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DISSERTATION

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THEME

Hybrid Brain Tumor Detection Using U-Net and SVM

Presented by :

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Publicly defended on : jj/mm/aaaa

In front of the jury composed of :

President : .....

Examiner : .....

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Dedication

To the architects of my dreams, my parents, whose unwavering love and guidance have been my compass ; to my family, the sanctuary of my heart, and to my friends, the sparks of joy in my journey.

This thesis is a testament to your belief in me, a reflection of your sacrifices, and a celebration of the bond we share. Thank you for being my pillars of strength and my endless source of inspiration.

- Mohammed

Dedication

To my parents, whose unwavering love, support, and guidance have been instrumental in shaping my dreams; to my family, who have been my rock and my safe haven; and to my friends, who have been the source of joy and laughter in my life.

This thesis is a reflection of their sacrifices, a testament to their faith in me, and a celebration of the bond we share. Thank you for being my pillars of strength and my endless source of inspiration.

- Assil

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Abstract

Brain tumors, particularly gliomas, pose a significant clinical challenge, requiring both precise localization and accurate grading to guide treatment. In this project, we present a hybrid framework that first segments tumor regions in brain Magnetic Resonance Imaging (MRI) scans using a U-Net model trained on the Brain Tumor Segmentation (BraTS2020) dataset and then classifies these regions as Low-Grade or High-Grade Gliomas with a Support Vector Machine (SVM) model based on features extracted from the segmented masks. On the held-out test set, our U-Net achieved an accuracy of 99.3%, while the SVM classifier delivered an overall accuracy of 93%.

Keywords : Brain Tumor, U-Net, SVM, MRI, BraTS, Segmentation.

Résumé

Les tumeurs cérébrales, en particulier les gliomes, posent un défi clinique important, nécessitant à la fois une localisation précise et un classement précis pour guider le traitement. Dans ce projet, nous présentons un cadre hybride qui segmente d'abord les régions tumorales dans l'imagerie par résonance magnétique (IRM) du cerveau en utilisant un modèle U-Net formé sur l'ensemble de données de segmentation des tumeurs cérébrales (BraTS2020) et classe ensuite ces régions comme faibleGliomes de grade ou de haut grade avec un modèle SVM (Support Vector Machine) basé sur les caractéristiques extraites des masques segmentés. Sur l'ensemble de test non exécuté, notre U-Net a atteint une précision de 99,3%, tandis que le classificateur SVM a fourni une précision globale de 93%.

Mots-clés : Tumeur cérébrale, U-Net, SVM, IRM, BraTS, Segmentation.

ملخص

تُشكل أورام الدماغ، وخاصة الأورام الدبقية، تحديا طبيا كبيراً، وتتطلب الى التحديد والتصنيف بشكل دقيق من أجل توجيه العلاج. في هذا المشروع، نقدم إطاراً هجينا يقوم أولاً بتقسيم مناطق الورم في عمليات مسح (MRI) للدماغ باستخدام نموذج (U-Net) المدرب على مجموعة بيانات أورام الدماغ (BraTS2020) ثم يقوم بتصنيف هذه المناطق على أنها أورام دبقيه منخفضة الدرجة أو عالية الدرجة باستخدام نموذج آلة الدعم المتجه (SVM) استناداً إلى الميزات المستخرجة من الأقنعة المجزأة. في مجموعة الاختبار، حققت شبكة (U-Net) الخاصة بنا دقة قدرها 99,3%، بينما قدم مصنف (SVM) دقة إجمالية قدرها 93%.

الكلمات المفتاحية: أورام الدماغ، الأورام الدبقية، U-Net، SVM، التصوير بالرنين المغناطيسي، BraTS، تقسيم الأورام، تصنيف الدرجات.

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List of abbreviations

AI Artificial Intelligence.

BraTS Brain Tumor Segmentation dataset.

CNN Convolutional Neural Network.

DL Deep Learning.

HGG High-Grade Glioma.

K-NN K-Nearest Neighbors.

LGG Low-Grade Glioma.

ML Machine Learning.

MRI Magnetic Resonance Imaging.

RF Random Forest.

SVM Support Vector Machine.

U-Net U-Net Convolutional Neural Network.

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Chapitre 1

General Introduciton

1.1 Introduction

Traditionally, radiologists rely on MRI scans to detect brain tumors, While this method is effective, it also has limitations analyzing hundreds of scans manually is time consuming and prone to human error. That is where technology comes in. With recent advances in artificial intelligence, especially deep learning, we now have powerful tools that can learn from medical images and help with faster and more accurate diagnosis.

In this project, we focus on building a hybrid system to detect brain tumors and determine whether they are low-grade or high-grade. We use a U-Net model for segmenting the tumor regions in MRI images. After identifying these regions, we extract important features and feed them into a Support Vector Machine (SVM) classifier to make the final prediction.

We use the BraTS2020 dataset, focusing on T2-weighted FLAIR images, to train and test our system. Our goal is to create a pipeline that is not only technically sound but also practical and helpful for medical professionals in real-world settings.

1.2 What is a Brain Tumor ?

A **brain tumor** is an abnormal mass of tissue in which cells grow and multiply uncontrollably, without the mechanisms that regulate normal cell behavior. Brain tumors can be broadly categorized into *benign* (non-cancerous) and *malignant* (cancerous) forms, each with varying

levels of severity and progression [1].

Brain tumors are generally divided into two main categories :

- **Primary brain tumors :** These originate in the brain and include common types such as :
  - *Gliomas* – tumors arising from glial cells, which provide support and insulation to neurons [2].
  - *Meningiomas* – tumors that form in the membranes surrounding the brain and spinal cord [3].
  - *Pituitary adenomas* – tumors that develop in the pituitary gland [3].
  - *Medulloblastomas* – fast-growing tumors more commonly seen in children [1].
- **Secondary (metastatic) brain tumors :** These originate from cancers elsewhere in the body (such as the lungs or breast) and spread to the brain [1].

Among gliomas, two major clinical subtypes are often considered for diagnostic and prognostic purposes [2] :

- **Low-Grade Gliomas (LGG) :** Slow-growing tumors that often have a better prognosis.
- **High-Grade Gliomas (HGG) :** Aggressive tumors with rapid progression and poor prognosis.

Accurate detection and classification of these tumor types are essential for clinical decision-making, which has led to the integration of artificial intelligence (AI) and deep learning (DL) methods into medical imaging workflows.

1.3 Problem Statement

Despite the advancements in medical imaging, the accurate identification and classification processes of the brain tumors in MRI scans remains a challenging task. Also the manual segmentation is time-consuming, not forgetting the human error, and the need fo expert knowledge. Existing automated methods often struggle with inconsistent tumor boundaries and data imbalance, especially when distinguishing between low-grade and high-grade gliomas.

There is a clear need for a robust and efficient system that can both segment brain tumors

accurately and classify their grade reliably. This project aims to address that gap by combining DL for tumor segmentation with classical ML for tumor grade classification providing a practical hybrid solution that balances performance and .

1.4 Objectives

1.4.1 General Objective

To develop an automated system for brain tumor detection, segmentation, and classification using DL and ML techniques on MRI scans.

1.4.2 Specific Objectives

1. Explore and preprocess the BraTS dataset, focusing on T2-weighted MRI images.
2. Train a U-Net model for precise segmentation of brain structures, including tumor regions.
3. Extract tumor regions from the segmentation masks and classify them as low-grade or high-grade gliomas using an SVM classifier.
4. Evaluate the performance of the segmentation and classification models using appropriate metrics.
5. Build a simple application that integrates both models for real-time inference and visualization.

1.5 Motivation

The potential of using DL and ML in brain tumor detection and classification is truly remarkable. It can help reduce the time required for diagnosis, which is life saving on early intervention. Moreover, it offers the promise of improved accuracy and consistency in medical decisions by minimizing the subjectivity and fatigue that can affect human experts.

Through this project, we aimed to contribute to that goal by building an automated system that segments brain tumors from MRI scans and classifies them into Low-Grade Glioma (LGG) or High-Grade Glioma (HGG). We used a U-Net architecture for precise segmentation of tumor

regions, followed by a SVM classifier to determine the tumor type. This combination ensures both spatial understanding of the tumor and a robust classification mechanism.

Our motivation stems from the desire to support the medical community with practical AI tools that can speed up diagnosis and reduce the burden on healthcare professionals, especially in regions where access to experienced radiologists may be limited.

1.6 Contributions

This thesis presents a complete pipeline that combines DL and ML techniques for brain tumor detection and classification using MRI scans. The primary goal was to build an accurate and practical system that can assist in identifying and distinguishing between Low-Grade Gliomas (LGG) and High-Grade Gliomas (HGG).

The key contributions of this work are as follows :

- **Tumor Segmentation with U-Net** : We trained a U-Net model to segment brain tumors from T2-weighted MRI images. This architecture was chosen for its proven effectiveness in biomedical image segmentation, allowing us to extract precise tumor regions. [4]
- **Tumor Classification using SVM** : After segmentation, we extracted features from the segmented tumor areas and used them to train a SVM classifier. This model classifies the tumor as either LGG or HGG, offering a straightforward yet powerful method for diagnosis.
- **Dataset Utilization and Visualization** : We utilized the BraTS dataset [5], specifically T2 modality images, and developed custom visualizations to help evaluate model predictions. These visualizations include overlays and individual class masks to clearly demonstrate the model's performance.

Chapitre 2

State of the Art

2.1 Medical Imaging in Brain Tumor Diagnosis

Magnetic Resonance Imaging (MRI) has emerged as the gold standard for brain tumor diagnosis due to its superior soft tissue contrast, high spatial resolution, and non-invasive nature [6]. Unlike other imaging modalities such as CT scans, MRI provides detailed structural information without exposing patients to ionizing radiation, making it particularly valuable for serial monitoring and treatment planning [7].

The multimodal nature of MRI is especially useful in brain tumor assessment, with each sequence highlighting different aspects of the tumor [8] :

- **T1-weighted (T1)** : Provides excellent anatomical detail and clearly delineates boundaries between gray and white matter. Tumors typically appear hypointense (darker) compared to surrounding tissue.

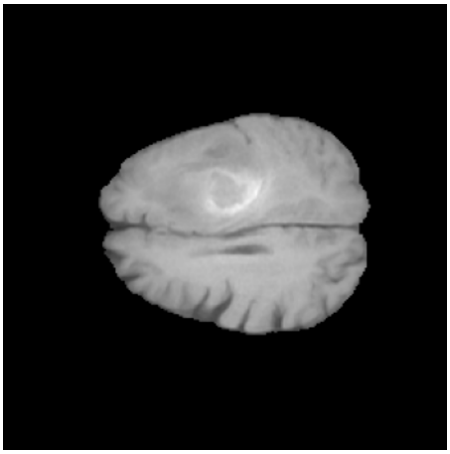

FIGURE 2.1 – Example of T1-weighted MRI sequence.

- **T1 with contrast enhancement (T1ce)** : After gadolinium administration, areas with disrupted blood-brain barrier (characteristic of high-grade tumors) enhance, appearing hyperintense and revealing the active tumor core.

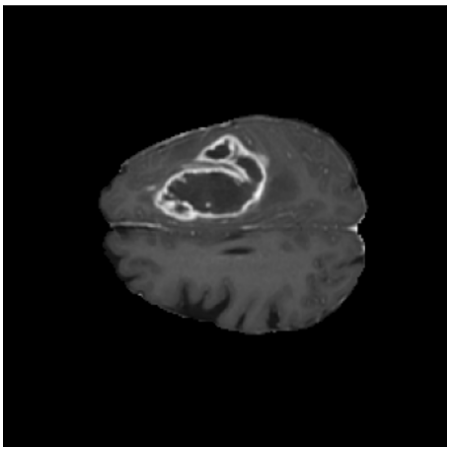

FIGURE 2.2 – Example of T1-weighted contrast-enhanced MRI sequence.

- **T2-weighted (T2)** : Highlights areas with increased water content, making it valuable for identifying edema and infiltrative tumor components. Tumors and surrounding edema appear hyperintense.

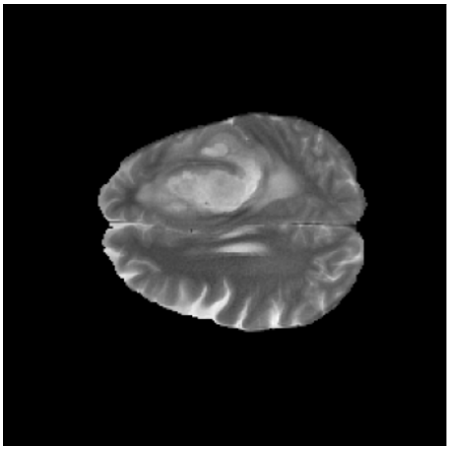

FIGURE 2.3 – Example of T2-weighted MRI sequence.

- **Fluid-Attenuated Inversion Recovery (FLAIR)** : Suppresses cerebrospinal fluid signals, enhancing the visibility of periventricular lesions and edema associated with tumors.

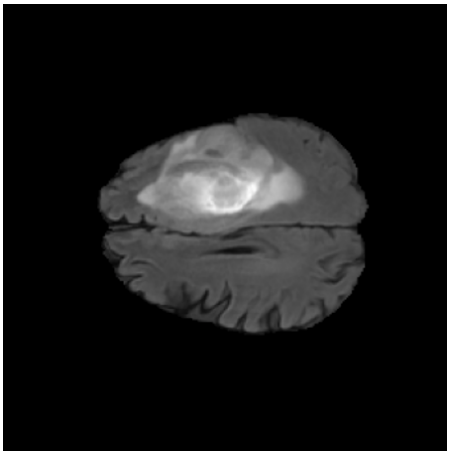

FIGURE 2.4 – Example of FLAIR MRI sequence.

Traditionally, neuroradiologists diagnose brain tumors by visually inspecting these multiple MRI sequences, mentally integrating information across modalities to determine tumor boundaries, assess grade, and identify critical structures [9]. This process is inherently subjective, time-consuming, and susceptible to inter-observer variability, with studies reporting considerable disagreement even among experienced radiologists These limitations have driven significant interest in developing computational approaches for automated and semi-automated tumor analysis.

2.2 The BraTS Dataset

The Brain Tumor Segmentation (BraTS) challenge and dataset represent a landmark initiative in standardizing the evaluation of brain tumor segmentation algorithms [7, 8]. Since its inception in 2012, BraTS has evolved into the most widely adopted benchmark for algorithm development and performance assessment in this domain [10].

The BraTS dataset is particularly valuable due to its :

- **Multimodal approach** : Each case includes four co-registered MRI sequences (T1, T1ce, T2, and FLAIR), enabling algorithms to leverage complementary information [11].
- **Standardized preprocessing** : All images undergo skull-stripping, resampling to isotropic 1mm³ voxels, and registration to a common anatomical template, reducing technical variability [8].
- **Expert annotations** : Each tumor is manually segmented by experienced neuroradiologists following a standardized protocol, with additional verification to ensure quality [7].
- **Multi-institutional data** : Images are acquired from multiple institutions using different scanners and protocols, promoting the development of robust algorithms [10].

1. **Enhancing Tumor (ET)** : Areas showing hyperintensity in T1ce relative to T1
2. **Tumor Core (TC)** : Encompassing the ET, necrotic components, and non-enhancing tumor
3. **Whole Tumor (WT)** : Including all tumor tissues and surrounding edema

This hierarchical annotation structure enables the evaluation of algorithms at multiple levels of detail, from gross tumor detection to fine-grained sub-region delineation [8]. The BraTS datasets and associated challenges have catalyzed significant methodological advances, with performance metrics improving consistently year over year [12].

2.3 Traditional Machine Learning Approaches

Before the deep learning revolution, brain tumor segmentation and classification relied heavily on traditional machine learning techniques coupled with handcrafted feature extraction [13]. These approaches typically followed a pipeline of preprocessing, feature extraction, and classification using conventional machine learning algorithms.

Support Vector Machines (SVM) were particularly popular for brain tumor classification and segmentation due to their strong theoretical foundations and effectiveness with high-dimensional data [14]. Zacharaki et al. [15] developed an SVM-based system that extracted 161 features including intensity, texture, and shape characteristics from multi-parametric MRI, achieving 85% accuracy in discriminating between different tumor types. Similarly, Reza and Iftekharuddin [16] combined texture features with fractal analysis and SVM classification to segment brain tumors, demonstrating competitive performance on earlier BraTS datasets.

Random Forest (RF) classifiers also showed promise due to their robustness to overfitting and ability to handle multi-class problems efficiently. Zikic et al. [17] employed RF with context-aware features for brain tumor segmentation, while Festa et al. [18] achieved strong results in the BraTS 2013 challenge using RF with handcrafted features. Tustison et al. [19] further refined this approach by incorporating an extensive feature set derived from multiple MRI sequences, winning the BraTS 2013 challenge.

K-Nearest Neighbors (K-NN) algorithms were explored by Simi and Joseph [20], who combined texture features with k-NN classification for tumor segmentation. Huang et al. [21] also investigated k-NN for brain tumor classification using multispectral MRI features.

Despite their success, these traditional approaches faced significant limitations :

- **Dependence on handcrafted features** : Their performance was heavily contingent on the quality of manually designed features, requiring substantial domain expertise [22].
- **Limited contextual understanding** : Most methods struggled to incorporate broader spatial context, often relying on voxel-wise or small-patch features [23].
- **Computational inefficiency** : Sequential processing of feature extraction followed by classification led to lengthy processing times impractical for clinical settings [24].
- **Suboptimal performance on heterogeneous tumors** : The high variability in tumor

appearance often challenged these methods, particularly for complex or atypical cases [7].

These limitations ultimately paved the way for the adoption of deep learning techniques, which could learn hierarchical features directly from data and better capture the complex patterns present in brain tumor images.

2.4 Deep Learning in Brain Tumor Segmentation

The adoption of deep learning, particularly Convolutional Neural Networks (CNN), has revolutionized brain tumor segmentation by enabling automatic hierarchical feature learning directly from imaging data [23]. This paradigm shift has eliminated the need for handcrafted features, and led to improving segmentation accuracy and robustness.

Among deep learning architectures, U-Net has emerged as the cornerstone for medical image segmentation, including brain tumor analysis [25]. Its distinctive encoder-decoder structure with skip connections effectively combines localization and contextual information, preserving fine details while capturing broader tumor patterns. Urban et al. [26] were among the first to apply CNNs to brain tumor segmentation, while Pereira et al. [27] demonstrated that carefully designed CNN architectures could outperform traditional methods on the BraTS challenge.

Several U-Net variants have been developed specifically for brain tumor segmentation :

- **3D U-Net** : Çiçek et al. [28] extended the original 2D architecture to process volumetric data, better capturing the three-dimensional nature of tumors. Isensee et al. [29] further refined this approach, achieving top ranking in the BraTS 2018 challenge with a 3D U-Net variant.
- **U-Net++** : Zhou et al. [30] proposed a nested architecture with redesigned skip pathways to bridge the semantic gap between encoder and decoder features. Experimental results showed improved performance on several medical segmentation tasks, including brain tumors.
- **Attention U-Net** : Oktay et al. [31] incorporated attention gates to highlight relevant features and suppress irrelevant regions, improving segmentation accuracy particularly

at tumor boundaries. Schlemper et al. [32] demonstrated the effectiveness of this approach for multi-class tumor segmentation.

The performance of these deep learning models on BraTS challenges has improved consistently over time. In BraTS 2018, Myronenko [33] achieved exceptional results with an encoder-decoder architecture incorporating variational components. McKinley et al. [34] further advanced the field with an ensemble of 3D U-Nets, achieving Dice scores of 0.91, 0.83, and 0.78 for whole tumor, tumor core, and enhancing tumor, respectively. The BraTS 2020 challenge saw even more impressive results, with top-performing methods consistently achieving Dice scores above 0.90 for whole tumor segmentation [12].

Despite these advancements, challenges remain in achieving clinically acceptable performance across diverse patient populations and imaging protocols, driving continuous innovation in the field.

2.5 Tumor Classification Using Deep Features

While segmentation delineates tumor boundaries, classification determines tumor type and characteristics—a critical aspect of diagnosis and treatment planning. Modern approaches increasingly leverage deep features, either independently or in conjunction with traditional machine learning classifiers like Support Vector Machines (SVMs).

Pretrained Convolutional Neural Networks (CNNs) have proven extremely effective as feature extractors for brain tumor classification. Afshar et al. [35] employed a modified ResNet architecture to extract deep features from brain MRI, achieving 93.68% accuracy in classifying tumors into different grades. Similarly, Deepak and Ameer [36] utilized DenseNet for feature extraction followed by SVM classification, reporting improved performance compared to traditional methods. Sajjad et al. [37] extended this approach by fine-tuning VGG-19 on brain tumor images, extracting features from intermediate layers for subsequent classification.

2.6 Multiclass Tumor Region Segmentation

Accurate delineation of different tumor sub-regions represents one of the most challenging aspects of brain tumor analysis, requiring discrimination between biologically distinct

components that may appear visually similar [8]. The BraTS challenge specifically evaluates algorithms on their ability to segment three tumor sub-components : Enhancing Tumor (ET), Tumor Core (TC), and Whole Tumor (WT).

Multi-class tumor segmentation approaches have evolved significantly in recent years. Zhao et al. [38] proposed a multi-scale CNN architecture specifically designed to address the hierarchical nature of tumor sub-regions, achieving meaningful improvements in enhancing tumor segmentation. Wang et al. [39] developed a cascaded approach where initial whole tumor segmentation guided subsequent sub-region delineation, reducing false positives in non-tumor regions. Kamnitsas et al. [40] introduced DeepMedic, a dual-pathway 3D CNN architecture that simultaneously processed input at different resolutions, effectively capturing both fine details and broader contextual information.

The continued advancement of multi-class tumor segmentation approaches promises to improve diagnostic accuracy and treatment planning by providing more detailed characterization of tumor heterogeneity.

2.7 Challenges in the Field

Despite the significant progress, several persistent challenges continue to impact the development and clinical translation of automated brain tumor analysis systems.

Class imbalance remains a fundamental issue in both segmentation and classification tasks. Brain tumors typically occupy less than 1% of the total brain volume, creating extreme imbalance that can bias models toward the majority (healthy tissue) class [27]. While techniques such as patch-based training [23], specialized loss functions [29], and data augmentation [41] have partially addressed this issue, performance on smaller tumor sub-regions (particularly enhancing tumor) continues to lag behind whole tumor segmentation.

The **interpretability of deep models** presents another significant hurdle, particularly for clinical adoption. The "black box" nature of deep learning approaches creates reluctance among clinicians to trust automated segmentations without understanding the underlying decision process [42]. Recent work by Natekar et al. [43] has explored visualization techniques to highlight features influencing segmentation decisions, while Lucieri et al. [44] demonstrated the value of

attention maps for explaining tumor classification outcomes. However, creating truly interpretable deep learning systems remains an open challenge.

Generalization across different MRI scanners and patients continues to limit clinical applicability. Models trained on specific datasets often experience performance degradation when applied to images acquired with different hardware, field strengths, or acquisition parameters [7]. Zech et al. [45] documented this domain shift problem in medical imaging, while Kamnitsas et al. [40] proposed domain adaptation techniques to mitigate its effects. More recently, Shaw et al. [46] explored adversarial domain adaptation specifically for brain tumor segmentation, showing promising results in cross-scanner generalization.

The **lack of labeled data** remains a fundamental limitation, particularly for rare tumor types or unusual presentations. While the BraTS dataset has grown substantially, it still represents a fraction of the true biological variability of brain tumors [10]. Semi-supervised approaches by Sedai et al. [47] leverage unlabeled data to improve generalization, while Zhao et al. [48] demonstrated promising results with data-efficient few-shot learning techniques. Transfer learning approaches by Ghafoorian et al. [49] have also shown potential in adapting pre-trained models to limited target datasets.

Additional challenges include :

- **Computational efficiency** : 3D deep learning models often require substantial computational resources beyond what's available in many clinical settings [40].
- **Longitudinal analysis** : Most current approaches treat each time point independently, missing the opportunity to leverage temporal information in patient monitoring [50].
- **Integration with other data types** : Combining imaging with clinical, genomic, and pathological data remains challenging despite its potential to improve diagnostic accuracy [10].
- **Clinically relevant evaluation metrics** : Standard technical metrics like Dice coefficients may not directly translate to clinical utility, creating a disconnect between research advances and clinical impact [51].

Addressing these challenges will require multidisciplinary collaboration between computer scientists, medical imaging experts, and clinicians to develop solutions that are not only technically sophisticated but also clinically relevant and practically deployable.

Chapitre 3

Le format

Chapitre 4

Figures, tableaux et références

Chapitre 5

Conclusion générale (2 pages max)

Références

[1] National Cancer Institute, "Brain tumors," https://www.cancer.gov/types/brain, 2024, accessed : 2025-04-15.

[2] D. N. Louis, A. Perry, G. Reifenberger *et al.*, "The 2016 world health organization classification of tumors of the central nervous system : a summary," *Acta neuropathologica*, vol. 131, no. 6, pp. 803–820, 2016.

[3] Mayo Clinic, "Brain tumor overview," https://www.mayoclinic.org/diseases-conditions/brain-tumor, 2024, accessed : 2025-04-15.

[4] O. Ronneberger, P. Fischer, and T. Brox, "U-net : Convolutional networks for biomedical image segmentation," in *International Conference on Medical image computing and computer-assisted intervention*. Springer, 2015, pp. 234–241.

[5] U. Baid, S. Ghodasara, S. Mohan, M. Bilello, E. Calabrese, E. Colak, K. Farahani, J. Kalpathy-Cramer, F. Kitamura, S. Pati, S. Pereira, P. Preetha, S. Reza, C. Sako, A. Sharma, C. Silva, J. Solomon, P. Vu, C. Yogananda, A. Flanders, C. Davatzikos, R. Colen, and S. Bakas, "The multimodal brain tumor image segmentation benchmark (brats) 2020 : Validating image segmentation and outcome prediction algorithms," in *International MICCAI Brainlesion Workshop*. Springer, 2021, pp. 133–145.

[6] S. Bauer, R. Wiest, L. P. Nolte, and M. Reyes, "A survey of MRI-based medical image analysis for brain tumor studies," *Physics in Medicine & Biology*, vol. 58, no. 13, p. R97, 2013.

[7] B. H. Menze, A. Jakab, S. Bauer, J. Kalpathy-Cramer, K. Farahani, J. Kirby *et al.*, "The multimodal brain tumor image segmentation benchmark (BRATS)," *IEEE Transactions on Medical Imaging*, vol. 34, no. 10, pp. 1993–2024, 2015.

[8] S. Bakas, M. Reyes, A. Jakab, S. Bauer, M. Rempfler, A. Crimi *et al.*, "Identifying the best machine learning algorithms for brain tumor segmentation, progression assessment, and overall survival prediction in the BRATS challenge," *arXiv preprint arXiv :1811.02629*, 2018.

[9] L. M. DeAngelis, "Brain tumors," *New England Journal of Medicine*, vol. 344, no. 2, pp. 114–123, 2001.

[10] S. Bakas, H. Akbari, A. Sotiras, M. Bilello, M. Rozycki, J. Kirby *et al.*, "Segmentation labels and radiomic features for the pre-operative scans of the TCGA-GBM collection," The Cancer Imaging Archive, 2019.

[11] ——, "Advancing the cancer genome atlas glioma MRI collections with expert segmentation labels and radiomic features," *Scientific Data*, vol. 4, p. 170117, 2017.

[12] F. Isensee, P. F. Jaeger, S. A. Kohl, J. Petersen, and K. H. Maier-Hein, "nnU-Net : A self-configuring method for deep learning-based biomedical image segmentation," *Nature Methods*, vol. 18, no. 2, pp. 203–211, 2021.

[13] N. Gordillo, E. Montseny, and P. Sobrevilla, "State of the art survey on MRI brain tumor segmentation," *Magnetic Resonance Imaging*, vol. 31, no. 8, pp. 1426–1438, 2013.

[14] S. Bauer, L. P. Nolte, and M. Reyes, "Fully automatic segmentation of brain tumor images using support vector machine classification in combination with hierarchical conditional random field regularization," in *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 2011, pp. 354–361.

[15] E. I. Zacharaki, S. Wang, S. Chawla, D. Soo Yoo, R. Wolf, E. R. Melhem, and C. Davatzikos, "Classification of brain tumor type and grade using MRI texture and shape in a machine learning scheme," *Magnetic Resonance in Medicine*, vol. 62, no. 6, pp. 1609–1618, 2009.

[16] S. M. S. Reza and K. M. Iftekharuddin, "Multi-class abnormal brain tissue segmentation using texture features," in *MICCAI Brain Lesion Workshop (BrainLes)*, 2013, pp. 38–42.

[17] D. Zikic, B. Glocker, E. Konukoglu, A. Criminisi, C. Demiralp, J. Shotton, O. M. Thomas, T. Das, R. Jena, and S. J. Price, "Decision forests for tissue-specific segmentation of

high-grade gliomas in multi-channel MR," in *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 2012, pp. 369–376.

[18] J. Festa, S. Pereira, J. A. Mariz, N. Sousa, and C. A. Silva, "Automatic brain tumor segmentation of multi-sequence MR images using random decision forests," in *Proceedings of NCI-MICCAI BRATS*, 2013, pp. 23–26.

[19] N. J. Tustison, K. L. Shrinidhi, M. Wintermark, C. R. Durst, B. M. Kandel, J. C. Gee, M. C. Grossman, and B. B. Avants, "ANTs and Arboles," *Proc BRATS Challenge*, pp. 47–50, 2015.

[20] V. Simi and J. Joseph, "Segmentation of glioblastoma multiforme from MR images - a comprehensive review," *Egyptian Journal of Radiology and Nuclear Medicine*, vol. 45, no. 4, pp. 1341–1348, 2014.

[21] M. Huang, W. Yang, Y. Wu, J. Jiang, W. Chen, and Q. Feng, "Brain tumor segmentation based on local independent projection-based classification," *IEEE Transactions on Biomedical Engineering*, vol. 61, no. 10, pp. 2633–2645, 2014.

[22] P. Pandit, M. Mandaviya, S. Shah, and N. Shah, "Brain tumor detection using convolutional neural network," *International Journal of Innovative Technology and Exploring Engineering*, vol. 8, no. 12, pp. 4164–4167, 2019.

[23] M. Havaei, A. Davy, D. Warde-Farley, A. Biard, A. Courville, Y. Bengio *et al.*, "Brain tumor segmentation with deep neural networks," *Medical Image Analysis*, vol. 35, pp. 18–31, 2017.

[24] C. Sompong and S. Wongthanavasu, "An efficient brain tumor segmentation based on cellular automata and improved tumor-cut algorithm," *Expert Systems with Applications*, vol. 72, pp. 231–244, 2017.

[25] O. Ronneberger, P. Fischer, and T. Brox, "U-Net : Convolutional networks for biomedical image segmentation," *arXiv preprint arXiv :1505.04597*, 2015.

[26] G. Urban, M. Bendszus, F. Hamprecht, and J. Kleesiek, "Multi-modal brain tumor segmentation using deep convolutional neural networks," in *MICCAI BraTS (Brain Tumor Segmentation) Challenge*, 2014, pp. 31–35.

[27] S. Pereira, A. Pinto, V. Alves, and C. A. Silva, "Brain tumor segmentation using convolutional neural networks in MRI images," *IEEE Transactions on Medical Imaging*, vol. 35, no. 5, pp. 1240–1251, 2016.

[28] Ö. Çiçek, A. Abdulkadir, S. S. Lienkamp, T. Brox, and O. Ronneberger, "3D U-Net : Learning dense volumetric segmentation from sparse annotation," in *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 2016, pp. 424–432.

[29] F. Isensee, P. Kickingereder, W. Wick, M. Bendszus, and K. H. Maier-Hein, "No new-net," in *International MICCAI Brainlesion Workshop*, 2018, pp. 234–244.

[30] Z. Zhou, M. M. R. Siddiquee, N. Tajbakhsh, and J. Liang, "UNet++ : A nested U-Net architecture for medical image segmentation," in *Deep Learning in Medical Image Analysis and Multimodal Learning for Clinical Decision Support*, 2019, pp. 3–11.

[31] O. Oktay, J. Schlemper, L. L. Folgoc, M. Lee, M. Heinrich, K. Misawa, K. Mori, S. McDonagh, N. Y. Hammerla, B. Kainz, B. Glocker, and D. Rueckert, "Attention U-Net : Learning where to look for the pancreas," *arXiv preprint arXiv :1804.03999*, 2018.

[32] J. Schlemper, O. Oktay, M. Schaap, M. Heinrich, B. Kainz, B. Glocker, and D. Rueckert, "Attention gated networks : Learning to leverage salient regions in medical images," in *Medical Image Analysis*, vol. 53, 2019, pp. 197–207.

[33] A. Myronenko, "3D MRI brain tumor segmentation using autoencoder regularization," in *International MICCAI Brainlesion Workshop*, 2018, pp. 311–320.

[34] R. McKinley, R. Meier, and R. Wiest, "Ensembles of densely-connected CNNs with label-uncertainty for brain tumor segmentation," in *International MICCAI Brainlesion Workshop*, 2019, pp. 456–465.

[35] P. Afshar, A. Mohammadi, and K. N. Plataniotis, "Brain tumor type classification via capsule networks," in *IEEE International Conference on Image Processing (ICIP)*, 2019, pp. 1570–1574.

[36] S. Deepak and P. M. Ameer, "Brain tumor classification using deep CNN features via transfer learning," *Computers in Biology and Medicine*, vol. 111, p. 103345, 2019.

[37] M. Sajjad, S. Khan, K. Muhammad, W. Wu, A. Ullah, and S. W. Baik, "Multi-grade brain tumor classification using deep CNN with extensive data augmentation," *Journal of Computational Science*, vol. 30, pp. 174–182, 2019.

[38] X. Zhao, Y. Wu, G. Song, Z. Li, Y. Zhang, and Y. Fan, "A deep learning model integrating FCNNs and CRFs for brain tumor segmentation," *Medical Image Analysis*, vol. 43, pp. 98–111, 2018.

[39] G. Wang, W. Li, S. Ourselin, and T. Vercauteren, "Automatic brain tumor segmentation using cascaded anisotropic convolutional neural networks," *arXiv preprint arXiv :1709.00382*, 2017.

[40] K. Kamnitsas, C. Ledig, V. F. Newcombe, J. P. Simpson, A. D. Kane, D. K. Menon *et al.*, "Efficient multi-scale 3D CNN with fully connected CRF for accurate brain lesion segmentation," *Medical Image Analysis*, vol. 36, pp. 61–78, 2017.

[41] G. Wang, W. Li, M. Aertsen, J. Deprest, S. Ourselin, and T. Vercauteren, "Aleatoric uncertainty estimation with test-time augmentation for medical image segmentation with convolutional neural networks," *Neurocomputing*, vol. 338, pp. 34–45, 2019.

[42] A. Holzinger, C. Biemann, C. S. Pattichis, and D. B. Kell, "What do we need to build explainable AI systems for the medical domain ?" *arXiv preprint arXiv :1712.09923*, 2017.

[43] P. Natekar, A. Kori, and G. Krishnamurthi, "Demystifying brain tumor segmentation networks : Interpretability and uncertainty analysis," *Frontiers in Computational Neuroscience*, vol. 14, p. 6, 2020.

[44] A. Lucieri, M. N. Bajwa, S. A. Braun, M. I. Malik, A. Dengel, and S. Ahmed, "On interpretability of deep learning based skin lesion classifiers using concept activation vectors," in *International Joint Conference on Neural Networks*, 2020, pp. 1–10.

[45] J. R. Zech, M. A. Badgeley, M. Liu, A. B. Costa, J. J. Titano, and E. K. Oermann, "Variable generalization performance of a deep learning model to detect pneumonia in chest radiographs : A cross-sectional study," *PLoS Medicine*, vol. 15, no. 11, p. e1002683, 2018.

[46] R. Shaw, C. H. Sudre, S. Ourselin, and M. J. Cardoso, "Brain tumour segmentation with uncertainty estimation for quality assessment," *arXiv preprint arXiv :2006.13799*, 2020.

[47] S. Sedai, D. Mahapatra, S. Hewavitharanage, S. Maetschke, and R. Garnavi, "Semi-supervised learning with semantic knowledge extraction for improved segmentation of brain structures," *ISPRS Journal of Photogrammetry and Remote Sensing*, vol. 151, pp. 223–232, 2019.

[48] A. Zhao, G. Balakrishnan, F. Durand, J. V. Guttag, and A. V. Dalca, "Data augmentation using learned transformations for one-shot medical image segmentation," *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*, pp. 8543–8553, 2019.

[49] M. Ghafoorian, A. Mehrtash, T. Kapur, N. Karssemeijer, E. Marchiori, M. Pesteie *et al.*, "Transfer learning for domain adaptation in MRI : Application in brain lesion segmentation," in *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 2017, pp. 516–524.

[50] L. Weninger, O. Rippel, S. Koppers, and D. Merhof, "Segmentation of brain tumors and patient survival prediction : Methods for the BraTS 2018 challenge," *arXiv preprint arXiv :1810.04274*, 2018.

[51] L. Maier-Hein, M. Eisenmann, A. Reinke, S. Onogur, M. Stankovic, P. Scholz *et al.*, "Why rankings of biomedical image analysis competitions should be interpreted with care," *Nature Communications*, vol. 9, no. 1, pp. 1–13, 2018.