN	T1, T2, FLAIR and & T1 post contrast MRI	ISLES + BRATS 2014
Chen and Konukoglu (2018) [179]	WGAN-GP	T2-weighted MRI	HCP (train) + BRATS2015 (test)
Baumgartner et al. (2018) [180]	WGAN + VA-GAN	T2-weighted MRI	ADNI
Han et al. (2018) [181]	PGGAN	T1c brain axial MR images	BRATS 2016
Han et al. (2019) [182]	PGGAN	T1-weighted (T1c) MRI	BRATS2016

Vu et al. (2019) [183]	Adversarial Dual Autoencoders (ADAE)	HGG and LGG	HCP + BRATS2017
Han et al. (2019) [44]	CPGGAN	T1-weighted (T1c) brain axial MRI	Self-acquired (National Center for Global Health and Medicine, Tokyo, Japan)
Sun et al. (2020) [184]	ANT-GAN	FLAIR MRI	BRATS2018 + LiTS
Shen et al. (2020) [185]	adGAN	FLAIR MRI	BRATS2017
Han C et al. (2021) [166]	MADGAN	T1w, T1c	OASIS-3 + Self acquired
Hu N et al. (2022) [186]	GAN-based Method	CT to MR (FLAIR)	Self-acquired
Saravanakumar S et al. (2022) [187]	semi-supervised GAN	MRI	ADNI
Kuttala D et al. (2022) [188]	Dense GAN + Dense Attentive GAN	sMRI	ABIDE II
Devika K et al. (2022) [189]	GAN-based encoder-decoder framework	longitudinal sMRI	ABIDE I + ABIDE II
Pan J et al. (2023) [190]	CT-GAN	DTI, rs-fMRI	ADNI
Sahoo S et al. (2023) [191]	GAN ensemble Hybrid CNN-based	CE-MR	Figshare
Datta P et al. (2024) [141]	ViT+ GAN	T1w	BraTS 2020 + Masoud2021 + SARTAJ + Figshare + BR35H
Siddiquee MM et al. (2024) [192]	Brainomaly	T1w	ADNI

could produce more detailed, COSMOS-like QSM maps from single-orientation efficiently.

In a different prospective, Dar et al. [92] introduced a GAN-based architecture to accelerate multi-contrast MRI acquisitions by exploiting low-spatial-frequency, high-spatial-frequency and perceptual priors at the same time. In order to maximize recovery of the target contrast, the proposed rsGAN uses high-spatial-frequency prior in-formation in the source contrast. In comparison to pure learning-based synthesis, rsGAN bases extracted images from data obtained from sampled acquisitions of the target contrast. The proposed rsGAN approach surpasses state-of-the-art methods of reconstruction and synthesis with enhanced high-frequency tissue structure recovery and efficiency improvements against degradation or loss of features.

Overall, the underlying methods are almost the same with all the reconstruction tasks. MR is a particular case since it has a well-defined forward and backward mechanism, i.e. Fourier transformation, so that raw K-space data can be integrated. Better reconstructed results can be achieved by using more data, either raw K-space or images from other sequences. Additionally, using adversarial loss provides more visually pleasing results in general than using pixel-wise reconstruction loss alone. But the model can hallucinate unseen structures by using adversarial loss to balance the generated and actual data distribution. However, Pixel-wise reconstruction loss tends to combat this issue if paired samples are usable, even if the model has been conditioned on all normal images, then used to recreate images of diseases, there would always be a hallucination problem due to domain overlap.

3.4 Brain Image Detection

Detecting anomalies from images using supervised Deep Learning algorithms involves a significant volume of annotated training data. GANs approach this issue in a separate way by either improving datasets with synthetic samples, or by mapping distributions by which deviations may be observed as outliers. In the following, Table (8). summarized available GAN-based brain detection medical images studies. The presented techniques demonstrate good success in the detection of anomalies while greatly decreasing the volume of training data despite getting more structural difficulty compared to other implementations since they belong to various facets of GANs. While in the aforementioned detection methods, the role of the discriminator is emphasized. However, the various databases and measures used for the analyses dispute a fair comparison between the approaches.

On MR images, Alex et al. [223] employed GAN for brain lesion identification. The generator has been used to simulate the distribution of regular patches and the discriminator has been used to measure the posterior likelihood of patches in the test image based on each pixel.

The modeling of the distribution of normal data with GANs is a different approach to unsupervised anomaly detection. The most comparable normal image to the query image is then reconstructed by the GAN and irregularities can be observed as differences between the query and the reconstructed image. To learn the data distribution of normal brain MR images, Chen and Konukoglu [224] utilized an adversarial auto-encoder. By examining the learned latent space, the lesion image was then mapped to an image without lesion, and the lesion could be highlighted by computing the residual of these two images.

Baumgartner et al. [225] suggested the Visual Attribution GAN (VA-GAN) for the detection of Alzheimer's disease, influenced by AnoGAN. VA-GAN extracts the map of adjustments that turn the image class from normal to diseased and uses it to detect abnormalities. Vu et al. [228] suggested a different semi-supervised GAN-based anomaly detection method, called Adversarial Dual Autoencoders (ADAE), such that both generator and discriminator are composed of autoencoders, where anomalies are observed using discriminator pixel-wise reconstruction error during the testing. Results from ADAE shows that the model in multiple problem domains is robust.

Patch reconstruction is based on the aforementioned GAN-based anomaly detection techniques, the main aim of which is to recreate the corresponding normal counterpart provided a new image patch. Shen et al. [230] recently proposed the adGAN model, which is a discriminative patch-level model that explicitly learns the boundary of normal data distribution and can output the anomaly score of a new image patch without the mechanism of reconstruction. The comprehensive experiments indicated that on all suggested datasets, adGAN is consistently superior to its rivals.

The above techniques demonstrate good success in the detection of anomalies while greatly decreasing the volume of training data despite getting more structural difficulty compared to other implementations since they belong to various facets of GANs. While in the aforementioned detection methods, the role of the discriminator is emphasized. However, the various databases and measures used for the analyses dispute a fair comparison between the approaches.

3.5 Brain Image Classification

In the domain of deep learning applications, classification is considered as the most successful task that has been deployed. It is possible to extract hierarchical image features from a deep neural network trained discriminatively with image-wise class labels. The complexity of obtaining medical records, however, hinders their employment opportunities. GANs' ability to increase training data and derive domain-specific features from each class will probably help solve this constraint. A two-stage process strategy is primarily applied for the classification studies, with the first stage learning to increase the images and the second stage learning to classify by implementing the appropriate classification network. These two stages are trained independently without any contact between them. In the following, Table (9). summarized available GAN-based brain classification images studies.

For the particular task of glioma classification, Ge et al. [73] suggested a pairwise GAN architecture to synthesize MR images in a cross-modality fashion. They also adopted a two-stage training strategy that proved that the approach introduced was efficient and robust, leading to a consistent improvement in test success in the classification of glioma. One year later, Ge et al. [238] have suggested a post-processing technique to incorporate the outcomes of the slice-level glioma subtype classification by plurality vote to produce the diagnostic outcome at the patient level. To learn the glioma feature using GAN-augmented MRIs followed by real MRIs, a two-stage coarse-to-fine training methodology is suggested. Results have shown that the proposed methodology is efficient and stable after testing the proposed training methodology using real and pairwise GAN-augmented MRIs as training results.

For brain tumor type classification, Ghassemi et al. [239] suggested a method for data augmentation across distinct datasets. On different sets of MRI scans, a GAN is first trained to generate MRI like images as the outputs of its generative model and to differentiate them by their discriminator from real ones. The discriminator model is then presented for tumor type classification as a pre-trained deep neural network model and is fine-tuned over the main limited set of labeled MRI scans. They claimed that the results of the proposed model obtained the highest precision compared to state-of-the-art models. In addition, they argued that pre-training of CNN as a GAN discriminator is a dominant approach with a small amount of data for the implementation of deep learning. The findings, as stated earlier, indicate that the classification tasks benefit from the samples produced by the GAN.

3.6 Brain Image Registration

Although CNNs have been successfully used to align medical images across the network in a single forward-pass, GANs have emerged as a contender for more optimal registration mapping with their excellent image transformation capability. Table 9. summarized available GAN-based brain registration images studies.

To automatically learn the similarity metric for training a deformable registration network, Fan et al. [242] suggested an unsupervised adversarial similarity network. A registration network that predicts the deformations is the model generator. Whereas the model discriminator is a discrimination network that decides when images are well matched and then supplies the registration network with misalignment information during training. Via adversarial training, both the registration and discrimination networks are trained, learning a metric for precise registration. The results of the proposed method show greater accuracy of registration relative to state-of-the-art registration methods.

In addition, a cross-modality generative model for cross-modality image registration was proposed by Yang et al. [67]. The proposed approach is inspired by an atlas-based registration in which a non-linear registration algorithm registers the source image to the target image. They reported that the proposed approach outperforms the state-of-the-art results on widely accepted MRI datasets in cross-modality registration.

With utilizing of autoencoder latent space feature maps that allow independent registration of datasets Mahapatra et al. [243] have suggested a GAN-based model for the registration of multiple forms of medical images using unsupervised domain adaptation and generative adversarial networks. The approach proposed achieves independent registration of the dataset where it is trained on one type of images and achieve state-of-the-art result in registering differing type of image. To produce the registered image and the corresponding deformation field, GANs are trained. Authors proved that the registration approach based on domain adaptation performs better than current methods that rely on large volumes of image registration training data.

Due to the necessity of learning both local and global features in different scales to model the difference between distributions, GANs provide this useful information. Although GANs greatly boost the efficiency of registration procedures, the necessary performance can still not be achieved in certain real medical settings.

3.7 Brain Image De-noising

Diagnostic radiology imaging often involves a trade-off between radiation risk and image contrast. Reduced radiation exposure results in poorer contrast and signal-to-noise levels, which can enhance diagnosis but expose the patient to more dangerous radiation. Deep Learning has been successfully applied to improve the clarity and reduce noise in low-contrast images. However, images produced by these methods are often fuzzy. GANs, which are thought to promote the creation of clear lifelike images, offer a way to mitigate this problem. Many studies have acknowledged this capability, and a variety of methods have been proposed to modify GANs in order to de-noise photos of noticeably greater quality. Table 9 is summarized the available GAN-based brain de-noising medical image studies.

By addressing the problems of image synthesis and image de-nosing as crucial elements of manifold learning, Bermudez et al. [45] investigated implicit manifold. By using DCGAN that has proved to generate high-resolution, high-fidelity images in an unsupervised manner, they utilized a skip-connected autoencoders for image denoising. Connections between convolutional layers in the autoencoder retain structural features to improve resolution. They revealed that this de-noising methodology outperforms the latest state-of-the-art FSL SUSAN de-noising tool.

For the simultaneous correction of rigid and non-rigid motion artifacts from multiple body areas, Armanious et al. [201] expand their previous MedGAN model. They further demonstrate the utility of jointly correcting rigid and non-rigid motion artifacts by contrasting them with an identical model trained solely on a single type of motion artifact. After quantitatively and qualitatively comparing the results against many state-of-the-art GAN-based strategies, the updated MedGAN demonstrated superior results in the motion correction task.

Although the findings appear convincing visually, it appears like an appropriate, quantitative criterion is not yet available to determine the strength of procedures in retaining essential medical image data. The results of the forementioned papers benefit from the ability of GANs to learn the key common features of the image domain.

4. GANs Potentials and challenges

The GANs models are an effective methodology for a wide range of tasks that has gained tremendous popularity in the area of medical image processing. The sections described above define GANs and the application of variants and their implementations in different brain medical image domains. The potential and challenges of using GANs are provided in this section. It also emphasizes the main difficulties and complications of using GANs.

4.1 GANs Potentials

GANs offer major benefits over other supervised or unsupervised learning methods. Its main advantage is that it does not include any description of the form of the generator model's probability distribution. Naturally, GAN thus avoids density forms that need to represent complex and high-dimensional distributions. GANs main advantages includes:

They are an unsupervised learning method: In medical imaging, collecting labelled data is a manual procedure that requires a lot of time and is costly to acquire. Because GANs learn the internal representations of the data they can be trained using unlabeled data, hence do not need labeled data.

Capable to generate data: The capacity of GANs to produce data that nearly looks like the genuine thing is one of its best features. Their ability to expand training datasets, operate in semi-supervised or unsupervised environments, and address issues like class imbalance makes them extremely useful in medical imaging. In cross-modality image synthesis, they have excelled, particularly in converting one sort of image to another. Conditional GANs reduce the expenses and dangers associated with medical imaging while producing data from several modalities, giving physicians access to richer, more varied datasets that aid in decision-making.

Ability to learn data density distributions: GANs can learn complex and hierarchical data distributions. The capacity to learn data distributions opens up the possibility of detecting in actual datasets unseen abnormal cases. Existing GANs methods demonstrate good success in the detection of anomalies in brain medical images while greatly decreasing the volume of training data.

Using discriminator as a classifier: A discriminator and a generator are the two primary parts of a GAN after training. Curiously, the discriminator may also function as a classifier, which makes it helpful for tasks like object classification, in addition to evaluating the generator's output. The classification capability of GANs has been extensively utilized in brain imaging. Furthermore, GANs excel in extracting valuable features from medical images, particularly when pixel-based approaches are insufficient. Their adversarial training methodology, which enables them to comprehend the most profound and semantic facets of the material, is responsible for this. In applications like brain image segmentation, registration, and classification, this property has proven especially useful.

4.2 GANs Challenges

In addition to such advantageous GAN utilities, there are also difficulties that need to be overcome for medical imaging to be effective. Although many improvements have been achieved to mitigate some of the training and evaluation issues of GANs, there are still some open challenges, includes:

Training challenges of GANs

There are several concerns involved with GANs such as training process difficulties which include mode collapse, vanishing gradients and internal covariate shifts.

Mode collapse: A typical problem with GANs is mode collapse, in which the generator produces outputs that lack variation and are strikingly similar, if not identical. This occurs because the probability distribution of the data is frequently multimodal and complicated, with several peaks denoting several sample groups. Mode collapse can occur when GANs are unable to adequately represent this complexity. In the worst situations, the generator may consistently provide almost the same output, a phenomenon known as total collapse. Thankfully, there are solutions for this issue, such as training separate GANs to handle different modes or encouraging the generator to generate a wider range of outputs during training by employing a broad collection of data samples.

Vanishing gradients: Neural networks frequently experience disappearing gradients, particularly when backpropagating. The gradient tends to get smaller as it goes backward through the layers, from the last to the first. It can occasionally grow so tiny that the early layers either learn very little or cease to learn at all. This basically freezes their training because the weights in those first levels are rarely adjusted. We refer to this issue as the "vanishing gradients problem." Activation functions like as ReLU, LeakyReLU, or PReLU can be used to address this issue. They ensure that the network trains more efficiently by preventing the gradients from decreasing excessively during backpropagation. Batch normalization is another useful technique that improves the stability and effectiveness of the training process by normalizing the inputs to the hidden layers.

An internal covariate shift: When the network's input distribution shifts, an internal covariate shift takes place. The training process is slowed down by the hidden layers' ongoing need to adjust to the changing input distribution. As a result, the model takes a lot longer to converge to a global minimum. Methods such as batch normalization and other normalizing techniques can be applied to solve this problem. By stabilizing the input distribution, these methods provide faster and more seamless training.

Table 9: Brain classification, registration and de-noising medical images studies

Paper Authors	GAN-based Methods	Modality	Dataset/s
Classification			
Ge et al. (2019) [41]	pairwise GAN (U-Net + Markovian)	Enhanced-T1-MRI and T2-MRI	TCGA
Ge et al. (2020) [193]	pairwise GAN	T1, T1e, T2, FLAIR IDH1 genotype	TCGA
Ghassemi et al. (2020) [194]	CNN + GAN	T1ce	Self-acquired
Gao X et al. (2021) [63]	TPA-GAN + PT-DCN	MRI to PET	ADNI-1 & ADNI-2
Fei Y et al. (2022) [169]	BiC-GAN	LPET to SPET	Self-acquired
Alrashedy HH et al. (2022) [78]	Vanilla GAN and DCGAN	MRI	Brain Tumor Classification-Kaggle
Neelima G et al. (2022) [126]	CAViaR-SPO + PO	T1, T1w, T1c, T2, T2w, FLAIR	BarTS2018
Cao Y et al. (2023) [195]	BNLoop-GAN	dMRI, rsfMRI	ADNI
Zhang M et al. (2024) [196]	PA-Net	MRI to PET	ADNI
Zhou X et al. (2024) [175]	GAN-NOV + GAN-VAN	T1w	ADNI + NACC
Registration			
Fan et al. (2018) [197]	GAN (cascades U-net)	3D brain images	LPBA40, IBSR18, CUMC12 and MGH10
Yang et al. (2018) [35]	cGAN	T1 To/From T2 MRI	BRATS2015
Mahapatra et al. (2020) [198]	CAEs + GAN	T1 and dual echo T 2 −weighted	ADNI-1
Zheng Y et al. (2021) [199]	SymReg-GAN	T1, T2, CT	BraTS 2018, ALBERTs, LPBA40, IBSR18, CUMC12, MGH10 and self-acquired CT-MRI dataset
Han R et al. (2022) [200]	JSR network	MR to CBCT	Self-acquired
Zhu X et al. (2022) [201]	TGAN (GAN_dr+GAN_ie)	3D brain MRI	Atlas, BrainWeb, RIRE
Zhu X et al. (2022) [202]	FSGAN	T1, T2w	BrainWeb, IXI, HGG, LPBA40
Fu J et al. (2023) [203]	MIG (AGM + QCM)	T1w	ADNI + OASIS-3 + GENIC (self-acquired)
Li M et al. (2023) [204]	GAN-based Method	T1w	HBN + ABIDE
Liu S et al. (2023) [205]	SCAM-GAN	CT to MRI	Self-acquired
Liu M et al. (2023) [206]	style-encoding GAN	T1w	UKBB + PPMI + ADNI + ABCD + ICBM
Xie K et al. (2024) [207]	MARINet	T1w	Self-acquired
Rahmani M et al. (2024) [208]	D²BGAN	T1w, T2-FLAIR	RESECT+ BITE
Park Y et al. (2024) [209]	GAN-MAT	T2- from T1-weighted MRI	HCP + SMC + ABIDE-II
De-noising			
Armanious et al. (2018) [157]	MedGAN (cGAN)	3D PET	Self-acquired
Bermudez et al. (2018) [17]	DCGAN	T1-weighted MRI	BLSA
Christilin DA et al. (2021) [210]	Residual Encoder- Decoder WGAN	T1w	TCIA
Tian M et al. (2021) [211]	conditional GAN	T1w, T2w, PDw	BrainWeb
Li Z et al. (2022) [212]	HDnGAN	3D T2 -SPACE FLAIR	Self-acquired
Yu M et al. (2023) [213]	RIRGAN	T1, T1ce, T2w, T2-FLAIR	BraTS 2019
Wang Q et al. (2023) [214]	DISGAN	T1w	HCP (Insample) + Epilepsy + BraTS2015
Zuo Q et al. (2023) [215]	DiffGAN	fMRI to SC	ADNI
Fu Y et al. (2024) [216]	MPGAN	LPET to FPET	Bern + UI
Wu Y et al. (2024) [217]	AttGAN-FT-2	LD PET, CT	Self-acquired
Cui J et al. (2024) [218]	PMC2-GAN	LPET to SPET	BrainWeb

Training instability: One of the most significant difficulties in using GANs is training instability. For both conceptual and numerical reasons, traditional GAN training is frequently unstable [264]. This can result in problems like mode-hopping or mode collapse, where the model finds it difficult to converge correctly. The majority of solutions are made for computer vision datasets, where it is simpler to visually examine the produced images and identify faults, even if there is a lot of research focused on finding answers for these challenges. To increase the stability of GANs, methods such as feature matching, mini-batch discrimination, historical averaging, one-sided label smoothing, and batch or instance normalization have been suggested. But things become more complicated with medical imaging. Because medical image modes are frequently less evident, it might be more difficult to identify erratic behavior or irrational results. Researchers have proposed unique loss functions and architectural modifications to address these issues. However, the medical industry lacks defined benchmarks and trustworthy assessment measures to accurately evaluate and gauge the effectiveness of various strategies.

5. Evaluation matrixes diversities

A potent and cutting-edge method for developing generative models is the use of GANs. In contrast to conventional neural networks, which are trained using a predetermined loss function until they converge, GANs function by comparing two models: a discriminator and a generator. The generator produces artificial images, while the discriminator gains the ability to discern between produced and real images. Simultaneously, these two models are taught, reining in one another. The disadvantage of this configuration is that there does not seem a simple loss function to gauge the generator's performance directly. Because of this, tracking training progress and evaluating the model's effectiveness in absolute terms are challenging Researchers have created a combination of qualitative and quantitative techniques to evaluate GANs according to the caliber and variety of images they generate in order to overcome this issue. These methods aid in assessing the model's performance even in the absence of a conventional loss metric [265].

5.1Quantitative measures: GAN generators are assessed quantitatively by allocating numerical scores that correspond to the degree of quality of images they produce. Metrics such as Average Log-likelihood, Coverage Metric, Inception Score (IS), Frechet Inception Distance (FID), Precision, Recall, and F1 Score are among the approximately 24 quantitative methods available for evaluating GAN models. Some of these measures are "model agnostic," which means they do not require to estimate the underlying probability distribution; instead, they regard the generator as a black box that simply has the capacity to sample images. However, measures like Average Log-likelihood are a little more complex since they need to approximate the probability distribution from the produced samples. Researchers may objectively evaluate a GAN's performance in terms of image quality and variety with the use of these quantitative techniques.

5.2 Qualitative measures: Non-numerical qualitative measurements are based on comparison analysis or subjective assessment. Among them are Nearest Neighbors, Rapid Scene Categorization, Rating and Preference Judgment, Mode Drop and Mode Collapse Evaluation, and Network Internals Investigation and Visualization. The most popular method of these is Rating and Preference Judgment, which entails examining and assessing the produced pictures by hand. Human participants are asked to rank or contrast models according to how accurate or lifelike the produced images seem in these investigations. A more intuitive understanding of the GAN's performance is provided by this type of practical assessment, which can reveal insights that statistics alone cannot.

There is still no consensus on the most effective method for assessing GANs. Quality, diversity, and realism are only a few of the features of picture production that are the subject of several measures, and no one score can encompass them all. However, by contrasting the statistical characteristics of produced and actual images, some measures, such as the Frechet Inception Distance (FID), have gained popularity since they provide a more impartial perspective. An effective assessment technique should be able to distinguish between authentic and fake images, identify problems such as mode collapse, which occurs when the generator generates outputs that are extremely similar, and detect overfitting, which occurs when the generator just replicates the training data. We should expect increasingly sophisticated and trustworthy methods to evaluate GAN performance as the field develops.

However, when evaluating GANs in medical imaging, researchers still frequently rely on conventional pixel-wise measurements like Mean Squared Error (MSE) or Peak Signal-to-Noise Ratio (PSNR). Ironically, GANs were created to get around the drawbacks of these measures, which frequently fall short of capturing the finer features or perceived quality of pictures. Another problem is that many of these measures depend on comparisons with ground-truth images, which is not always feasible in semi-supervised or unsupervised environments. Because of this, it is challenging to assess GANs in jobs where ground-truth data may be lacking or insufficient, such as image synthesis or reconstruction.

The difficulty is increased by the fact that GANs are notoriously difficult to train because of their overall instability and unpredictability in initialization and optimization. This implies that in order to accurately assess their effectiveness, we require certain measures, as mentioned in [266]. Metrics that emphasize the clinical utility of produced images, such as how well they support diagnosis, might be significantly more significant in the field of medical imaging than conventional ratings. Regretfully, the research examined here have not looked at these customized measures too much. Future research should focus on improving assessment techniques since doing so will not only enhance our ability to evaluate GANs but also increase their usefulness and dependability for actual medical applications.

6. Privacy and Credibility Issues in Data Generated by GANs

Significant privacy issues and questions about the reliability of the produced data are brought up by the usage of GANs. The possibility that GANs will unintentionally remember and replicate particular details from the training data, raising the possibility of sensitive information leaking, is a major privacy concern. In medical imaging, for instance, if a GAN model were trained on a collection of patient scans, it may produce pictures that contained recognizable private information, jeopardizing patient privacy and breaking data protection laws. Since synthetic data does not always accurately reflect real-world data distributions, trustworthiness is still another crucial issue. This calls into doubt the clinical or operational usefulness of data generated by GANs, especially in high-stakes applications like diagnostics where even little mistakes can have a big impact. It is frequently necessary to do thorough validation, be open about the constraints of the data produced, and conduct thorough testing against real-world datasets in order to ensure reliability. To address these concerns, privacy-preserving strategies like secure federated learning and differential privacy are being investigated; nonetheless, building confidence in synthetic data is still a significant obstacle that requires further study and regulatory supervision.

7. Real-World Applications of GANs in Brain Imaging: Scenarios and Case Studies

GANs have been deployed in real-world applications for brain analysis, particularly in medical imaging and neuroscience research. While many applications are still in the research or clinical trial phase, some have already been integrated into clinical workflows or are being actively used in healthcare settings. Below are examples of real-world deployments and case studies where GANs are making an impact in brain analysis:

Synthetic Data Generation for Rare Disease Analysis

Training AI models to detect rare brain conditions (e.g., gliomas, multiple sclerosis lesions) using synthetic data. For example, NVIDIA Clara AI: NVIDIA's healthcare platform uses GANs to generate synthetic brain MRI scans for training AI models in hospitals where patient data is scarce [267]. This has been deployed in partnerships with institutions like the Mayo Clinic to improve tumor segmentation models. This approach has been particularly useful in developing models for rare diseases, where real-world data is limited.

Super-Resolution MRI in Alzheimer's Diagnosis

Enhancing low-resolution MRI scans to improve visualization of brain structures like the hippocampus. For example, Alzheimer's Disease Neuroimaging Initiative (ADNI): Researchers have integrated GAN-based super-resolution tools into ADNI's pipeline to enhance MRI scans for early Alzheimer's detection [268]. Additionally, Siemens Healthineers: Collaborated with academic hospitals to deploy GAN-powered MRI reconstruction tools (e.g., Deep Resolve) on Siemens scanners, reducing scan times while maintaining diagnostic quality [269].

Cross-Modal Synthesis for Radiation Therapy Planning

Generating synthetic MRI scans from CT images to improve brain tumor targeting. As MD Anderson Cancer Center uses GANs to synthesize MRI-like images from CT scans for patients who cannot undergo MRI (e.g., those with implants), streamlining radiation therapy planning [270]. Also, RaySearch Laboratories integrated GAN-based tools into their RayStation treatment planning system to reduce reliance on multiple imaging modalities [271].

Noise Reduction in fMRI for Decides Monitoring

Removing motion artifacts from fMRI scans to improve brain activity mapping. GANs have been used in fMRI studies to remove motion artifacts caused by patient movement during scans. This has improved the reliability of brain activity mapping, which is crucial for research in neuroscience and clinical applications like epilepsy monitoring. For example, BrainVoyager a neuroimaging software suite that incorporates GANs for preprocessing fMRI data, used in research labs worldwide [272].

GANs for Stroke Rehabilitation Prediction

Simulating brain recovery patterns to personalize rehabilitation strategies by using GANs to predict post-stroke recovery trajectories by analyzing MRI scans, enabling tailored rehabilitation programs. Arterys a cloud-based medical imaging platform that employs GANs to model stroke outcomes, deployed in partnership with hospitals like Stanford Health Care [273].

Ethical and Regulatory Considerations

Addressing challenges in deploying GANs in clinical settings is essential. The U.S. FDA has cleared GAN-based tools like Subtle Medical's SubtleMR, which enhances brain MRI quality using GANs. It is clinically deployed in over 100 imaging centers [274]. In addition, EU's GDPR Compliance hospitals in the EU use GANs to generate synthetic data for research while adhering to strict patient privacy laws [275][276].

8. Discussion

Recent years have seen a huge increase in the usage of GANs in research; the sections above describe how GANs function, their various variations, and their uses in brain image processing. **Fig. 5** illustrates that around 39% of these researches concentrate on brain image synthesis, with the most prevalent use case being cross-modality or conditional synthesis shown in **Fig.6**. The reason for this is that GANs are especially adept at creating one kind of brain image from another, which is highly beneficial for medical imaging.

The most often cited imaging method in GAN-related research is MRI because of the large number of publicly accessible MRI datasets and the time-consuming nature of gathering many MRI sequences. Patients and physicians can save a great deal of time and money by using GANs to efficiently generate one sequence from another. The adaptability and promise of this technology in increasing brain image analysis are demonstrated by the several innovative GAN-based techniques that researchers have presented for both unconditional and conditional image synthesis.

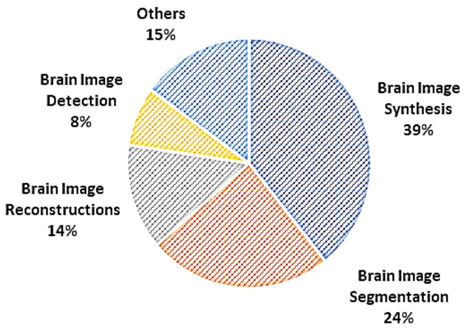

Figure 5. Brain imaging GAN-Based Studies

The efficacy of GAN-based methods frequently prompts doubts and calls for more research. For example, research such as that conducted by Frid-Adar et al. and Chuquicusma et al. has demonstrated that artifacts in the created samples can make it reasonably straightforward to discern between genuine and synthetic images in visual Turing tests [34] [35]. Furthermore, it might be difficult to get exact alignment across several imaging modalities, such CT and MRI. In an effort to address this, Nie et al. [61] combined adversarial feedback from a discriminator with voxel-wise loss from a CNN regression to produce more realistic synthetic CT images from MRI. For training, this approach still requires ideally aligned MR-CT pairings, which are not always accessible.

Wolterink et al. [60] suggested employing CycleGANs for MR-to-CT synthesis in order to get around the requirement for paired data. A forward CycleGAN is trained to convert MR images into CT and back to MR, and a reverse CycleGAN is trained to convert CT images into MR and back to CT. The model is more adaptable and useful because of its cyclic consistency, which enables it to function without paired training data. Notwithstanding these developments, there are still issues with the artificial realism of images, artifacts, and other characteristics that set GAN-generated samples.

The wider effects of these parameters on the performance and dependability of GAN-based models are still unclear, despite the fact

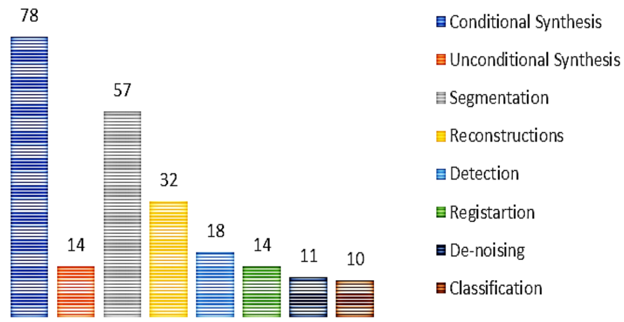

Figure 6. Numbers of Brain imaging GAN-Based Studies in Different Application

that GANs have shown promise for data simulation and augmentation in tasks like classification and segmentation. To find out how these factors affect GANs' overall efficacy in medical imaging and other fields, more investigation is required.

Approximately 24% of the research concentrated on brain image segmentation due to the increasing popularity of image-to-image translation frameworks. In these situations, the generator is able to keep fine control over form and texture because to adversarial training, which makes it a potential method for segmentation tasks. The discrepancy between reference segmentations' discrete label masks and the generator's continuous probability values for every voxel and class, however, presents a problem for adversarial segmentation techniques. The discriminator may learn to take use of this difference instead of concentrating on enhancing the segmentation quality when it is taught to distinguish between the continuous outputs of the generator and the discrete reference masks. This demonstrates a significant drawback of using adversarial networks directly for segmentation tasks and emphasizes the necessity of creative fixes to close this gap.

Designing the discriminator to assess the input image and its segmentation is a practical way to overcome this difficulty. An adversarial encoder network was suggested by Xue et al. [27] that looks at the reference (ground truth) segmentation in addition to the input image and the projected segmentation. They added a scalar adversarial loss based on the L1 loss between the multi-scale features that were extracted from the input and the projected segmentation. This method showed notable gains in accuracy and proved to be very successful for brain tumor segmentation in MRI.

In a similar vein, Kamnitsas et al. [141] used domain adversarial networks to tackle the problem of domain changes between MR collection procedures. By adding multi-connected adversarial networks to the basic design, they improved it and made it possible for the domain discriminator to process data from several feature extractor layers. A more resilient domain classifier resulted from this approach, which also improved the gradients returning to the core network and increased domain adaption. They also demonstrated how 3D CNNs for volumetric image processing may use this domain adversarial training technique. Their approach proved useful in managing domain changes when it was successfully tested on multi-modal MR brain scans of traumatic brain injuries, where one of the modalities varied between datasets. Both papers show creative approaches to using adversarial training for segmentation tasks, whether it is to handle domain changes in multi-modal data or to increase segmentation accuracy through multi-scale feature analysis. These methods highlight adversarial networks' adaptability and potential in medical image processing.

Brain image reconstruction accounted for about 14% of those surveyed studies. While several GAN architectural modifications are suggested, it appears that ResNet is the most common generator architecture. In addition to the adversarial loss, most of the methods enforce a pixel-wise loss. In order to retain critical information in the missing data reconstruction, other loss functions are also applied. GANs can have satisfactory accuracy in the reconstruction of missing data in medical images due to their synthesis abilities. In comparison, for the quantitative assessment of proposed approaches, much of the analysis for image reconstruction uses conventional metric system methods. Particularly where GAN introduces additional losses, in the absence of a standardized reference metric, there is difficulties in improving the visual standard of an image.

In order to fully analyze the quality of GAN-generated images, Armanious et al. [203] has suggested that MedGAN evaluations should incorporate both subjective assessments by subject matter experts, such as seasoned radiologists, and perceptual analysis. Although this method offers in-depth insights, it has some serious disadvantages, including being costly, time-consuming, and challenging to generalize in other situations. This calls into doubt the validity and applicability of such measurements for broad use.

The possible loss of data fidelity in GAN-based techniques is another significant issue, especially in unpaired training situations. GANs sometimes have trouble preserving information from small or subtle aberrant areas during cross-domain image-to-image translation, which can be important in medical imaging. Notwithstanding these drawbacks, the results of the experiments under evaluation indicate that GANs execute faster and more accurately than alternative techniques for tasks like data reconstruction. This demonstrates both their promise and the necessity of more improvement to meet current obstacles.

A further 8% of brain imaging studies are concerned with anomaly detection. In contrast to previous applications, papers proposed for anomaly detection by GANs have more structural sophistication because they gain from multiple facets of GANs. In particular, in detection methods, the importance of the discriminator is emphasized. While significantly lowering the amount of training data, the aforementioned techniques demonstrate good effectiveness in anomaly identification. The trials' diverse datasets and metrics, however, make it difficult to compare the approaches in a practical way. In the unpaired image transfer based on CycleGAN, lesions inside an image may be excluded because of the distribution matching effect if the intended distribution is created from medical images without pathology. It is also possible to use this negative impact to discover abnormalities if the source and target domains are of the same imaging modality and just differ in terms of normal and pathological tissue Sun et al. [57]. Lastly, the little amount of research that is still available on classification, registration, and de-noising makes it challenging to draw any conclusions.

The remining 15% brain imaging studies is aggregating the studies that have been carried out on brain image classification, registration and denoising as shown in Figure2. Despite being extensively used for tasks like as image synthesis and brain imaging segmentation, GANs' application in classification, registration, and denoising is restricted because of a number of unique difficulties. Because GANs are primarily built for creating new data rather than differentiating between classes, they are not well suited for classification jobs that need exact class separation. While several versions try to include classification skills, such auxiliary classifier GANs (AC-GANs), these models frequently lack the accuracy and durability needed for trustworthy diagnostic application. The difficulty of registration is in matching multi-modal or multi-timepoint brain pictures, which calls for extremely precise spatial changes.

In addition, GANs are not built to tackle spatial alignment challenges and might not be precise enough, researchers prefer more conventional approaches, such non-rigid registration techniques, which yield more dependable results. Finally, because the adversarial training process does not naturally emphasize maintaining tiny, diagnostically significant features, GANs may find it difficult to remove noise from images without unintentionally creating artifacts or deleting important details. Because of this, researchers are concentrating on models that are especially tailored for the complex needs of classification, registration, and denoising in brain imaging, leaving the potential of GANs in these domains underutilized.

Finally, GANs lack meaningful metrics to determine the performance of GANs. It is therefore very difficult to compare various variants of GANs and still based on the visual evaluation of the generated images. Furthermore, due to lack of rigorous and reliable criteria, it is difficult to determine which are the best GANs algorithms. A reasonable evaluation is required because it will allow a very wide variety of appropriate algorithms to be identified. Also, to have the best algorithms and their understanding and which algorithms in practice would make a significant difference [266]. Researchers have suggested different evaluation methods for GANs in order to resolve the above-mentioned problems [55]. In addition, various measurement criteria are preferred for different implementations, as different applications need different trade-offs for various metrics. A mixture of training and evaluation metrics for the target application is critical to consider.

9. The Impact of GANs Application in the Healthcare Domain

Generative Adversarial Networks (GANs) are revolutionizing medical imaging by improving diagnostic precision and addressing data scarcity. For instance, GANs enable super-resolution enhancements, transforming low-quality CT or MRI scans into high-resolution images, which is particularly impactful in resource-limited settings where advanced imaging equipment is unavailable [277]. This capability reduces reliance on costly hardware and expands access to accurate diagnostics globally. Additionally, GANs facilitate tasks like lesion segmentation and tumor detection by generating synthetic data that augment training datasets, thereby improving the robustness of AI models used in radiology and pathology [277]. Such advancements not only elevate diagnostic confidence but also democratize access to advanced healthcare tools, bridging gaps between high- and low-resource regions.

Additionally, GANs are pivotal in synthesizing patient-specific medical data, enabling personalized treatment strategies while mitigating privacy concerns. By generating synthetic yet realistic patient images, GANs allow researchers to create diverse datasets for training predictive models without compromising sensitive information [278]. For example, GAN-based image-to-image translation can convert MRI scans into synthetic CT images, aiding in radiotherapy planning without exposing patients to additional radiation. Beyond imaging, GANs are used in predictive analytics, such as forecasting patient readmission risks by augmenting imbalanced datasets with synthetic samples, which improves model accuracy in identifying high-risk individuals. This synthesis of multimodal data supports tailored interventions, from precision oncology to chronic disease management, fostering a shift toward individualized care paradigms [278].

While GANs offer transformative potential, their deployment raises ethical and operational challenges. Biases in training data can propagate into synthetic outputs, potentially exacerbating health disparities if underrepresented populations are excluded from datasets [279]. For instance, GANs trained on homogeneous data may fail to generalize across diverse patient demographics, leading to inequitable diagnostic outcomes. Moreover, the lack of standardized validation frameworks for synthetic data poses risks in clinical adoption, as inaccuracies could compromise patient safety. Regulatory bodies must establish guidelines to ensure transparency, fairness, and accountability in GAN applications. Collaborative efforts between technologists, clinicians, and policymakers will be critical to harness GANs' benefits while addressing ethical pitfalls, ensuring these tools align with equitable and patient-centered healthcare goals [280]. These impacts underscore GANs' dual role as both a catalyst for innovation and a subject of scrutiny, demanding balanced integration into healthcare systems to maximize societal benefit.

10. Research Directions and Key Research Pathways

The redesign network architectures, adding new loss functions, and creating alternative optimization algorithms are the three primary strategies that recent research has suggested to overcome the difficulties with GANs. As demonstrated by research such as in [37] [39] [43] redesign network architectures seek to optimize the structure of GANs. In works like [40] [44], new loss functions are put forth with the goal of enhancing output quality and training stability. To improve convergence, various optimization methods adjust or regularize the optimization procedure. Many creative approaches have been developed to address the inherent difficulties of GANs as a result of the increasing amount of study on the subject, opening the door for more reliable and efficient models.

In addition, we also look at more general topics for further research to expand on previous findings. In order to overcome frequent problems including unstable training, disappearing gradients, and mode collapse, a number of academics have suggested solutions, including creating more resilient network designs, regularizing goals, improving training techniques, and adjusting hyperparameters. However, because these issues are intrinsically linked, these solutions frequently involve trade-offs, especially between variety and image quality. In order to develop more reliable and efficient GAN models for medical imaging applications, future research will need to carefully weigh these trade-offs.One potential path for study might be to focus on image quality without suffering from the poor variety of images. In order to explore more tractable formulations and to make training stable and transparent, another important research path is to provide a theoretical framework for managing problems in the training phase of GANs. In addition, it was shown to approach the creation of solutions with algorithmic enhancements for improved performance rather than better precision, as the majority of related works largely stressed the achievement of state-of-the-art accuracy.

Complex geometric connections are often overlooked by current data synthesis methods in medical imaging, which limits their use in modalities like MRI, CT, and ultrasound where maintaining structural integrity is essential. The next generation of GAN designs will probably concentrate on incorporating sophisticated geometric modeling skills in order to get beyond these restrictions. For example, architectures such as Spatial GANs (SAGANs) and Geometric GANs (GeoGANs) have demonstrated potential in producing data that more closely resembles the anatomical structures and spatial connections seen in actual medical imaging. In medical imaging, where even little spatial irregularities can affect the validity of a diagnosis, these models promote spatial consistency and continuity by utilizing spatial attention processes and customized loss functions.

Furthermore, bidirectional mapping capabilities are introduced by Bidirectional Generative Adversarial Networks (Bi-GANs) and Invertible Conditional GANs (IcGANs), which enable high-quality synthesis while maintaining geometric properties unique to the anatomy of interest. In order to efficiently recreate genuine pictures while synthesizing new ones, bi-GANs, for instance, use an encoder network to build a shared latent space. This makes the model extremely versatile for complicated tasks like multi-modal image translation and alignment. In applications like MRI to PET translation, where anatomical alignment is crucial, IcGANs further improve this by conditioning on certain geometric features, enabling fine control over synthetic picture qualities.

Besides, by resolving issues with registration and alignment, models such as Spatially-Conditioned GANs (SC-GANs) and Deformable GANs offer an extra degree of refinement. The ability of SC-GANs to conditionally produce images in response to spatial limitations is especially useful for registration tasks that call for the alignment of structures across several imaging modalities. Conversely, deformable GANs use deformable convolutional layers that adjust to the spatial geometry of the input data, making them more useful for creating pictures that need precise spatial distortion, such as in some forms of elastography or ultrasound imaging.

GANs can better manage the many geometric properties and correlations present in many medical imaging applications by merging these specific designs. This makes them reliable tools for real-time clinical applications that demand accuracy and spatial coherence, in addition to increasing their potential for producing synthetic data. These advancements open the door to more extensive GAN applications, from robust synthetic training data that satisfies the exacting validation requirements of medical imaging to realistic anatomical simulations.

Although GANs were first created as entirely unsupervised models, real-world applications have demonstrated that adding some labeled input greatly improves the quality and control of their creation. This method, which is frequently used with Semi-Supervised GAN (SS-GAN) architectures, shows that even a small number of labels may direct the model to produce outputs that are more precise and significant. For example, by anchoring the model to these important properties, a medical GAN might significantly increase the therapeutic relevance and variety of the produced images by using a small number of annotated photos of certain brain pathologies or anatomical locations.

One well-known example is the Auxiliary Classifier GAN (AC-GAN), which adds an auxiliary output to predict labels in addition to creating images. Even with sparse labels, the generator may learn more focused features with the aid of an auxiliary prediction, resulting in higher-fidelity images that correspond to the designated classes. In a similar vein, the Semi-Supervised GAN (SS-GAN) is an extension of conventional GANs that incorporates a discriminator that divides images into labeled and unlabeled categories. This improves the discriminator's capacity to differentiate between generated and realistic images, thereby improving the quality of the generator. A different strategy is the Label Propagation GAN (LP-GAN), which propagates labels using pseudo-labeling techniques on a tiny labeled set. This successfully amplifies the influence of limited labeled data without having to pay the high costs of complete labeling.

Advanced models that can more adaptably and dynamically use both labeled and unlabeled data are probably where GAN integration with semi-supervised learning is headed. Examples of potential solutions are Self-Training GANs and Few-Shot GANs, which allow models to repeatedly refine themselves after self-generating labels based on the labeled subset. Furthermore, Conditional GANs (cGANs) may be used in semi-supervised contexts to generate varied, realistic data that generalizes effectively while conditioning on a restricted number of labels for certain features. By improving model resilience and lowering reliance on large labeled datasets, this semi-supervised method may revolutionize the application of GANs in areas where labels are expensive or hard to get, such as uncommon medical illnesses or highly specialized diagnostic imaging.

The use of GANs for text production is being investigated more and more in the context of semi-automated medical report generation. Attentional GANs and Transformer-based GANs are two models that have the ability to provide thorough, diagnostically relevant image reports. By using attention methods to rank disease-critical information in the output text, these designs make sure that every report stays focused on important diagnostic markers that are pertinent to the particular imaging scenario.

In order to provide structured and contextually correct text outputs that closely match physician standards, Attentional GANs, for instance, can weigh the significance of characteristics associated with diseases such as tumors, lesions, or fractures. Additionally, because Transformer GANs can capture long-range dependencies within complex medical narratives, they are especially well-suited for the nuanced task of report generation. This is because they integrate transformer layers, which are known for their strengths in sequence modeling, and produce reports that reflect the coherence and detail of documents authored by clinicians.

Looking toward the future, to improve these designs to satisfy clinical requirements, cooperation between medical experts and AI researchers is essential. Doctors' knowledge of data annotation and clinically relevant feature selection is crucial, particularly when it comes to spotting subtle imaging patterns that automated algorithms could miss. Their participation guarantees that the attention mechanisms of the GAN are adjusted to the most diagnostically important characteristics, hence improving the quality of the reports that are produced. By including physician input into model improvement and diagnostic validation, this multidisciplinary synergy might possibly revolutionize physician roles and maximize the effect of GANs in medical imaging and report creation. As these technologies advance, GAN-assisted reporting may help enable a more accurate and efficient diagnostic process by lowering effort and improving report accuracy and consistency.

Finding suitable measures to assess the consistency and quality of samples produced by GANs is, last but not least, a major difficulty. Determining how to evaluate this realism is not simple, even though many research use adversarial techniques to create realistic samples.

It becomes challenging to compare various implementations in the absence of uniform assessment criteria. Since various applications necessitate distinct trade-offs between parameters like picture quality, variety, and clinical relevance, a benchmarking framework is crucial. Developing a set of training and evaluation criteria appropriate to the intended application is essential to addressing this issue and guaranteeing a fair and insightful evaluation of GAN performance.
Following are summarization the Key Research Pathways:

Geometric Consistency in Medical Data Synthesis

Current GANs often fail to preserve complex anatomical geometries in modalities like MRI, CT, and ultrasound, where structural integrity directly impacts diagnostic validity. Emerging architectures address this limitation by integrating spatial and geometric priors:

- Spatial Attention Mechanisms: Models like Spatial GANs (SAGANs) use attention layers to enforce spatial coherence, producing anatomically plausible structures.
- Bidirectional Mapping: Bi-GANs and Invertible cGANs (IcGANs) employ encoder-decoder frameworks to map between latent spaces and image domains, preserving geometric fidelity during tasks like MRI-to-PET translation.
- Deformable Convolutions: Deformable GANs adaptively adjust kernel receptive fields to model tissue elasticity and distortions, enabling applications in ultrasound and elastography.

These innovations enhance GANs' ability to maintain spatial relationships, making them viable for tasks requiring precise alignment (e.g., multi-modal registration) and synthetic data generation for rare pathologies.

Semi-Supervised Learning for Enhanced Generalization

Incorporating limited labeled data into GAN training has proven effective for improving output controllability and clinical relevance:

- Auxiliary Classifiers (AC-GANs): By predicting labels during generation, AC-GANs anchor outputs to clinically meaningful features, such as tumor morphology.
- Self-Training Architectures: Few-shot and label-propagating GANs (LP-GANs) amplify small labeled datasets through pseudo-labeling, reducing dependency on costly annotations.
- Hybrid Architectures: Transformer-GANs and attention-based models (e.g., Attentional GANs) integrate sequence modeling for tasks like automated report generation, prioritizing diagnostically critical features through learned attention weights.

Future semi-supervised frameworks could enable dynamic label refinement and domain adaptation, particularly for rare diseases or specialized imaging protocols.

Standardized Evaluation and Clinical Validation

A major unresolved challenge is the lack of standardized metrics for assessing GAN outputs in medical contexts. Current adversarial metrics (e.g., Fréchet Inception Distance) often fail to capture clinically relevant features. To address this:

- Domain-Specific Benchmarks: Develop task-specific evaluation criteria (e.g., structural similarity index for MRI, lesion consistency scores) co-designed with clinicians.
- Multi-Dimensional Assessment: Balance metrics across quality (e.g., SNR, resolution), diversity (e.g., coverage of anatomical variations), and clinical utility (e.g., diagnostic accuracy of synthetic-augmented datasets).
- Validation Pipelines: Implement rigorous human-in-the-loop validation, where radiologists assess synthetic images and reports for diagnostic plausibility.

Collaborative Roadmap for Clinical Translation

The next frontier lies in bridging AI innovation with clinical expertise:

- Clinician-AI Collaboration: Integrate physician insights into feature selection, model training, and output validation to ensure outputs align with diagnostic workflows.
- Regulatory Alignment: Establish guidelines for synthetic data usage in training and validation, addressing ethical and regulatory concerns.
- Real-World Deployment: Optimize models for edge devices and PACS integration, ensuring compatibility with existing clinical infrastructure.

By addressing these challenges, GANs could revolutionize medical imaging—from enabling low-cost synthetic training datasets to assisting in real-time diagnostics and personalized treatment planning.
We can summarize these fsuture revolutionize to three main aspects:
1. Quality-Diversity Synergy: A critical goal is improving image quality without sacrificing diversity. Current methods often prioritize one at the expense of the other, limiting their clinical utility. Novel architectures that decouple these objectives or introduce adaptive loss functions could resolve this tension.
2. Theoretical Frameworks: Developing rigorous mathematical frameworks to analyze GAN training dynamics (e.g., convergence guarantees, equilibrium conditions) is essential for stabilizing training and improving interpretability. Such frameworks could unify disparate solutions and guide the design of more tractable optimization landscapes.
3. Algorithmic Innovation Over Precision: While many studies focus on achieving state-of-the-art accuracy, future efforts should emphasize algorithmic robustness and computational efficiency. This shift would better align with clinical workflows, where reliability and speed are paramount.

11. Conclusion

Generative Adversarial Networks (GANs) have gained significant popularity not only due to their ability to learn intricate, non-linear mappings between latent and data spaces but also because they can leverage large volumes of unlabeled image data, which are often underutilized in deep representation learning. This review paper provides an in-depth discussion on the various applications, architectures, available brain imaging datasets, and unresolved research challenges of GANs in medical image processing for brain-related disorders. Despite their potential, GANs are notoriously difficult to train, with challenges such as instability, non-convergence, and mode collapse posing substantial obstacles. Addressing these issues should remain a focus of future research. Overcoming the difficulties associated with GANs may be possible by designing more efficient models through the adoption of suitable network architectures, activation functions, and optimization strategies.
Although several GAN variants with distinct features have been introduced, challenges remain. There is still significant room for improving the theoretical foundations and methodologies behind GAN training. Additionally, the growing capabilities of deep networks present exciting opportunities for novel applications in brain imaging research. Adversarial guidance, for instance, can assist in generating images that more closely resemble real images in the target domain, enhancing their potential for clinical applications in tasks such as image synthesis or segmentation, where designing an efficient loss function is particularly challenging. To achieve the consistency and reliability required for GAN-based imaging techniques to be widely adopted in clinical practice, continued research is essential.

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