

# Few Shot Cross-Domain Image Generation for Data-Scarce Domains - A Medical Imaging Case Study

## Introduction:

Deep learning excels at classification, segmentation, and detection—especially when trained on large, balanced datasets (e.g., ImageNet [16]). In practice, assembling such datasets in domains like manufacturing inspection, materials science, remote sensing, and medical imaging is expensive and time-consuming. Data scarcity and imbalance lead to overfitting and weaker generalization [5]. Many domains inherently yield limited labeled data (e.g., pediatric medicine, rare defects) and evolving task sequences frequently require additional training [4,5].

Generative AI tackles this problem in a principled way. Traditional models like Generative Adversarial Networks (GANs) and Latent Diffusion Models (LDMs) get trained on a larger dataset and can be guided in such a way to generate data in the same or a different domain where the data is scarce [14,1-3]. This method is called **cross-domain image generation**. Traditionally basic augmentation techniques (eg., rotations, flips or noise injection) have been applied to datasets to increase the number. However, cross-domain image generation tests whether structural or statistical features learned in one context can be **repurposed** to another [2,3,6,10]. Many other ways have been introduced to tackle this problem in recent studies including Data-efficient generative models, Few-shot generative adaptation, one-shot image generation [1,6,10]. Collectively, these approaches aim to reduce dependence on large datasets while maintaining image fidelity and functional utility. Together these studies indicate that cross domain image generation remains promising, and generative AI can play a crucial role in enabling robust learning data-scarce environments across not only multiple disciplines [1-3,5].

Among data-scarce settings, **medical imaging** is especially consequential [4-5]. Brain cancers, particularly diffuse glioma, are among the most severe pediatric malignancies in the modern age among children aged 5-10 years. Once a child is diagnosed, survival generally only ranges from 8 to 11 months. Early detection is difficult and labeled data is limited. This study investigates whether generative models can help alleviate this scarcity by synthesizing realistic, anatomically coherent MRIs for underrepresented conditions.

We study a **general cross-domain framework** and validate it via a medical **case study**: train a **conditional GAN (cGAN)** on a data-rich **glioblastoma (GBM)** MRI source domain, then condition it to synthesize **diffuse glioma** images in a data-scarce target domain. The hypothesis is that related diseases within the same organ share transferable structure that a generative model can exploit to produce useful synthetic data.

MRI image synthesis presents unique challenges because of its **spatial-temporal complexity** and the need to preserve **3-D anatomical continuity** across slices. Unlike 2-D photographic data, MRI volumes contain rich contextual information in three dimensions, meaning that inconsistencies between adjacent slices can distort anatomical realism [3]. This motivates careful conditioning (e.g., masks) and standardized preprocessing to stabilize training.

## Research gap and hypothesis:

Prior work demonstrates few-shot generative transfer mostly in natural images or within a single disease subtype. **This study tests whether a model trained on a data-rich tumor type (GBM) can synthesize realistic and diagnostically useful MRIs for a related, data-scarce tumor (diffuse glioma) under few-shot and zero-shot conditions.** We position this as a general framework that can extend beyond medicine to other low-resource domains.

## **Literature Review:**

Over the past decade, with the rapid improvements of deep learning models and state of art models like ImageNet [16] and Convolutional Neural Networks (CNN's), the performance for tasks like segmentation, classification and detection have improved significantly. However, most of these have been tested significantly on labeled abundant datasets. In the real world-applications having abundant labeled datasets is very expensive and restricted especially in domains like medical imaging [2,5], remote sensors, manufacturing inspections.

To mitigate this problem, traditional approaches like image augmentation have been looked at more often. These steps included image cloning, image rotation clockwise and anti-clockwise and at different angles. Regions of interest (ROIs) in the images were manually displaced or augmented to increase the sample count [2,3]. But **this process did not add new pathology diversity**; it **replays** existing distributions and still **overfits** when the target class is rare. Hence augmentation cannot substitute for **distribution-level transfer** from a data-rich source.

A more powerful alternative emerged with **Generative Adversarial Networks (GANs)** (Goodfellow et al., 2014). GANs employ two competing neural networks - a generator and a discriminator - trained in opposition to synthesizing realistic samples. This framework enables the model to learn high-dimensional latent distributions and produce diverse, data-driven augmentations. Over time, multiple GAN variants have been introduced:

- **DCGAN (2015)**: improved stability for image generation.
- **WGAN (2017)**: addressed mode collapse through Wasserstein loss.
- **CycleGAN (2017)**: enabled *unpaired* image-to-image translation.
- **PGGAN (2018)** and **StyleGAN (2019)**: enhanced image resolution and controllability.
- **SAGAN and RANDGAN**: focused on spatial attention and segmentation-driven generation.

Methods that adapt to a **pretrained source model** work best when the target domain **resembles** the source and when **some target images** are available. Neither is guaranteed for **cross-subtype MRI**.

Recently, **Diffusion Models (DDPMs and LDMs)** have overtaken GANs in image fidelity, using iterative denoising processes to generate high-quality images with stable convergence [1].

There has been a good amount of research done on generative AI techniques in the medical domain. But pediatric cancer types remain underexplored [2,4,5]. With rapid advancements in deep learning. Much research is focused on tumor detection. Before 2012 most detections models included traditional machine learning based models like SVM (Support vector machines), KNN (K-means nearest neighbor). But after 2012 - CNN (Convolutional Neural network) has been regarded as one of the best models with utmost accuracy to successfully detect any tumors [16,4,5]. Early detection remains challenging, partly because people seek imaging only when symptoms appear and because labeled datasets are limited [2,5].

One other problem people were facing was detecting the overlapping region of the tumors. for example, it is hard to know if the tumor has affected any other regions within the organ with the likelihood of cancer cells spreading to other tissues. Since the MRI's are bulky in volume, it is physically impossible to segment the images layer by layer. To overcome this problem, professionals have introduced U-NET-based segmentation architecture [15].

**Table 1** summarizes representative few-shot/cross-domain generators and medical applications, focusing on **assumptions** and **what they validate**.

1. **Domain generalization gap:** validated mostly on natural/curated images; limited evidence for **MRIs with anatomical constraints**.
2. **Utility gap:** many papers stop at **FID/SSIM**; **downstream task gains** are rarely quantified.
3. **Transfer scope gap:** **no full cross-subtype MRI generation** shown with **source-only** training (few/zero-shot) [1-13].

Study / Year	Model / Focus	Main Contribution	Limitations / Critique
<b>Wang et al. 2019 (MineGAN) [7]</b>	Latent “miner” network for few-shot GAN adaptation	Efficient transfer by sampling relevant latent regions from source GANs	Assumes source latent space already covers target domain; heuristic hyperparameters; not tested on medical data; no downstream validation
<b>Xiao et al. 2022 [17]</b>	Cross-domain alignment with relaxed structural correlation	Maintains spatial relationships during few-shot transfer	Correlation assumptions break for structurally different domains; compressed latent space reduces detail; no medical testing
<b>Duan et al. 2023 (WeditGAN) [9]</b>	Latent-space relocation using $\Delta w$ offsets	Lightweight, one-to-one mapping maintaining diversity	Linear latent shift oversimplifies domain change; untested on MRI; lacks downstream performance analysis
<b>Mondal et al. 2023 [18]</b>	Inference-stage latent module for multi-domain adaptation	Adapts pretrained GANs without retraining full generator	Limited flexibility; relies on heuristic latent modules; tested only on photographic datasets
<b>Wu et al. 2022 (D3T-GAN) [8]</b>	Knowledge distillation + latent alignment	Improves few-shot GAN transfer via data-dependent mapping	Requires good latent inversion; domain dissimilarity limits success; lacks medical validation
<b>Ojha et al. 2021 (Cross-Domain Correspondence) [10]</b>	Preserves relational structure across domains	High diversity in extreme low-data settings	Relational assumption fails for structurally constrained data (e.g., MRIs); evaluation limited to FID
<b>Park et al. 2021 [11]</b>	GAN for IDH-mutant glioma synthesis	Improved classifier accuracy (~90 %) vs. real-only (~85 %)	Limited to one molecular subtype; still needs hundreds of target samples; no true cross-subtype test
<b>Moon et al. 2024 [12]</b>	Score-based diffusion for glioma augmentation	110 k synthetic MRIs improved AUC = 0.94, outperforming radiologists	High compute cost; strong domain overlap (same tumor type); not tested on unseen subtypes

<b>Mukherjee et al. 2022 [13]</b>	Multi-GAN ensemble with style transfer	Synthesized realistic brain tumor MRIs (SSIM $\approx 0.83$ )	Evaluated only by visual metrics; no downstream task validation
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However, in the medical domain, GANs and other generative AI techniques have not been widely applied across diverse cancer types [2,3,5]. Most existing work focuses on adult cancers, leaving pediatric diseases such as diffuse glioma largely unexplored [2,4,5]. Moreover, even when generative models are used, they typically rely on well-balanced datasets within a single disease domain [2,3,11–13]. Few studies have investigated cross-disease generation, where knowledge from one cancer type could help synthesize another related type with limited data [1,6–13]. In contrast to same-subtype augmentation (e.g., IDH-mutant glioma), **cross-subtype** synthesis forces the model to **invent** target-specific patterns from **only source structure** - a stricter test than style transfer within one class.

**Research question:** Can a model trained on data-rich **GBM** synthesize **diffuse glioma** MRIs that are **both realistic and diagnostically useful** under **few-/zero-shot** constraints?

**Claim:** Answering this tests a **general cross-domain framework** for **data-scarce** settings, with medical imaging as a stringent case.

**Research Gap:** Recent few-shot generative models have made progress in adapting a source-trained GAN to new domains with limited data (e.g., via latent-space knowledge mining in MineGAN [19], latent code relocation in WeditGAN [20], or multi-level distillation in D3T-GAN [21]). These techniques mitigate mode collapse and leverage the source domain’s learned diversity [20], but they often emphasize global realism over the target domain’s unique structural attributes. In practice, when source and target MRI distributions differ substantially (such as adult versus pediatric tumors), even state-of-the-art adaptations can produce anatomically implausible results, as models may carry over inappropriate source features into the target domain [22]. Regularization strategies that constrain the generator too tightly to its source distribution can backfire – for instance, preserving adult anatomical traits while attempting to generate pediatric tumor images leads to unnatural hybrids [22]. Even emerging score-based diffusion models face similar challenges: without special adaptation, a fine-tuned diffusion generator on scarce medical data tends to overfit, degrading image detail and diversity [23]. **Thus, as of 2025, it remains an open problem to create a generative model that can bridge significant domain shifts in medical imaging, ensuring that synthetic MRI scans of a rare tumor subtype are not only visually realistic but also faithfully reflect the target domain’s anatomical and pathological structures [24].**

## Research design and methods:

The overall main goal of this research is to explore how we can optimize cross-domain image generation across many domains [1,6–10]. The proposed method is designed to generalize to other data-scarce domains such as remote sensing, manufacturing defect detection, or material microstructure imaging [4,5]. However, this study focuses on generating diffuse glioma images from glioblastoma [11–13]. And I am going to investigate this in 2 ways: zero-shot image generation and few-shot image generation [1,6–10].

For the zero-shot setup, pretrained multimodal models such as **GLIP** or **CLIP** may be leveraged to extract semantic visual-language features that guide the CGAN generator toward the target domain, even when no target-domain samples are available. This integration allows the model to ground generative conditioning in semantic similarity rather than pixel-level correspondence, improving generalization across domains [25–27].

The methodology is divided into three main stages:

1. Data preprocessing and standardization,
2. Conditional generative model training, and
3. Evaluation of visual and functional performance [1,6–10].

Each stage is structured to maintain domain-agnostic flexibility while allowing specific implementation within the medical imaging context [2,3,5].

## Dataset:

The dataset for glioblastoma is available at <https://doi.org/10.7937/TCIA.709X-DN49> and the dataset for diffuse glioma is available at <https://doi.org/10.7937/tcia.bdgf-8v37>. The modalities include T1, T2 and FLAIR. The glioblastoma dataset contains ~828,000 image slices derived from 3D MRI volumes of multiple subjects, spanning T1, T2, and FLAIR modalities. and diffuse glioma consists of 12k images. The data types for each of them are as follows: MR, Molecular Test, Demographic for glioblastoma and MR, Measurement, Demographic, Follow-Up, Diagnosis for diffuse glioma.

Although the medical datasets have been chosen for this project, this could be generalized for other domains [4,5].

## Dataset preprocessing:

Both the glioblastoma and diffuse glioma datasets contain MRI scans stored primarily in NIfTI format, along with associated metadata such as patient demographics, molecular test results, and diagnostic information. Because these datasets originate from different studies and may vary in acquisition parameters, a consistent preprocessing pipeline is required to ensure uniformity and compatibility for training generative models [2,3,5].

- The MRI scans from the cancer archive are arranged as T1, T2 and flair. Non-image files contains demographic information which will be stored separately and be made use of when training.
- MRI intensities vary across scanners and acquisition protocols. To reduce this variability, voxel intensities will be normalized to a consistent range (e.g., [0, 1] or z-score normalization). This standardization improves model convergence and reduces modality bias [2,3].
- All volumes will be resampled to a fixed voxel dimension (e.g.,  $1 \times 1 \times 1 \text{ mm}^3$ ) and cropped or padded to a uniform spatial size (e.g.,  $64 \times 64 \times 64$  voxels). This ensures uniform input size for the generative network [2,3,5].
- For the conditioning part of the CGAN, the images should contain segmentation masks which would be extracted from glioblastoma and be fed into the CGAN model. If the segmentations of masks are not available, a U-NET may be trained to obtain them [15].
- Data augmentation steps like cloning, flipping, and rotating may be performed to keep the data consistent among all classes [2,3]. However, special care will be taken when applying rotation or spatial transformations to segmentation masks to ensure label alignment and prevent anatomical inconsistencies between masks and corresponding MRI volumes [2,3].

Through these preprocessing steps, the datasets will be standardized and normalized, enabling the conditional generative model to effectively learn mappings between glioblastoma and diffuse glioma domains [1,6-10].

## Model Architecture & Training

A Conditional GAN (CGAN) will be used to generate diffuse glioma images [14]. To achieve this, The CGAN will be conditioned using segmentation masks extracted from the glioblastoma dataset, enabling it to generate structurally plausible diffuse glioma MRI volumes from random latent vectors. The generator will receive as input (1) segmentation masks or low-resolution structural maps and (2) random latent vectors sampled from a Gaussian distribution. After the generator outputs a random noisy image, the discriminator uses a “PatchGAN” to check the realism of the image [14].

In the zero-shot scenario, GLIP embeddings can be incorporated as auxiliary conditioning vectors alongside segmentation masks, providing the model with high-level contextual cues (e.g., “diffuse glioma MRI”) derived from text–image pretraining. This allows semantic alignment between source and target domains without explicit paired data.

Loss functions:

- Both the generator and discriminator will be optimized using **Binary Cross-Entropy (BCE)** loss with the **Adam optimizer** (learning rate = 0.0002,  $\beta_1 = 0.5$ ). This configuration provides stable adversarial training and helps the generator produce anatomically plausible images [14].

## The Generator:

- The generator receives a noise vector and a condition input
- Reshape and concatenate label embedding with the input image.
- Process noise through dense layers with LeakyRELU activation.
- Reshape and concatenate label embedding with noise features.
- Use Conv3DTranspose layers to up-sample into  $64 \times 64 \times 64 \times 1$  images.
- Output layer uses tanh activation to scale pixels between -1 and 1 [14].

## The Discriminator:

- Use Conv3D layers with LeakyReLU activations from the torch framework to extract features.
- A minimum of 4 layers with 32 to 64 neurons
- Flatten features apply dropout to prevent overfitting
- Final dense layer with sigmoid activation outputs probability of real or fake [14].

## Evaluation:

To evaluate the effectiveness of the generated images and whether synthetic images contain sufficient structural features for downstream tumor classification., a **CNN-based classifier (AlexNet)** will be trained on real diffuse glioma dataset to detect and localize tumor regions [16].

- A baseline CNN classifier (e.g., AlexNet-inspired) with 3–4 convolutional layers with 32–64 neurons each, trained with **ReLU** activations and **Adam optimization (The layers and neurons altered depending on the performance later)**
- Once trained, this classifier will be tested on the **synthetic diffuse glioma images** generated by the cGAN [14].
- Comparative metrics such as **classification accuracy**, **Structural Similarity Index (SSIM)**, and **Fréchet Inception Distance (FID)** will be used to assess the quality and realism of generated data.

This approach not only validates the realism of the generated MRI scans but also measures their **utility in improving diagnostic model performance**—a crucial step toward developing reliable AI systems for rare pediatric cancers [2,3,5].

## **Optimization (Tuning hyper parameters):**

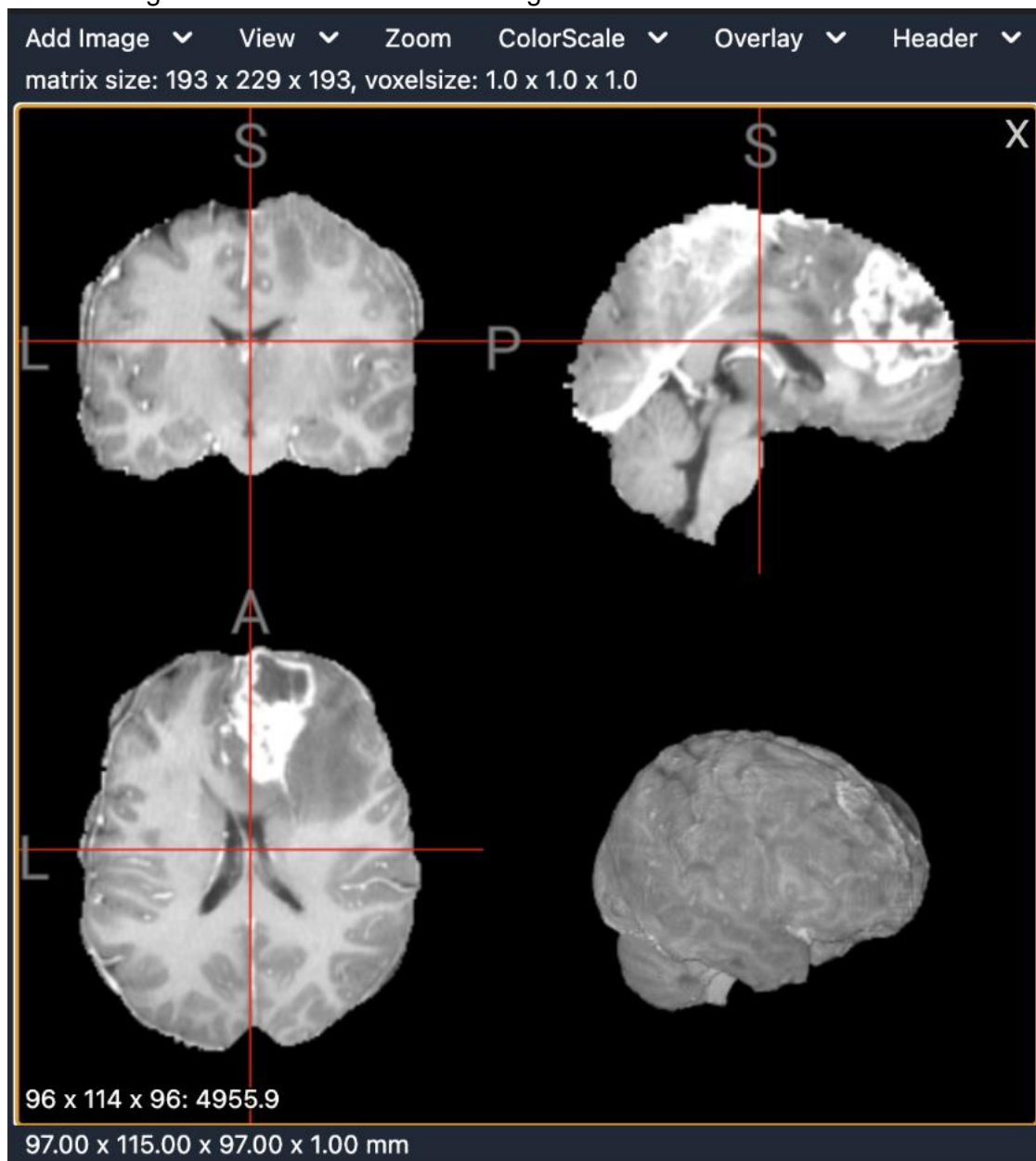
If the generated images or classifier results show significant signs of instability - such as blurring, mode collapse, or poor anatomical fidelity - hyperparameter tuning will be performed to improve both visual quality and convergence [14]. GAN training is known to be highly sensitive to parameter selection, so iterative experimentation will be essential [14]. In addition to these standard adjustments, optimization may also involve incorporating **Focal Loss** to better address class imbalance during training. And these parameters will be adjusted:

- Learning rate
- Batch size
- Dropout and regularization
- Noise vector dimension

Each configuration will be evaluated using quantitative metrics such as **FID**, **SSIM**, and classifier accuracy, as well as qualitative visual inspection by overlaying generated images against real MRI scans [1,6-10]. The best-performing parameter set will then be selected for final training runs.

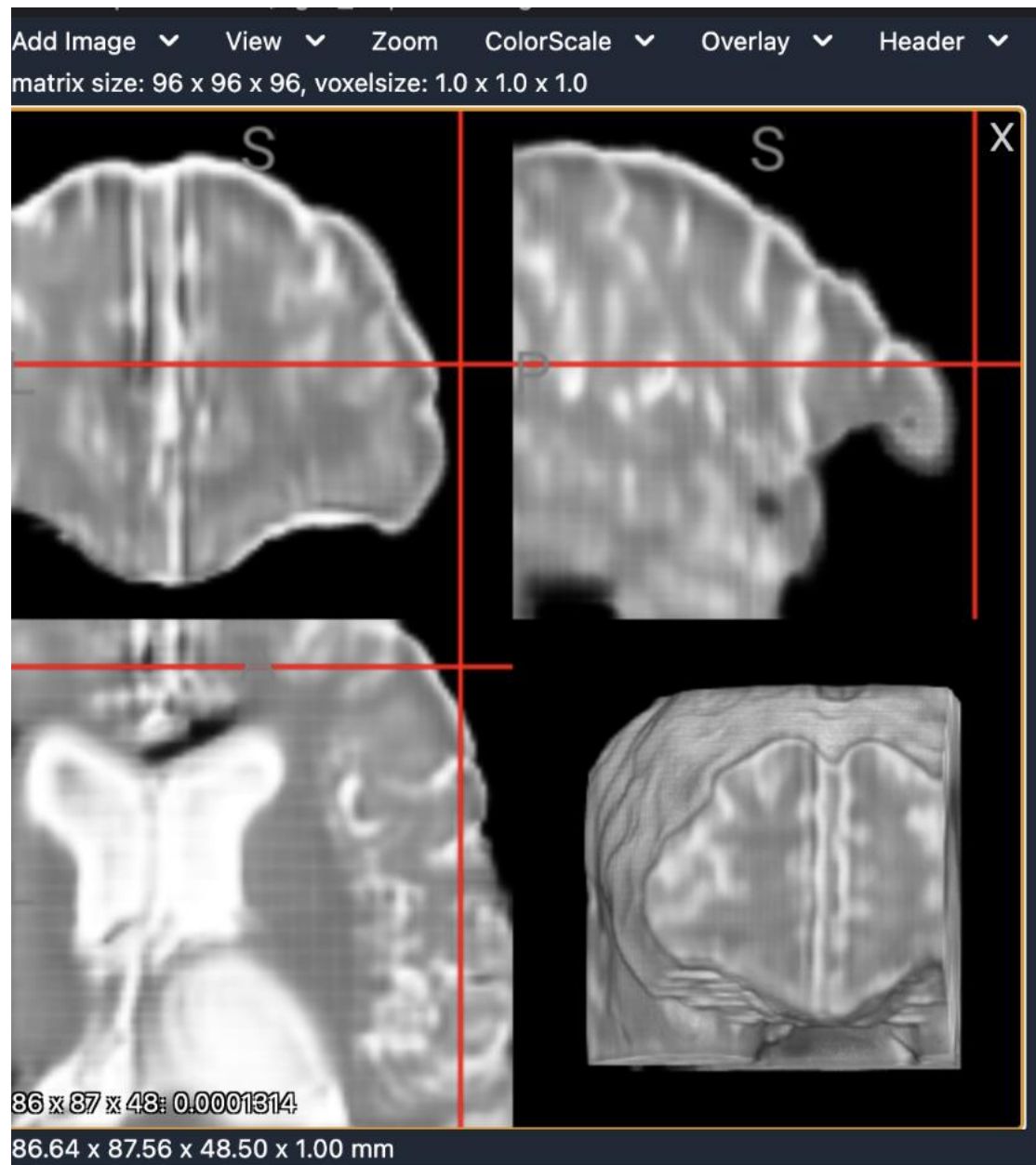
### Test Run:

This is how the real image data is stored for the diffuse glioma dataset:



To validate preprocessing and assess baseline feasibility, a classical GAN was trained on a subset (~33 subjects) from the diffuse glioma dataset. The output format and spatial resolution confirmed compatibility with planned pipeline requirements.





## Implications and contributions:

The main projected contributions can be seen as follows:

- Introduces the use of a data-rich cancer type (glioblastoma) to synthesize realistic MRI images of a rare cancer type (diffuse glioma) using conditional Generative Adversarial Networks (cGANs) [14]. This demonstrates that diseases originating in the same organ can share learned structural similarities and features, facilitating cross-disease synthesis [2,3,5]
- Investigates how far a generative model can generalize when trained on a large source domain (glioblastoma) and guided toward a target domain (diffuse glioma) with little or no target domain data. By evaluating both **few-shot** (limited samples) and **zero-shot** (no samples) scenarios, the study explores the limits of generative transferability under data scarcity. By evaluating both few-shot (limited samples) and zero-shot (no samples) scenarios - where GLIP-based semantic conditioning supports generative transfer - the study explores the limits of generative adaptability under data scarcity.
- Goes beyond visual quality metrics by assessing how generated images perform in downstream classification and segmentation tasks using CNN-based models [16]. This helps determine the real-world effectiveness of synthetic data in computer-aided diagnosis systems [2,3,5].

Scientific and technical implications:

- This study explores the broader potential of generative AI in healthcare or any other domain by extending conditional generation to cross-disease scenarios [1,6-10]. It aims to validate whether pathological similarities between related cancers can be exploited to generate anatomically consistent synthetic data [2,3,5]. The findings will contribute to the growing field of data-efficient deep learning in medicine, where model robustness depends on both dataset diversity and structural fidelity [2,3,5]. While this research is validated through a medical case study, the underlying cross-domain generative framework is designed to generalize across disciplines. Within medicine, it can extend beyond brain tumor synthesis to other areas such as cancer subtype modeling, drug discovery, and molecular image generation. Beyond healthcare, the same principles can apply to industrial inspection, materials science, or remote sensing—where data scarcity and structural variability present similar challenges.

The societal contribution would be as follows:

Once validated, this framework could be applied to broader disease categories to generate synthetic data for rarer subtypes [1,2,3,5]. This technique can be applied not only to create diffuse glioma images but also to any domain facing severe data imbalance [4,5]. In healthcare, this means that even when rare diseases lack sufficient MRI data, researchers could create high-quality synthetic datasets to:

- Train detection and segmentation models for early diagnosis [15,16],
- Support computer-aided diagnostic systems in resource-limited settings [2,3,5], and
- Accelerate research on underrepresented or pediatric diseases without compromising patient privacy [2,3,5].

In the longer term, such generative data synthesis could improve computer aided diagnosis and promote open, reproducible research in data scarce fields [2,3,5].

## Gantt chart:

Phase / Task	Description	Timeline	Deliverables / Milestones
Phase 1 – Setup and Proposal	Finalize topic, research scope, and background study. Prepare proposal and presentation.	Oct 1 – Oct 17 2025	Proposal submission (5%) – Due Oct 17
Phase 2 – Planning and Data Preparation	Collect glioblastoma and diffuse glioma datasets. Set up compute environment, verify file formats, begin preprocessing (normalization, resampling, segmentation masks).	Oct 18 – Nov 21 2025	Project Plan (5%) – Due Nov 21
Phase 3 – Model Design and Preprocessing Completion	Complete preprocessing pipeline; build baseline cGAN architecture; test data loaders and visualization.	Nov 22 – Jan 23 2026	Progress Report #1 (5%) – Due Jan 23
Phase 4 – Model Training and Generation	Train cGAN on glioblastoma data; implement zero-shot and few-shot generation of diffuse glioma images. Perform initial synthetic image validation.	Jan 24 – Feb 20 2026	Progress Report #2 (5%) – Due Feb 20
Phase 5 – CNN Evaluation and Cross-Domain Validation	Train CNN models on real vs. synthetic data; evaluate classification/segmentation performance. Begin image-quality metric evaluation (FID, SSIM).	Feb 21 – Mar 20 2026	Thesis Draft (10%) – Due Mar 20
Phase 6 – Analysis and Refinement	Conduct parameter-sensitivity analysis, iterative improvements, and extended validation with external datasets or expert review.	Mar 21 – Late Mar 2026	Seminar Presentation (10%) – Late Mar 2026
Phase 7 – Thesis Writing and Final Submission	Finalize analysis, figures, and report writing. Submit completed thesis and defend.	Apr 1 – Apr 13 2026	Final Thesis (60%) – Due Apr 13

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