CS491: Senior Design Project I

Project Specification Document

MRacle

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1. Introduction

1.1 Description

Detecting brain tumors early and accurately is crucial for giving patients the best chance of recovery. Delays or mistakes in diagnosing can cause serious problems, making treatments less effective and affecting quality of life. However, the imbalance between the number of radiologists and the total workload emphasize need for tools like MRacle.

MRacle is an innovative AI-based solution designed to address these challenges and change how brain tumors are detected and diagnosed. While taking ethical and professional issues into consideration, by analyzing images quickly and accurately, MRacle helps identify potential tumors and marks affected areas for easier review using advanced neural networks. Furthermore, MRacle helps radiologists concentrate on the most critical patients by giving priority to those that are more likely to have tumors. The purpose behind MRacle is to improve diagnostic accuracy, enhance patient outcomes and help radiologists without replacing their role.

1.2 High-Level System Architecture & Components of Proposed Solution

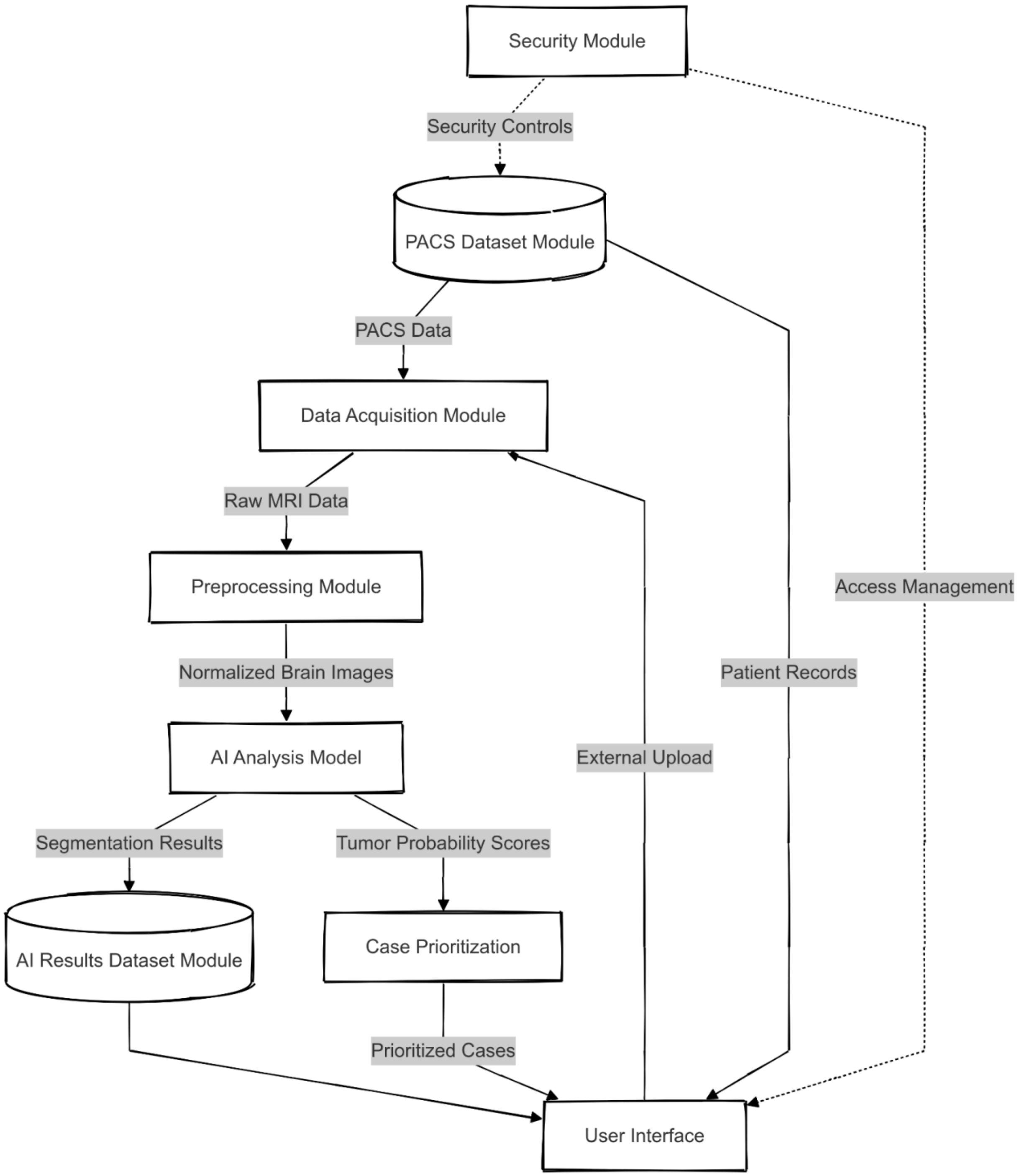

Figure 1: High-Level System Architecture Diagram

<u>Components:</u>

1. Security Module:

- Implements data encryption and access control mechanisms to ensure patient confidentiality.
- Monitors system activity to detect and prevent unauthorized access.

2. PACS Dataset Module:

- Interfaces with Picture Archiving and Communication Systems (PACS) to acquire and store MRI images.
- Integrates seamlessly with hospital radiology systems.

3. Data Acquisition Module:

- Manages acquisition of MRI scans in formats such as NIfTI (.nii/.nii.gz) and DICOM (.dcm).
- Supports incorporation of multiple MRI sequences (e.g., T1-CE, T2-FLAIR).
- Validates incoming data to ensure quality and format compatibility.

4. Preprocessing Module:

- Aligns MRI sequences, resamples images to a uniform voxel size, and performs skull-stripping.
- Ensures consistent data representation via normalization.

5. AI Analysis Model:

- Utilizes MRacle AI model for tumor detection and segmentation.

6. AI Results Dataset Module:

- Stores results generated by the AI analysis model, including tumor detection and segmentation outputs.

7. Case Prioritization System:

- Algorithms to prioritize cases based on tumor likelihood.
- Integration with radiologists' workflow for efficient case management.

8. User Interface (UI):

- An interface where the user can view all results from the model, such as segmentation results and tumor likelihood.
- A system where authorized users can upload MRI images externally to the system and request analysis.

1.3 Constraints

1.3.1 Implementation Constraints

Data Diversity and Quality:

- The open-access datasets may not fully represent the diversity of real-life cases.
- Potential biases due to overrepresentation of certain tumor types or demographics.
- Danger of bias due to lack of diversity in age and ethnicity background.
- Difficulty in obtaining sufficient data for rare tumor types.

MRI Sequence Variability:

- Different MRI machines produce varying image qualities and sequences.
- Older MRI machines may produce images with low quality.
- Need to handle variations in image contrast, noise levels, and artifacts.

Computational Resources:

- Training and deploying deep learning models require significant computational power.
- Real-time analysis demands optimized algorithms and hardware acceleration.

Integration Challenges:

- Compatibility with various MRI devices without hardware changes.
- Integration into current PACS systems easily.
- Ensuring adaptation with DICOM (Digital Imaging and Communications in Medicine) [1] and other interoperability standards.

1.3.2 Economic Constraints

Development Costs:

- High costs associated with acquiring and annotating medical imaging data.
- Rental fees for the infrastructure to be used to train the model, such as high-performance GPUs

Certification Expenses:

- Significant financial investment required for FDA [2] and CE [3] approvals.
- Ongoing costs for maintaining compliance and updating certifications.

Maintenance Costs:

- Regular software updates to improve AI model performance, integrate new features, and address new challenges.
- Costs associated with retraining AI models to adapt to changes in medical imaging technology or new diagnostic requirements.
- Data security must be maintained, following laws like GDPR[4] and HIPAA[5].

1.3.3 Ethical Constraints

Patient Privacy:

- Strict adherence to data protection laws such as HIPAA [5] and GDPR [4].
- Risks associated with data breaches or unauthorized access.

Algorithmic Bias:

- Potential for the AI model to exhibit biases based on the training data.
- Ethical implications of unequal diagnostic accuracy across different patient groups.

Transparency and Trust:

- Necessity to ensure that radiologists understand and trust AI recommendations.
- Ambiguity in generation of results due to black box aspect of AI technology.
- Risk of over-reliance on AI or dismissal of AI alerts due to lack of trust.

Informed Consent:

- Ethical considerations in using patient data for model training.

1.4 Professional and Ethical Issues

When using AI systems like MRacle in healthcare, there are important issues to consider regarding responsibility, data use, professional acceptance, and ethics. It's important to define who is responsible if a misdiagnosis happens or if a tumor is missed, especially when doctors rely on AI suggestions. Legal concerns must also be addressed, as it may be unclear who is at fault, especially with AI models that are hard to understand (black box structure). Clear guidelines should be set for doctors and AI systems to work together, so the AI supports but does not replace the doctor's judgment.

It's also necessary to clarify who owns the data generated by AI and ensure that patient information is used ethically, especially when training AI systems. Policies should be clear about how data is handled, stored, and shared. Another challenge is getting healthcare professionals to accept AI. Some may fear that AI will replace their jobs, so it's important to explain that AI is a tool to help doctors, not take their place. Doctors and other staff need training to use AI properly, and there should be clear guidelines on how AI fits into their work.

MRacle AI is designed to help doctors make decisions, not make them on its own, especially in complex cases where the doctor's experience is needed. Lastly, AI systems need to be checked regularly to make sure they are working well and that they stay accurate over time. This includes updating models to prevent errors and keep up with medical changes.

1.5 Standards

Medical Imaging Standards:

- DICOM: Standard for handling, storing, and transmitting medical imaging information [1].
- NIfTI: Standard format for neuroimaging data [6].

Software Development Standards:

- IEEE 830-1998: Software Requirements Specifications [7].

Regulatory Standards:

- FDA Regulations: For Software as a Medical Device (SaMD) [2].
- CE Marking: Compliance with EU medical device directives [3].

Data Security Standards:

- HIPAA: Health Insurance Portability and Accountability Act [5].
- GDPR: General Data Protection Regulation [4].

Modeling Standards:

- UML 2.5.1: For system modeling and documentation [8].

2. Design Requirements

2.1 Functional Requirements

The radiologists should be able to:

- Upload and manage MRI scans in various formats depending on the MRI type.
- View multi-sequence images with synchronized navigation.
- Initiate AI analysis on selected scans, view AI-generated tumor segmentation overlays.
- Inspect the potential risks shown by the labels generated by the AI analysis.
- Order the results according to the risks, a dashboard displaying prioritized cases and customize alerts for high-risk findings.
- Compare current scans with previous ones and track changes in tumor size and characteristics over time.
- Annotate AI results with corrections or confirmations, and submit feedback to improve AI performance if necessary.
- Generate detailed reports for patient records and scans.
- Add notes on their suggestions to the final diagnosis and further steps.

2.2 Non-Functional Requirements

2.2.1 Usability

The system will have an intuitive interface designed to align seamlessly with radiologists' workflows, ensuring a consistent and user-friendly experience. Common tasks will be implemented to minimize user effort, allowing users to focus on their core responsibilities. Customization options enable users to adjust interface settings according to their preferences. To further enhance usability, comprehensive user manuals and documentation will be supplied.

2.2.2 Privacy & Security

The system is designed with a focus on the sensitivity of medical data, ensuring compliance with healthcare-specific data protection standards and regulations. Given the critical nature of patient information, strong measures will be in place to protect privacy and confidentiality. Data must be protected during transmission and storage, minimizing risks of interception or unauthorized access. Role-based access controls (RBAC) are going to be implemented to ensure only authorized healthcare professionals can access specific patient data, and multi-factor authentication (MFA) will be required for secure logins. Additionally, measures such as anonymization must be applied where possible to protect patient identities, further increasing the system's commitment to privacy and security in the medical domain.

2.2.3 Performance

The system should have a high enough performance, completing AI analysis within a short interval of time per scan and maintaining UI response times of under one second for user interactions. It is designed to handle scalability, support multiple concurrent analysis requests.

2.2.4 Supportability

A modular architecture should ensure clear separation of components, simplifying updates and maintenance. Update mechanisms will be designed to be seamless, enabling software updates without service disruption, with a notification system in place for scheduled maintenance. The system will provide a full suite of manuals, including FAQs, troubleshooting guides, and system architecture documentation, accessible for radiologists.

2.2.5 Scalability

The application should easily scale up in order to meet the needs of the growing needs of users. The server should scale up to handle an increasing number of scans. We aim to develop our application so that our model is usable across multiple hospitals in Türkiye.

3. Feasibility Discussions

3.1 Market & Competitive Analysis

3.1.1 Global Market Analysis

Globally, the AI-enabled diagnostic imaging sector is growing with huge investments. Brain tumor detection, in particular, has emerged as a rapidly growing segment due to the integration of AI and machine learning that increases diagnostic accuracy and efficiency. Conferences and challenges such as Brain Tumor Segmentation (BraTS) are held in this field annually [9]. Rapidly developing technologies and investments in this field are growing worldwide with innovations such as automatic tumor detection, segmentation, and prioritization. Leading companies like Philips and Siemens are integrating AI and diagnostic technologies into MRI devices [10][11]. Major players in the global market include independent companies such as AIRAmed, Annalise.ai, and AI Medical, which offer AI-driven platforms focused on lesion detection, case prioritization, and protection of personalized health data [12]. The integration of AI not only improves diagnostic capabilities but also acts as a triage mechanism for radiologists to prioritize high-risk cases. These innovations are creating a rapidly growing global market for AI-enabled diagnostic tools, especially in brain tumor detection, where early detection plays a significant role in patient outcomes.

The licensing and certification processes are the biggest obstacle to entering this emerging market worldwide. In the European Union, CE (Conformité Européenne) certification and in the US, FDA (Food and Drug Administration) approval are required for medical devices and healthcare equipment to be placed on the market [2][3]. However, due to high costs and long approval periods, these processes can be a significant obstacle for entrepreneurs and new companies. For MRacle, these certification processes are also the biggest obstacle to entering the market.

3.1.2 Local Market and Competitive Analysis

In Türkiye's local market, the current healthcare system presents a need for MRacle to be met. While 52 MRI scans are performed per 1000 people per year in OECD countries, this number is 119 per 1000 people in Türkiye. However, the number of radiologists in Türkiye is significantly low, with 15 per 100,000 people in OECD countries, this number is only 5 per 100,000 people in Türkiye [13]. In other words, while our country performs more than twice as many MRIs as OECD countries, the number of radiologists is one-third of OECD countries. In Türkiye, a radiologist may have to report up to 300 daily examinations, spending only 1-2 minutes on each [13]. This situation forces the radiologist to make mistakes or results in reports that are later than expected. This imbalance highlights the urgent need for AI-supported tools to prevent radiologists with excessive workloads from reporting images so late that they pose a life-threatening risk. In addition, the radiologist needs to be able to make early and accurate diagnoses in life-threatening cases such as brain tumors. Approximately 15,000 people are diagnosed with brain tumors in Türkiye each year [15]. In brain tumors, where early diagnosis is vital, the need for prioritization in cases also comes to the fore. Our goal in the market is not to build a system that will replace radiologists and doctors, but to assist them in making their diagnosis easier and faster.

Contrary to global trends and local needs, the diagnostic imaging market in Türkiye has yet to embrace AI-enabled diagnostic tools. In 2020, a product called Türk-Beyin was introduced in a project carried out in collaboration with Gazi University and the “Cumhurbaşkanlığı Dijital Dönüşüm Ofisi”. This product integrates with Gazi University Hospital's PACS system, analyzes every brain MRI taken, and notifies the doctor in case of an abnormality [16]. However, despite the promising nature of the project, it is not currently used, probably due to licensing or certification issues. We aim to contact the coordinators of the Türk-Beyin project on this issue and develop our local market analysis. Apart from this project, there are no other prominent local projects. This deficiency creates a significant market opportunity for the MRacle.

3.1.3 Go to Market Strategy

We have built the market entry strategy for MRacle in two main phases. First is the clinical validation step, which provides the evidence needed to demonstrate the efficacy and safety of the product. We hope to provide validation of MRacle by establishing partnerships with volunteer and open-concept healthcare facilities. By partnering with healthcare facilities, MRacle can collect real-world data that will support its clinical validation and help form the basis for regulatory approvals. Research shows that doctors tend to trust AI decisions in clinical decisions [17]. Collaboration with doctors in the clinical validation step is one of the most important steps for the MRacle to enter the market. We can also integrate our product into MRI devices that healthcare institutions already have in their inventory and bring it to market at a cost much lower than the budget required for new devices. Unlike solutions from companies like Siemens and Philips that require expensive investments in new MRI devices, MRacle can already work with the existing MRI infrastructure in Türkiye. This integration significantly reduces the cost for healthcare institutions, making the product more affordable and accessible compared to these solutions. This integration with existing systems, strategic partnerships, and clinical validation will establish MRacle in the local market. Clinical validation forms the basis for regulatory requirements prior to certification processes.

Obtaining FDA and CE certifications is the second phase of entering the market, as these approvals are mandatory for any medical device entering the market. MRacle is categorized as Software as a Medical Device (SaMD); it must meet strict requirements to prove its safety, reliability, and transparency [2][3]. These certifications are critical for market entry, gaining the trust of healthcare providers, and for MRacle to be used safely and effectively in clinical settings.

3.2 Academic Analysis

The technical feasibility of the MRacle project has been assessed from multiple perspectives, including the availability of suitable datasets, data augmentation techniques, and the selection of machine learning models.

3.2.1 Dataset Availability and Diversity

A diverse dataset is important for training a brain tumor detection model. We have identified several publicly available datasets relevant to our project:

- **Brain Tumor Segmentation (BraTS) Challenge Datasets**: The 2024 BraTS Post-Treatment Glioma Challenge dataset offers a comprehensive collection of multi-institutional MRI scans with expert annotations of gliomas of different grades. This dataset includes four MRI modalities for each patient: T1-weighted, T1-weighted contrast-enhanced (T1CE), T2-weighted, and T2 Fluid Attenuated Inversion Recovery (T2-FLAIR). With over 2,000 patients' this dataset provides a solid foundation for training and validating our models [18].
- **ReMIND The Brain Resection Multimodal Imaging Database:** The ReMIND contains pre- and intra-operative data from 114 patients surgically treated with image-guided tumor resection between 2018 and 2022. For each patient, the dataset includes pre- and intra-operative MRI scans (T1, T1CE, T2, and T2-FLAIR). Additionally, it provides various segmentations such as the preoperative whole tumor, cerebrum, previous resection cavities, and residual tumors identified on intraoperative MRI. Including intraoperative data and detailed segmentations enhances the diversity of our training data and allows for more comprehensive modeling of brain tumors, including the challenges of residual tumor detection [19].
- **Pretreat-MetsToBrain-Masks:** This dataset is an open-access collection of brain metastasis 3D segmentations on MRI, along with clinical and imaging feature information. It includes patients with pathologically proven brain metastases with pre-treatment scans with standard MRI sequences (T1, T1CE, T2, and T2-FLAIR). The dataset also provides clinical metadata such as demographic information, survival outcomes, and qualitative imaging features. This dataset enhances our ability to train models to detect and segment metastatic brain tumors and understand their clinical implications [20].

3.2.2 Data Augmentation Techniques

We plan to employ data augmentation techniques to enhance data diversity and prevent overfitting. This approach is critical in medical image analysis, where obtaining new high-quality annotated data is costly and time-consuming. We plan to implement the following data augmentation strategies:

3.2.2.1 Affine Transformations

- **Flipping:** Creating mirror images of MRI scans along certain axes can help the model learn invariant features [21].
- **Rotation:** Applying small rotations helps the model become invariant to the orientation of tumors resulting from patient positioning variations. Rotations are kept within a limited range to avoid creating anatomically incorrect images [21].
- **Translation:** Slightly shifting the images along the x, y, or z axis allows the model to learn spatially invariant features, helping to detect tumors in different parts of the brain [21].

3.2.2.2 Elastic Transformations

Data augmentation using elastic transformations can generate variations of medical images for training, typically using B-splines or random deformations. While these can sometimes produce unrealistic images (such as distorted brain MRIs), diffeomorphic mapping is a widely used technique in data augmentation. It preserves the topology of the original image while generating slight variations, helping to create biologically accurate training data that can improve deep learning model performance [21].

3.2.2.3 Pixel-Level Transformations

Pixel-level data augmentation modifies image intensity values without changing the geometric shape of the images. This is particularly valuable in medical imaging, where images from different scanners or locations may have different intensity levels. Standard techniques include adding random or Gaussian noise, adjusting brightness, applying gamma correction, and sharpening or blurring [21].

3.2.2.4 Generation of Artificial Data

Data augmentation through artificial data generation using Generative Adversarial Networks (GANs) has emerged as an approach to enhance medical datasets. GANs work by creating synthetic images that are close to real medical data. Other methods include using tumor growth models with domain adaptation and "mixup" techniques that combine existing training samples. These approaches are especially valuable for medical imaging, where datasets are imbalanced and real data is scarce. However, care must be taken to ensure that the synthetic data matches the characteristics of real medical images [21].

3.2.3 Model Selection and Methodology

The selection of appropriate model architectures and the design of a practical methodology are critical for the success of our project. Below, we provide a detailed overview of our model selection and methodology.

3.2.3.1 Model Architectures

We analyzed the following models for their effectiveness in medical image segmentation, in particular in brain tumor detection and segmentation tasks:

- **U-Net:** The U-Net architecture is a convolutional neural network designed for biomedical image segmentation. Introduced by Ronneberger et al. in 2015, U-Net has become a foundational model in medical imaging due to its ability to produce high-quality segmentation results even with limited training data [22].
- **3D U-Net:** The 3D U-Net architecture extends the original U-Net model to three dimensions, allowing for volumetric segmentation of 3D medical images. It consists of an encoder-decoder structure with skip connections that enable the model to capture contextual and spatial information effectively. The encoder path captures the context of the input image, while the decoder path enables precise localization using transposed convolutions [23].
- **nnU-Net:** The nnU-Net (no-new-Net) is a semantic segmentation method that automatically adapts to a given dataset. It is an automated framework configuring itself by analyzing the provided training cases and automatically setting up a matching U-Net-based segmentation pipeline. It automates preprocessing, architecture selection, training, and post-processing steps, eliminating the need for manual tuning [24].
- **Swin UNETR:** Swin UNETR integrates the Swin Transformer architecture into a U-Net framework, replacing the traditional convolutional encoder with Swin Transformer blocks. This allows the model to capture long-range dependencies and hierarchical representations efficiently [25].

3.2.3.2 Handling Class Imbalance

Class imbalance is a critical issue in medical image segmentation, where regions of interest (e.g., tumors) may fill a small portion of the image compared to the background. This imbalance can lead to biased models that favor the majority class (background) and potentially miss diagnostic features. To address this issue, several specialized loss functions developed:

- **Dice Loss:** Focuses on the overlap between the predicted segmentation and the ground truth, effectively handling class imbalance [26].
- **Focal Loss:** Reduces the relative loss for well-classified examples, focusing more on complex, misclassified examples [27].

3.2.3.3 Evaluation Metrics

We will use the following evaluation metrics to evaluate the performance of our models:

- **Dice Similarity Coefficient (DSC):** A measure of the overlap between the predicted segmentation and the ground truth, ranging from 0 (no overlap) to 1 (perfect overlap). It is particularly suitable for medical image segmentation tasks [18].
- **95% Hausdorff Distance (HD95):** Measures the distance between the boundaries of the predicted segmentation and the ground truth, focusing on the worst-case scenarios by excluding the top 5% of distances [18].

3.2.3.4 Methodology

Based on these insights, our methodology will involve:

1. Data Preparation

- **Preprocessing:** Standardizing the MRI scans, including co-registering, resampling, and skull-stripping.
- **Data Augmentation:** Implementing affine transformations, elastic deformations, pixel-level modifications, and synthetic data generation using GANs.

2. Model Training

- **Hyperparameter Tuning:** Utilizing automated tools like nnU-Net's configuration system to optimize model parameters.
- **Loss Functions:** Using a combination of loss functions that address class imbalance.

3. Model Ensemble

- **Diversity of Models:** Training multiple models (3D U-Net, nnU-Net, Swin UNETR) to capture different aspects of the data.
- **Ensemble Strategy:** Combining model predictions through majority voting or weighted averaging techniques.

4. Evaluation

- **Metric Calculation:** Computing DSC and HD95 metrics on validation sets.

4. Glossary

Term	Definition
AI	Artificial Intelligence
MRI	Magnetic Resonance Imaging
CNN	Convolutional Neural Network
DICOM	Digital Imaging and Communications in Medicine
NIfTI	Neuroimaging Informatics Technology Initiative
FDA	Food and Drug Administration
CE	Conformité Européenne Certification
BraTS	Brain Tumor Segmentation Challenge
OECD	Organisation for Economic Co-operation and Development
SaMD	Software as a Medical Device
PACS	Picture Archiving and Communication System
GDPR	General Data Protection Regulation
HIPAA	Health Insurance Portability and Accountability
RBAC	Role-Based Access Controls
MFA	Multi-Factor Authentication
UML	Unified Modeling Language
GAN	Generative Adversarial Network
T2-FLAIR	T2 Fluid Attenuated Inversion Recovery
T1CE	T1 Contrast-Enhanced
FAQ	Frequently Asked Questions

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