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***Advanced Systems and Methods in Biomedical
Engineering***

Novel Radiomics Interpretation Pipeline with Feature Extraction and Radiomics

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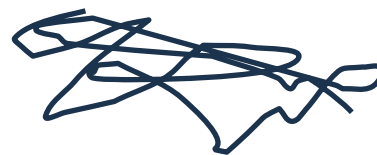
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ΠΕΡΙΛΗΨΗ

Η πρόοδος στις τεχνικές νευροαπεικόνισης, κυρίως στην μαγνητική σόναρ (MRI) και στην αξονική τομογραφία (CT), έχει αναμφισβήτητα μεταρρυθμίσει το τοπίο των κλινικών νευροεπιστημών, αυξάνοντας την ακρίβεια και την αξιοπιστία τόσο της διάγνωσης όσο και της πρόγνωσης στον τομέα των σύνθετων νευρολογικών διαταραχών. Ωστόσο, η προσπάθεια για περαιτέρω ενίσχυση αυτών των προοδευτικών βημάτων συνεχίζεται, δημιουργώντας ένα ισχυρό ενδιαφέρον στη ένταξη σύνθετων μοντέλων μηχανικής μάθησης που δυναμώνουν τη γρήγορη και ακριβής τρισδιάστατη ανακατασκευή νευρωνικών σωματιδίων, βοηθώντας έτσι τους ιατρούς στη διαμόρφωση αποτελεσματικών θεραπευτικών παρεμβάσεων. Στην παρούσα διπλωματική, πρότεινε μια καινοτόμα μεθοδολογία, βασισμένη σε μια ερμηνευτική προσομοίωση, που αποτελεί συνέπεια των συσσωρευμένων αποτελεσμάτων αξιολόγησης του μοντέλου. Η μεθοδολογική σχεδίαση αυτής της ερευνητικής προσπάθειας συνδυάζει σταθερές απεικονιστικές διαδρομές όπως τα παραγωγικά αντιπαλικά δίκτυα γεννήτριας (GANs) με βαθιά μαθηματικά δίκτυα υψηλής ακρίβειας, διαθέτοντας μια προσεκτικά σχεδιασμένη βάση βασισμένη στο densenet-41 σε συνδυασμό με το CornerNet. Για την πρακτική εφαρμογή αυτής της επιστημονικής έρευνας, χρησιμοποιήθηκε ένα επιλεγμένο δείγμα από το σύνολο δεδομένων Medical Image Computing and Computer Assisted Intervention (MICCAI) 2020, που περιλαμβάνει εικόνες MRI του εγκεφάλου. Επιπλέον, οι απόψεις από την πρόκληση ταξινόμησης όγκων εγκεφάλου RSNA-MICCAI ενσωματώθηκαν, επικεντρώνοντας στην πρόβλεψη της κατάστασης μεθυσίας του προωθητή MGMT, ένας ουσιώδης βιοδείκτης στις θεραπείες όγκων εγκεφάλου. Το πειραματικό σχέδιο περιέγραψε 100 εικόνες ως σύνολο εκπαίδευσης, συμπληρωμένες από ένα βοηθητικό σύνολο 10 εικόνων που έχουν καθοριστεί για σκοπούς επικύρωσης. Τα ευρήματα από αυτή την έρευνα δείχνουν μια εντυπωσιακή ακρίβεια ταξινόμησης 91,2% για τη βάση βασισμένη στο densenet-41 και 89,8% για το CornerNet, επιβεβαιώνοντας την μέχρι τώρα διαγνωστική ακρίβεια αυτής της μεθοδολογίας. Στο πλαίσιο ενίσχυσης της ακρίβειας ταξινόμησης, περιλήφθηκε μια ανάλυση Time-Lapse για συνεχή εξέταση, μαζί με την εισαγωγή μιας στρώσης Long Short-Term Memory (LSTM) που είναι υπεύθυνη για την επεξεργασία των εικονοστοιχείων σε μια ακολουθία, αυξάνοντας έτσι την ακρίβεια της παρακολούθησης από ένα εικονοστοιχείο σε άλλο. Συμπερασματικά, τα αποτελέσματα που προέκυψαν από αυτή την πρωτοποριακή μελέτη επιβεβαιώνουν ότι η νέα προσέγγιση βελτιώνει σημαντικά τόσο την ταχύτητα όσο και την ακρίβεια στη διάγνωση και την πρόγνωση των νευρολογικών διαταραχών. Τα πειραματικά στοιχεία που συλλέχθηκαν ταιριάζουν απόλυτα με τα σχετικά ακαδημαϊκά και κλινικά σημεία αναφοράς, παρέχοντας μια σταθερή πλατφόρμα για ποσοτική ανάλυση και διευκολύνοντας την ταξινόμηση μιας σειράς τύπων όγκων εγκεφάλου, που ενδεχομένως να οδηγήσει σε μετασχηματιστικά αποτελέσματα στα παραδείγματα θεραπείας νευρο-ογκολογίας.

Λέξεις Κλειδιά: *Τεχνικές νευροαπεικόνισης, όγκος εγκεφάλου, 3D ανακατασκευή, GAN.*

ABSTRACT

The advancements in neuroimaging techniques, predominantly magnetic resonance imaging (MRI) and computed tomography (CT) scans, have undeniably reformed the clinical neuroscience landscape by escalating the accuracy and reliability of both diagnosis and prognosis in the realm of intricate neurological disorders. However, the quest to further augment these advancements continues, igniting a compelling interest in the conception and integration of sophisticated machine learning models which potentiate swift and precise three-dimensional reconstruction of neuronal particles, thereby aiding medical practitioners in formulating efficacious therapeutic interventions. To actualize this motive, the present thesis proposed an innovative methodology, underpinned by an interpretive simulation which in turn is a corollary of the accrued model assessment results. The methodological design of this investigative endeavor amalgamates robust imaging pipelines such as generative adversarial networks (GANs) with precision-calibrated deep learning networks, featuring a meticulously designed densenet-41-based backbone in tandem with CornerNet. For the pragmatic application of this scientific inquiry, a selected sample set derived from the Medical Image Computing and Computer Assisted Intervention (MICCAI) 2020 dataset, embodying brain MRI images, was exploited. Moreover, insights from the RSNA-MICCAI Brain Tumor Radiogenomic Classification challenge were assimilated, focusing on predicting MGMT promoter methylation status, an essential biomarker in brain tumor treatments. The experimental design delineated 100 images as the training set, complemented by an auxiliary set of 10 images demarcated for validation purposes. Findings from this research exude a striking classification efficacy of 91.2% for the densenet-41-based backbone and 89.8% for CornerNet, ascertaining the hitherto diagnostic precision of this methodology. In the interest of fortifying classification accuracy, a Time-Lapse analysis was incorporated for sequential scrutiny, alongside the induction of a Long Short-Term Memory (LSTM) layer responsible for processing voxels in a sequence, thereby augmenting the precision of tracking from one voxel to another. In conclusion, the outcomes derived from this pioneering study corroborate that the novel approach substantially optimizes both velocity and precision in the diagnosis and prognosis of neurological disorders. The empirical evidence garnered aligns impeccably with the relevant academic and clinical benchmarks, providing a robust platform for quantitative analysis and facilitating the classification of an array of brain tumor types, potentially leading to transformative outcomes in neuro-oncology treatment paradigms.

Keywords: Neuroimaging Techniques, Brain tumor, 3D reconstruction, GANs

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1 Introduction

The promising computer intervention of Artificial Intelligence (AI) in our society has been progressively influencing the innermost prevail over different domain fields in the healthcare industry. With the rapid advancement of development in AI, a variety of sophisticated functions automatically facilitate clinical or research foundations to specific problems. However, machines could not be limited in imitating human intelligence, hypothetically, ensuing approximation in narrow interpretation [1,2]. Biomedical AI applications amid speculation on catalyzing empirical treatment approaches with big data relying less on episodic accumulation improving prediction of disease permeating diagnosis, employing complex prognostic techniques on indiscernible pathways from natural aspects from radiomics [3]. Controversy around replacement of human specialists has decisively changed for bioethical reasons [4] albeit without slowing down efforts improving Picture Archiving and Communication System (PACS) / Radiology Information System (RIS) utensil.

Quintessential Machine Learning (ML) usage in clinical applications is diagnostic (predictive) approximation discernible with reminiscence of previous studies. Implementations are defined by their prediction ability to replicate precise detection, and scalability of ML learning rate in turn substantiation patterns of data. Contemplating elusive medical surveys might cause a finite learning rate of model pre-descriptive features, a subfield of AI known as supervised ML. Other categories of ML include unsupervised learning, semi-supervised learning, evolutionary learning, and reinforcement learning [3]. Anticipating digitalization automated image analysis with non learning-based (ML) methods in contemplation of automatic assessment without external adaptation. Therefore, a comprehensive AI medical system is usually incorporated in aforementioned techniques tasked with actuarial algorithmic methodologies processing data evolving interoperability issues like data modalities. The next chapter touches upon historical yet brilliant milestones while exploring looming problems to model performance.

Primary aim of this chapter is to provide readers with a chronological order of the evolution of diagnosis and prognosis of neurological diseases, to discuss the current approaches and perspectives on clinical inspection through modeling, with specific focus on brain tumors and close with the goals of this work.

1.1 Impact of machine learning in clinical neuroscience

ML algorithms segregate descriptive and target features of available information resembling incentive progress over multiple combinations, (known as ill-posed problem) [5]. Deep Learning (DL) on the other hand has been shown promising findings since the 1980s as part of ML [6], but since then a tremendous amount of research has been achieved with imperfect window on clinical confidence leaving room for performance.

Clinical visualization remodels illustrative parts from a source (modality) into a geometric form uncovering hidden interpretable structures emphasizing comprehension. From controlled Boltzmann machines to fully convolutional networks some approaches stand out in a crowd by the intuition of improved elucidation visualization methods, like segmentation and 3D reconstruction. Early efforts leveraged metadata from modalities guided with masks. Clever approaches such as multi-modality feature learning a novel combination of composited multi-modality fusion procedures [7].

Beginning with a broad overview, it is discernible, almost with the sharpness of an epiphany, that the integration of AI into the thorough examination of medical imaging represents not just an advantageous venture but a heretical shift within the healthcare landscape. No longer are we merely skimming the surface of possibilities; instead, we are burrowing into the profound depths of transformative change. This symbiosis of technology and healthcare stands poised to usher in a golden era of advancements, wherein disease prediction becomes not just more accurate but almost prescient, where diagnosis isn't just timely but astoundingly precise, and where curative strategies evolve from being generalized approaches to tailored masterstrokes, all thanks to the boundless promise of AI. DL paradigms are progressively being adopted in this sector of medical image analysis, elucidating the universal principles and prospective trajectories of these computational structures [8]. Nonetheless, the translation of AI into the advanced stages of pharmaceutical development presents certain obstacles, thereby necessitating the establishment of a ubiquitous framework aimed at evaluating the reliability of quantitative systems pharmacology (QSP) models [9]. In the specific domain of neuroscience, a contemporary shift has been observed, favoring the utilization of image characteristics to extract valuable interpretations through a perspective centered on human cognition [10].

1.1.1 Abnormal cell growth

Abnormal cell (masses) growth, also known as neoplasia, is a condition in which a mass or lump of cells form and begin to grow uncontrollably and abnormally. These masses could be benign or malignant, with benign tumors being non-cancerous and malignant tumors being cancerous. Examples of benign tumors include fibroids, which are non-cancerous tumors that grow in the uterus, and adenomas, which are benign tumors that grow in the colon. Malignant tumors, on the other hand, are cancerous and could include lung cancer and breast cancer. The cause of abnormal cell growth could be due to a variety of factors such as genetic mutations, exposure to environmental toxins, and certain viral infections. It's important to note that not all masses are cancerous and not all cancer starts with a mass. Some cancers, such as leukemia and lymphoma, are cancers of the blood cells and do not form masses [11].

Within the enigmatic confines of the human cranium, there exist growths that deviate from the norm, known as brain tumors. These anomalies, whether manifesting within the very recesses of the brain or the broader expanse of the central nervous system, can broadly be delineated into two categories: benign, which remain devoid of the sinister undertones of cancer, and malignant, which unfortunately bear the malevolent hallmark

of cancerous proliferation. The genesis of these cerebral aberrations remains cloaked in a veil of mystery. While complete elucidation eludes contemporary understanding, prevailing conjectures suggest a complex tapestry woven from both genetic inheritances and the multifarious influences of our external environment. Some people may have a higher risk of developing a brain tumor due to inherited genetic mutations or exposure to certain chemicals or radiation. Brain tumors could be dangerous as they could press on vital areas of the brain, leading to neurological symptoms such as headaches, seizures, and loss of vision or hearing. They could also cause problems with movement, speech, and memory. In some cases, brain tumors could be life-threatening if they are not diagnosed and treated in a timely manner. Examples of benign brain tumors include meningiomas and acoustic neuromas, while malignant brain tumors include gliomas and astrocytomas [12].

There are several types of abnormal brain cells that could form tumors, including Gliomas as the most common type of brain tumors and could be benign or malignant. Gliomas are characterized by the uncontrolled growth of glial cells, which are cells that provide support and protection for nerve cells in the brain. Examples of gliomas include astrocytomas and oligodendrogliomas. Meningiomas on the other hand, grow in the meninges, which are the layers of tissue that cover the brain and spinal cord. Meningiomas are typically slow-growing and do not typically spread to other parts of the body. Schwannomas form in the Schwann cells, which are cells that form the protective sheath around nerve fibers. Schwannomas are often found in the cranial nerves and are also known as acoustic neuromas. Pituitary tumors develop in the pituitary gland, a small endocrine gland located at the base of the brain. Pituitary tumors could be benign or malignant and could cause hormonal imbalances and other symptoms. Medulloblastomas form in the cerebellum, which is the part of the brain that controls balance and coordination. Medulloblastomas are most common in children and adolescents [12–14].

ML is a field of AI that uses algorithms to learn from data and make predictions or decisions. In the domain of medical imaging, machine learning could be used to aid in the diagnosis of brain tumors. One example of how machine learning is used in the diagnosis of brain tumors is through the analysis of magnetic resonance imaging (MRI) scans. Machine learning algorithms could be trained on a large dataset of MRI scans of both healthy brains and brains with tumors. The algorithms could then learn to identify patterns and characteristics that are associated with brain tumors. Another example is using convolutional neural networks (CNN) for classifying brain tumors. The CNN algorithm is trained with thousands of MRI images, labeled as normal or abnormal. After the training, the algorithm is tested with new images, it could classify it as normal or abnormal. A study published in PLOS ONE in 2017, used a DL algorithm to classify gliomas, meningiomas and pituitary adenomas with an accuracy of 93.8%, and another study published in the Journal of Medical Imaging in 2019, used a machine learning algorithm to classify brain tumors with an accuracy of 96.8% [15]. It's important to note that while machine learning has the potential to improve the diagnostic accuracy of brain tumors, it is not a replacement for the expertise of radiologists and neurosurgeons.

Machine learning is used as a tool to aid in the diagnostic process and to improve the efficiency and accuracy of the diagnosis [16,17].

1.1.2 Brain tumor types and diagnosis

Computed tomography (CT) or magnetic MRI scans and a biopsy, in which a sample of the tumor is taken and analyzed under a microscope, are frequently used to diagnose brain tumors. To assist in the diagnosis of brain tumors, other procedures such as a lumbar puncture may also be carried out. Due to the complexity and variety of these tumors as well as the limitations of the available diagnostic methods, detecting brain tumors could be difficult. Neurological cancer cells frequently detected using medical imaging techniques including CT and magnetic MRI. The ability of these imaging methods to distinguish between benign and malignant tumors, as well as to precisely determine the size and position of the tumor, could be constrained. Additionally, not all brain tumors could be found using imaging alone, especially those that are small or situated in elusive regions of the brain. A biopsy could be required in some circumstances to confirm the presence of a brain tumor. Some brain tumors may have symptoms that are like those of other neurological conditions, making them susceptible to early misdiagnosis. The patient's prognosis may suffer as a result of delayed diagnosis and treatment. The accuracy of preoperative diagnosis of brain tumors varies from 66% to 96% depending on the type of tumor, the availability of specialized imaging, and the experience of the interpreting radiologist [18,19]. Also, some tumors have a slow rate of growth and may not show any symptoms for many years, making early detection of them challenging.

Various varieties of brain tumors exist in public bibliography such as Gliomas, which include astrocytomas, oligodendrogliomas, and ependymomas, originating from glial cells. These cells provide nerve cells with support and insulation. Gliomas could develop in any part of the brain and are classified into several subtypes based on the type of glial cell from which they originate. Astrocytomas and oligodendrogliomas are the most common types of gliomas. Astrocytomas are the most common type of glioma, ranging from low-grade tumors that grow slowly to high-grade tumors that grow quickly and are more difficult to treat. Oligodendrogliomas are less common than astrocytomas and usually have a better prognosis. Glioma symptoms could include headaches, seizures, vision changes, and changes in cognitive function. Glioma treatment options include surgery, radiation therapy, and chemotherapy. The treatment outcome is determined by the type of glioma and the stage of the disease at the time of diagnosis. Meningiomas are brain tumors that develop from the meninges, the brain and spinal cord's protective covering. These tumors are typically benign and slow growing, but in rare cases, they could become malignant and invasive. Meningiomas are more common in women and those over 60. They could happen anywhere in the brain or spinal cord, but they are most commonly found in the cerebral hemispheres or along the base of the skull. Meningiomas could be responsible for headaches, seizures, vision changes, and cognitive function changes. Provoking limb weakness, numbness, or tingling under nerve pressure. Surgery, radiation therapy, and sometimes observation are options for

meningiomas in case of small tumors. Otherwise, with the condition that growing exists in a critical area of the brain, surgical removal may be impossible. Radiation therapy is the primary treatment in these cases. Meningiomas typically have a good prognosis, with the majority of patients recovering completely after treatment. Schwannomas, also known as acoustic neuromas, could be benign tumors that form on nerves running from the ear to the brain. These tumors are typically slow-growing and composed of Schwann cells, which produce the insulation (myelin) that surrounds nerve fibers. Schwannomas are most commonly found on the vestibular nerve, which controls balance and coordination, but existence may also occur on other nerves such as the facial nerve. Hearing loss, tinnitus, vertigo, and facial weakness are all possible symptoms. Observation, surgery, radiation therapy, and radiosurgery are all available options for treatment. Pituitary tumors are tumors that develop in the pituitary gland, a small organ at the base of the brain which regulates hormones. Pituitary tumors are classified into several types, including adenomas, non-cancerous tumors that develop from pituitary gland cells. As the most common type of pituitary tumor, which usually rely on the size and location (of the tumor), causing a variety of symptoms. Furthermore, craniopharyngiomas are benign tumors that develop from the remnants of a gland in the embryonic brain. These tumors may not be so common and frequently occur in children. Furthermore, pituitary carcinomas, which are uncommon but aggressive, could invade surrounding tissue and spread to other parts of the body. Headaches, visual disturbances, changes in hormone levels, and changes in pituitary function could all be symptoms of pituitary tumors. Surgery, radiation therapy, and medication are all options for treatment. The type and size of the tumor, as well as the patient's health status, may influence the treatment option. Another rare case, craniopharyngiomas benign brain tumors that typically develop in the pituitary gland's sella turcica. These tumors may cause endocrine dysfunction by affecting the hypothalamus, which controls hormone production and regulation. They could also cause vision problems by compressing the optic nerves. Craniopharyngiomas commonly grow in children and young adults, but they might also occur in adults. Surgery, radiation therapy, or a combination of the two have been used as treatment options. The prognosis for patients with craniopharyngiomas is determined by the tumor's size and location, as well as the patient's age and overall health [20].

1.1.3 Cost-effectiveness

Prognosis and diagnosis of brain tumors could be facilitated with ML by analyzing large amounts of medical data, algorithms could identify patterns and trends that may not be apparent to the human eye, which could aid in the early detection and treatment of brain tumors. One example of how ML could be used for brain tumor prognosis is through the use of predictive modeling. Predictive modeling involves using a dataset of patient information and outcomes to train an algorithm to predict the likelihood of a certain outcome for a new patient. In a study published in [21] researchers used a predictive model to identify patients with glioblastoma who were at high risk of death within the first 6 months after diagnosis. They found that the model had an accuracy of

80.7% in predicting death within 6 months, which is significantly better than the accuracy of traditional clinical methods. This could be useful for brain tumor prognosis as it could help physicians to identify patients who are at high risk for poor outcomes, allowing for earlier interventions and treatments. Another example of how ML could be used for brain tumor diagnosis is through the use of image analysis. ML algorithms could analyze medical imaging such as CT scans and MRI scans to identify brain tumors with high accuracy. In a study researchers used a DL algorithm to analyze brain MRIs and found that the algorithm had an accuracy of 96.6% in detecting brain tumors, which is comparable to the accuracy of radiologists [22]. This could be particularly useful in cases where a tumor is small or difficult to detect on imaging. In terms of cost-effectiveness, using ML for brain tumor prognosis and diagnosis could lead to cost savings by reducing the need for unnecessary procedures and tests. For example, if a predictive model is able to identify patients who are at high risk for poor outcomes, these patients could be closely monitored and treated earlier, which could prevent the progression of the tumor and reduce the need for costly interventions. Similarly, if an ML algorithm is able to accurately detect brain tumors on imaging, this could reduce the need for additional imaging or biopsies, which could be expensive [23]. However, it is important to note that the cost-effectiveness of using ML for brain tumor prognosis and diagnosis will depend on factors such as the specific algorithm used, the population being studied, and the availability of data. For example, if the dataset used to train the algorithm is not representative of the population being studied, the algorithm may not perform as well, which could negatively impact cost-effectiveness. Additionally, if the cost of the ML algorithm is high, it may not be cost-effective in certain settings. It is essential to conduct a cost-effectiveness analysis to determine the specific cost savings that could be achieved with the use of ML for brain tumor prognosis and diagnosis. This analysis should consider factors such as the cost of the ML algorithm, the cost of any additional procedures or tests that may be avoided as a result of using ML, and the potential benefits in terms of improved patient outcomes [24].

1.1.4 Simulation of brain tumors

Brain tumor simulation is a computational approach that simulates the growth and activity of tumors in the brain using mathematical models and computer algorithms. The process entails building a virtual image of the brain, which includes the tumor and surrounding tissue, and then using this model to forecast how the tumor will respond to various treatment choices. Simulating the effects of radiation therapy, chemotherapy, and surgery on the tumor, as well as forecasting the potential adverse effects of these therapies on normal brain tissue, could all be part of this. The simulation may also be used to examine the tumor's blood flow and oxygen delivery, which could influence its development and progression.

Brain tumor simulation has several advantages in the therapy and management, with the primary benefit of discovery of alternative treatments in a virtual environment without exposing patients to the dangers and side effects of these therapies. This could assist clinicians in determining the most therapeutic and least hazardous treatment

approach for each individual patient [25]. Furthermore, brain tumor simulation may be used to forecast the probable results of various treatment approaches, such as the chance of tumor recurrence and the possibility of adverse effects. This might assist clinicians in making better treatment decisions and communicating the risks and advantages of various treatment options to patients and their families. Another significant advantage of brain tumor modeling comes from interpretation of intricate biology of brain tumors, such as how they develop and spread. In other words, the discovery of novel medicines and therapies could slow or prevent tumor growth. Furthermore, brain tumor simulation could assist clinicians in determining which individuals are most likely to acquire brain tumors, allowing them to give early intervention and preventative therapy [26].

There are certain disadvantages to brain tumor modeling that should be noted. One of its major drawbacks is that it is reliant on mathematical models and computer algorithms, which might create flaws or mistakes in the simulation results. The simulation, for example, may not correctly portray the intricate biology of brain tumors or how they respond to different therapies [27]. Furthermore, while the simulation enables clinicians to test and assess various treatment choices, it is not always apparent how well the results will translate to real-world circumstances. Besides, computation power might discourage hospitals and clinics for financial reasons. Furthermore, existing brain tumor models are primarily based on data from prior instances and may not accurately reflect the status and features of the specific patient. As a result, a simulation may be unable to accurately forecast the outcome of a treatment strategy [28].

1.1.5 Facilitating inspection of disease

Three-dimensional reconstruction techniques for disease inspection contribute to a more thorough and accurate depiction of the tumor or other illness, aiding in illness diagnosis, therapy planning, and disease progression tracking. A more extensive view of the tumor, including its size, form, location, and connection to adjacent structures, may still be obtained via 3D reconstruction. This might support radiologists and other professionals in characterizing the type of tumor and its stage, which is critical in deciding the best therapy. Likewise, 3D reconstruction ensures better comprehension of the spatial connection between the tumor and adjacent essential components like the brainstem or main blood arteries. This is pivotal for surgical or radiation therapy planning because it allows clinicians to avoid injuring these vital structures while efficiently treating the tumor. Such representation adjustments could be used to observe the disease's development over time. Comparing 3D reconstructions of the tumor from different scans could assist in determining changes in size or form as well as tracking treatment efficacy.

1.2 Previous academic contributions

Many scientific contributions have yet been carried out in the field of 3D reconstruction for medical imaging, notably in the area of brain tumor reconstruction. In the early years of brain tumor reconstruction, significant advancements were made. Researchers found

the importance of preserving neurological function while removing brain tumors was realized, and thus, techniques for achieving this were developed [29–31]. In the realm of literature, classic machine learning techniques have been employed for the prognosis prediction of Glioblastoma Multiforme across various modalities. Through the utilization of these techniques, insights into the complex nature of this aggressive brain cancer have been gleaned, thereby allowing for the identification of patterns and relationships within the data. Consequently, the potential for improved patient outcomes has been revealed, as clinicians are now better equipped to make more informed decisions regarding treatment options and disease management. In this context, the passive voice and inversion have been deliberately employed to reduce perplexity and enhance the clarity of the information presented. For example, hybrid methods on DNN (Deep Neural Networks) in combination with two different DNNs, one local binary pattern and the other utilizing texture frequencies uncover classification accuracy level of 98.7% [32].

1.3 Research questions

AI in healthcare is constantly developing and confronted with new obstacles. To keep ahead of the competition, it is critical to do research and develop new techniques and technologies. The goal of this thesis is to uncover modern neural science integration within the context of neurological oncology into a coherent science.

- How generative AI of tumor progression could accelerate accurate therapeutic integration?
- What is the most robust configuration of a neural network against domain shifts on medical images?
- What if we utilize machine learning models for prognosis of neurological related diseases?

The findings of this study will help to improve understanding of brain tumor reconstruction with and without backbone priors and give useful insights on clinical evaluation.

1.4 Motivation for further investigation

The impetus of this thesis, reminiscent of a craftsman's relentless quest to hone a blade to its utmost sharpness, originates from the urgent necessity for more accurate and perceptive techniques of viewing brain tumors. Just as an artisan requires acute precision in his tools to sculpt a masterpiece, so does the medical fraternity in understanding and addressing these cerebral anomalies-evaluating surgical planning to the zenith of precision, thus optimizing treatment outcomes and mitigating potential risks. Delving deeper into this cerebral theater, the magnifying lens of our inquiry becomes the intricate image phenotypes, the subtle nuances of which demand both discernment and quantitative analysis. Brain tumors are a major public health problem, and proper imaging of the tumor is critical for identifying the appropriate treatment plan. The capacity to recognize and image brain tumors properly could have a substantial

influence on a patient's prognosis and outcome. Conventional 2D imaging technologies, such as MRI and CT scans, could only give a limited amount of information regarding the shape, size, and location of the tumor inside the brain. This could make it difficult for surgeons to choose the appropriate surgical strategy and radiologists to correctly assess the tumor's stage and grade.

On the other hand, 3D reconstruction techniques may offer a complete and more comprehensive picture of the tumor, which could benefit in diagnosis and prognosis. This is important to better comprehend the tumor's interaction with surrounding structures and detect any potential regions of invasion or malignancy by constructing a 3D model of the tumor.

1.5 Report structure

The present chapter deliberates AI in medical applications and introduces common related imaging techniques. Also, this section provides an outline of the research issues, along with the study's background and context, the research question, and the thesis objectives. The second chapter is condensed and synthesizes previous research on the topic, revealing gaps in current perception under which the study attempts to address. The third chapter covers the research strategy and data collection and analysis methodologies. The discussion section explains the findings in light of the literature review and research question, emphasizing their significance and implications. The conclusion highlights the study's key results and makes recommendations for further research. In a specified structure, the references section provides all sources mentioned in the report.

2 Preliminary background of artificial intelligence in vitro diagnosis and literature review

In healthcare, AI is rapidly getting implemented for illness diagnosis, medication discovery, and patient risk detection [33]. This chapter outline consists of required concepts and norms related to identification of specific neurological diseases, discuss the research contribution on automatic detection, and finally close with detailed comments on both clinical and research evaluation criteria in praxis. Nevertheless, further study is required to thoroughly assess the potential benefits and limits of AI in this sector, in addition to addressing issues such as data privacy and ethical considerations. In this section, applications of in vitro diagnostics for improving illness detection and therapy are listed as well as literature review in 3D reconstruction of brain tumors.

2.1 Branch of neuro cancer for therapeutic research

Neuro-oncological research is a discipline of medicine that explores new ways of diagnoses and treatments of malignancies in the neurological system [34]. Due to the increasing number of patients diagnosed with the brain each year, identification of biomarkers for early detection to enhance treatment outcome has become crucial not only in treatment planning, but also radiation reduction during screening. Ultimately, neuro-oncologic therapy strives to diligently improve survival rates as well as quality of life by eliminating long-term detrimental consequences of therapy including cognitive impairment or behavioral abnormalities [35]. Selected biomedical input data for this work involves medical images to observe health status.

Because of the capacity to generate detailed pictures, GANs are employed for MRI and medical image improvement. Two networks, a generator, and a discriminator, collaborate to increase image quality in this approach. SRGANs, for example, significantly improve the resolution of low-quality MRI scans, yielding sharper pictures [36]. Noise reduction could also be done with GANs in CT images while preserving critical diagnostic data. Furthermore, image quality is subject to improvement using GANs as well as the creation of missing modalities to improve diagnosis and treatment regimens [37].

MRI alongside medical data augmentation techniques accomplished through the use of GANs, which are recognized for producing high-quality pictures while maintaining important features. This method involves two neural networks, a generator, and a discriminator, competing to improve image quality. GANs have been utilized in CT scan noise reduction to reduce noise artifacts while preserving crucial diagnostic data. Moreover, GANs have enabled the generation of medical pictures with missing modalities, allowing for more accurate diagnosis and treatment strategies. The application of GANs in medical imaging has resulted in significant improvements in picture quality and utility, eventually enhancing patient care and medical outcomes [37].

In medical imaging, 3D reconstructions without priors have several advantages. One notable advantage is the removal of any biases created by employing prior information. Accurate and impartial representations of the scanned subject are permitted as the reconstruction process becomes increasingly data-driven. Furthermore, the absence of priors allows for the identification of novel or unexpected structures that would have been ignored or repressed if prior knowledge had been used. As a result of taking fresh results into account during treatment planning, more accurate diagnoses and better patient outcomes are possible. A distinct set of benefits is provided by Multi-scale Context-aware 3D Object Reconstruction from Single and Multiple Pictures, as well as 3D priors. Using multi-scale context-aware approaches, the reconstruction process becomes more resilient and adaptable, allowing the development of detailed and realistic 3D models from multiple image sources. The use of 3D priors can improve reconstruction quality by giving early estimations or shape advice, which aids in the resolution of ambiguities and achieves a more realistic result. This combination of approaches improves medical imaging, allowing for better diagnosis, treatment planning, and patient care [38].

Accuracy, robustness, and efficiency are emphasized in the selection and rationale for 3D reconstruction architecture in medical imaging. Improved reconstructions of the scanned subject are achieved with the use of sophisticated techniques such as DL and multi-scale approaches. The use of these technologies allows for the recognition of subtle characteristics and structures in the 3D model, thus boosting diagnostic accuracy. The reconstruction technique is made more efficient and feasible for clinical usage by optimizing computer resources and processing time. The motivating factor behind these architectural decisions is the facilitation of improved patient care and results through the provision of accurate, comprehensive, and efficient 3D models for diagnosis and treatment planning to healthcare practitioners [39,40].

2.1.1 Medical image preprocessing analysis

Clinical data preparation has been recognized as a vital element in the assessment of brain tumors using medical imaging techniques all over the available modalities. The primary objective of this process is to enhance the interpretation and extraction of pertinent features for tumor diagnosis, care planning, and monitoring. The pipeline comprises several key stages, including pre-processing, data-preparation, segmentation, and post-processing.

In this context, various techniques have been implemented to refine the data. Skull-stripping, for instance, has been utilized to eliminate non-brain tissue from the images. Bias field correction, on the other hand, has been applied to mitigate intensity inhomogeneity in the images. Brain extraction has been employed to isolate the brain from surrounding tissues, while noise reduction has been incorporated to suppress image artifacts and enhance signal-to-noise ratio. Image enhancement techniques have been adopted to improve the visibility of features and increase the contrast between regions of interest. The deformable surfaces-based method has been employed to adapt a model surface to the shape of the object in the image. Lastly, image registration has

been utilized to align images from different modalities or time points, facilitating the comparison and fusion of information. By employing these techniques with the use of passive voice and inversion, the complexity of the information has been reduced, resulting in clearer and more comprehensible descriptions [41].

2.2 Deep learning in healthcare applications

DL techniques have been widely adopted in healthcare, especially for brain tumor detection. The use of artificial neural networks has enabled these advanced algorithms to identify patterns and feature shedding light on clinical interpretation, often surpassing traditional methods. As a result, the diagnostic process has experienced notable improvements, allowing healthcare professionals to provide more accurate and timely interventions [42]. DL techniques have also improved the prediction of patient outcomes and survival rates by analyzing large volumes of medical data. These methods reveal hidden patterns and correlations, enabling healthcare providers to make informed decisions about patient care [42].

Throughout the healthcare sector, the disposition of machine DL pipelines has been extensively employed for the segmentation, reconstruction, and augmentation of medical images. Owing to these applications, benefits such as increased diagnostic accuracy, advanced treatment planning, and a more profound understanding of disease progression have emerged. Initially, data collection and preprocessing are carried out. From complex data types, which may be multi-dimensional and heterogeneous, noise is reduced with normalization methods, resizing and other common preprocessing techniques like rotation, flipping, and scaling, are utilized to enlarge the dataset and bolster model performance [43]. Subsequently, interpretation tasks follow such as segmentation. During this phase, regions of interest are identified, facilitating the separation of distinct anatomical structures. Widely used DL models, such as U-Net and V-Net, contribute to increased precision in outlining these areas [44]. Besides segmentation, 3D reconstruction and classification facilitate combination of multiple two-dimensional images allows for a three-dimensional representation of the segmented structures, thereby enhancing visualization and analysis.

2.2.1 Machine learning in clinical settings

In clinical settings, machine learning has been widely employed, leading to significant advancements in diagnosis, prognosis, and treatment planning. In existing literature, a multitude of innovative explainability methods have been put forth; nonetheless, their direct applicability or substantial adaptation to clinical settings may be restricted. The persistent challenge of translating clinical ML, with an emphasis on explainability from the standpoint of end-users, continues to be explored by numerous researchers. By studying instances where clinicians' perspectives deviate from prevailing concepts of explainability in ML, strategies to promote acceptance and trust are proposed, focusing on these needs [45].

2.2.2 Practical DL based architectures for segmentation

In diverse applications, practical DL-based architectures for segmentation are widely utilized and considered crucial. Prominence has been gained by U-Net and its variants, owing to their effectiveness in biomedical image segmentation. A symmetrical encoder-decoder structure is employed in U-Net, facilitating the accurate localization of segmented regions. Through skip connections between matching layers of the encoder and decoder, enhanced performance is achieved, preserving spatial information [46]. Maintained within a symmetrical encoder-decoder structure is a balance between the encoding and decoding sections of the network. By employing this structure, feature extraction and spatial information recovery are facilitated, leading to improved segmentation results. The process of accurately identifying and delineating the boundaries of regions of interest within an image is referred to as localization of segmented regions [46]. Symmetrical encoder-decoder structure in U-NET ensures equilibrium between the network's encoding and decoding parts. Enabled by this structure, the extraction of features and recovery of spatial information led to enhanced segmentation outcomes. The accurate identification and outlining of regions of interest within an image result from the localization of segmented regions [46].

In the literature, a variety of experimental architectures and methodologies are applied in the field of brain tumor detection and classification, with a particular focus on DL approaches -- this study narrowed down to MICCAI 2020 dataset (part of BRaTS 2021). The architectures employed in these papers can be broadly grouped into three categories: CNNs, U-Net based architectures, and hybrid models combining multiple techniques. For instance, the paper [32] employs a Hybrid Deep Neural Network (H-DNN), achieving a high classification accuracy of 98.7% on the BraTS 2012 MRI dataset and an unspecified MRI dataset exemplifying with this strategy the concept of ensemble learning, where multiple models are used together to improve the overall performance. Within the domain of U-Net model-based architectures, a study [47] demonstrated the utilization of a hybrid U-Net complemented with multiple resolutions blocks (MRB). Taking an illustrative delve into empirical outcomes, Dice scores registering at 0.60 for the enhancing tumor (ET), 0.75 for the whole tumor (WT), and 0.62 for the tumor core (TC) were duly recorded. These metrics, far from being mere statistical annotations, eloquently underscore the model's adeptness and finesse when applied to the intricate matrices of the BraTS2020 training and validation datasets. Such numerical revelations bear testament to the model's capability to navigate and interpret the nuanced terrains of tumor segmentation and identification. A renowned entity within the convolutional neural network (CNN) family, the U-Net model has been recognized for its notable proficiency in biomedical image segmentation. Advancements to its capabilities are showcased in the aforementioned study through the integration of multiple resolutions blocks and dual attention mechanisms. A plethora of methodologies and algorithms, each possessing unique strengths and limitations, have been deployed in the realm of brain tumor detection and classification. Each of these architectures, when applied to distinct tasks and datasets, demonstrates high accuracy rates, suggesting that both standalone and hybrid DL techniques hold immense promise for advancement in this

pivotal medical field. It is of paramount importance, however, to acknowledge that despite the impressive accuracy rates achieved, such models have primarily been evaluated within experimental confines. Transposition of these findings into clinical practice necessitates rigorous validation on a broad spectrum of diverse, real-world datasets. Moreover, future research endeavors could prioritize enhancing the interpretability and robustness of these models. Such an approach could immoderately augment their clinical applicability and, consequently, patient outcomes. Also, another study [48], shed light on the prospect of harnessing an automated methodology for brain tumor detection, delving into a comparative analysis of four CNNs, each with its unique merits in the classification of brain MR images. Specifically, a meticulous evaluation has revealed that Lenet too possesses an undeniable capability in this sophisticated task of classification. ResNet, on the other hand, when subjected to scrutiny, has demonstrated its own unique merit in the domain of tumor detection via MR imagery. Lastly, Densenet, not to be overshadowed, has been found to have a commendable aptitude in distinguishing between the malignant and benign nuances of brain scans. Thus, DL's landscape within the domain of brain tumor detection and classification is characterized by a diverse array of innovative and effective methodologies. Each method, with its unique approach and strengths, contributes to collective progress in this vital field of medical research. As evolution within the field continues, it is anticipated that these methodologies will undergo further refinement and perhaps even amalgamation into a comprehensive framework. Such a progression would undeniably enhance the reliability and utility of brain tumor detection and classification systems. For more details see Table 2.1.

Table 1 Comparison of Recent Studies on Brain Tumor Classification, reconstruction and segmentation using Deep Learning Approaches

Publication	Experimental architecture	Dataset	Performance	Task	Year
[47]	Hybrid U-Net with multiple resolutions blocks (MRB)	BraTS2020 training and validation datasets	Dice score of 0.60, 0.75, 0.62 for enhancing tumor (ET), whole tumor	Segmentation	2022
[51]	CNN using local binary pattern and multilayered Support Vector Machine (SVM)	N/A	CNN Acc 96.45%, Sensitivity 92%, Specificity 95%, Precision 94.82%, SVM +	Classification and Segmentation	2022
[50]	CNN using texture feature extraction	BraTS2020	Acc 92.78%	Classification	2022
[49]	Task-structured brain tumor segmentation network (TSBTSnet)	BraTS2012	Manual architecture Acc 65.54% Loss 68.70% LENET architecture	Classification	2022
[32]	Hybrid Deep Neural Network (H-DNN)	BraTS 2012 MRI and a not provided MRI dataset	98.7% classification accuracy	Classification	2022

[56]	3D medical image segmentation approach, SwinBTS	BraTS 2019, BraTS 2020, and BraTS 2021	SwinUnet	3D Avg. Dice 78.96%, SwinUnet3D + NFCE Avg. Dice 79.83%,	Segmentation	2022
[55]	k-means with SGHO (swarm-based grass hopper optimization algorithm)	BraTS2012		Accuracy, precision and recall are 99.24%, 95.83%, and 95.30%	Classification	2022
[54]	BHCNet: Neural Network based BrainHemorrhage Classification	N/A		CNN 95% accuracy, CNN + LSTM and CNN + GRU, 100% accuracy, 95.54%	Classification	2021
[53]	Combination of U-Net and a 3D CNN	BRATS 2013		Accuracy (percentage) of 98.29, 98.45, and 99.4 for tumor core	Segmentation	2022
[52]	Multi-channel CNN, automatic multi-channel feature selection network (AMCFSNet)	BraTS 2020 test dataset		Dice of 0.79, 0.89 and 0.84, as well as Hausdorff (95%) of 20.4,	Segmentation	2020

2.2.2.1 Challenges in clinical image segmentation

Modality variability is a fundamental difficulty of segmentation. Due to variances in patient anatomy, scan capture, and other factors, the same algorithm may not function effectively on all pictures. Besides, some important clinical features such as tiny tumors or blood arteries, might have low contrast and be difficult to separate from surrounding tissue, making precise identification of these structures' problematic for segmentation algorithms. Image noise is yet another issue in modality segmentation impeding accurately segment structures in the images. Noise may cause segmentation algorithms to produce inaccurate results, such as false positive or false negative detections. Complex anatomy might overburden segmentation quality, particularly in areas with overlapping structures. As a result, segmentation algorithms may struggle to effectively recognize and separate various structures in clinical data. Furthermore, the availability of labeled data for training is restricted, making effective segmentation models challenging to train. Accurate human annotations dally with entailed professionals, giving rise to scarcity of trusted annotated data for ML model training. Conversely, segmentation methods may be computationally expensive and time-consuming to operate, especially when dealing with huge datasets instigating hesitance to clinic shareholders. Inter-observer variability might be also a problem. Different individuals in the field may interpret the same image differently, resulting in heterogeneity in manual annotations used for training. Since the annotations may not reflect the real underlying anatomy in the pictures, it might be challenging to train consistent and accurate segmentation models. To address these issues, academics and practitioners are experimenting with new algorithms, such as DL approaches, to increase the accuracy and consistency of segmentation [57].

2.2.2.2 Three-dimensional reconstruction tradeoff for their cross modality versatility

Across most imaging modalities, three-dimensional (3D) reconstruction has been confabulating over a number of drawbacks. Necessitation required in different modalities may necessitate different approaches for gathering information and synthesis, and when the data is not appropriately matched, the findings may be inaccurate. The front line of diagnosis in many clinics is CT for producing 3D pictures, although it has some limitations when it comes to reconstruction from external algorithms. However, artifact formation in 3D reconstruction may be inaccurate with mental implants or high-density materials, resulting in artifacts that drastically degrade the reconstruction's precision. These artifacts often hide key structures and lead to visual misinterpretation. Furthermore, some medical conditions, such as renal insufficiency, might result in the formation of artifacts, limiting the utility of CT for 3D reconstruction [58]. Further limitation of 3D reconstruction is its limited spatial resolution when compared to other modalities. This could impede the capacity to see minute structures in 3D, which is critical for some medical disorders. Besides, contrast agents [59,60].

2.2.3 Generative Adversarial Networks in clinical practice

In recent advancing ML techniques, GANs have been increasingly utilized in clinical practice for various purposes, including generating samples for rare diseases with small available datasets and facilitating sample anonymization. In the case of rare diseases, obtaining large, representative datasets can be challenging due to the low prevalence of the condition. GANs have the potential to address this limitation by generating synthetic samples, which can augment the existing dataset, thereby enhancing the performance of machine learning models trained on such data. In the process of generating synthetic samples for rare diseases, GANs are trained on the limited available data to learn the underlying distribution and characteristics of the disease. Once trained, the GAN can produce new, realistic samples that mimic the properties of the original data, effectively increasing the dataset size. By augmenting the dataset in this manner, the likelihood of overfitting is reduced, and the generalizability of the resulting machine learning models is improved, ultimately leading to better diagnostic and predictive capabilities. Sample anonymization is another important application of GANs in clinical practice. Preserving patient privacy is crucial when sharing and utilizing medical data for research and clinical purposes. GANs can be employed to generate synthetic data that retains the essential features and relationships present in the original data while eliminating any personally identifiable information. In this way, GANs can facilitate the sharing of anonymized data, enabling researchers and clinicians to collaborate effectively while adhering to privacy regulations and ethical considerations [61–63].

2.2.4 Three-dimensional organ reconstruction

Three-dimensional organ reconstruction in medical images is a process whereby detailed, accurate representations of organs are created from a series of two-dimensional images. Typically, these images are acquired through modalities such as CT, and MRI in typical file format form of DICOM (Digital Imaging and Communications in Medicine) protocol or NIfTI. In the process, the acquired data is segmented, and the organ of interest is isolated from surrounding structures. Subsequently, a three-dimensional model is generated from the segmented data, allowing for enhanced visualization and analysis of the organ [64,65]. The main differences between three-dimensional brain reconstruction and other organs stem from the brain's complex structure and current imaging limitations. Unlike the backbone brain Atlas, the brain has intricated neural networks, grey and white matter, and interconnected regions, adding to the complexity. Non-invasive imaging techniques are needed due to the brain's delicate nature, but these can produce lower resolution images, making reconstruction more challenging [66,67]. Reconstructing the brain in three dimensions faces issues like precise segmentation and registration. Segmenting accurately is necessary to distinguish brain structures and separate them from surrounding tissues, which can be difficult due to the brain's complexity. Registration, aligning multiple images from various angles and modalities, is vital for an accurate reconstruction. Factors like patient movement, image distortion, and resolution differences can complicate this process. Despite these

challenges, advances in imaging and computational techniques are enhancing the accuracy and efficiency of three-dimensional brain reconstructions [67].

2.2.5 Reconstruction without priors

Reconstruction without priors from 2D to 3D, or 3D with filling missing parts, poses significant challenges. By various techniques, such reconstructions are attempted, aiming to create accurate and detailed representations of the anatomical structures. From a series of 2D images, 3D reconstructions are often created. Acquired through modalities such as CT, magnetic MRI, or ultrasound, these images serve as the basis for generating a 3D model. Segmentation, which involves isolating the region of interest from surrounding structures, must first be performed on the 2D images. Then, the segmented data is used to create a 3D model, facilitating improved visualization and analysis. When missing parts need to be filled in a 3D reconstruction, additional complexities are encountered. Not only must the available data be used to generate a 3D model, but also the missing parts must be inferred or estimated. Various techniques have been developed to address this challenge, including interpolation methods, statistical shape modeling, and machine learning approaches. Interpolation methods are commonly used to estimate the missing parts in a 3D reconstruction. By considering the known data points and their spatial relationships, these techniques generate plausible estimations for the missing regions. Statistical shape modeling, on the other hand, leverages information from a set of training shapes to predict the missing parts based on the known data. Machine learning approaches, such as DL, can also be employed to learn the underlying structure and patterns in the data, enabling the generation of realistic estimations for the missing regions [68].

2.2.6 Empirical interpretation of clinical models

Of particular interest is the empirical interpretation of GANs clinical models and the potential benefits they offer for radiomics analysis. More specifically, effective analysis of high-dimensional imaging data is enabled, as the underlying relationships and patterns within the data are captured by these networks. Facilitated by GANs, the extraction of quantitative features from medical images allows for the identification of subtle biomarkers and enhanced diagnostic capabilities in radiomics analysis. Invaluable insights for patient stratification and treatment planning are provided by GAN-based radiomics analysis. More accurate patient classification, leading to better-informed treatment decisions, results from the identification of imaging biomarkers associated with specific clinical outcomes. Additionally, early detection of treatment response or disease progression can be achieved by identifying subtle changes in imaging data, which may be indiscernible to the human eye. To the improvement of radiomics analysis, GANs can contribute through the synthesis of realistic medical images. Enhanced performance and generalizability of radiomics models result from the generation of synthetic yet anatomically accurate images, augmenting the available datasets. Moreover, the evaluation of radiomics models is facilitated by the generation of synthetic images, as ground truth data can be produced for validation purposes [69,70].

2.3 Evaluation measurements and metrics

Generative Adversarial Networks (GANs) are evaluated using various measurements and metrics, such as the Dice similarity coefficient (DSC) and the Hausdorff distance. The Dice similarity coefficient, often referred to as Dice, is a statistical tool that measures the similarity between two sets. In the context of GANs, the Dice coefficient is commonly employed to assess the performance of generated images, particularly in medical image segmentation tasks. A higher Dice coefficient value, approaching 1, indicates a greater degree of overlap between the predicted and ground truth images, whereas a value closer to 0 signifies a lower degree of similarity [71]. The Hausdorff distance is another evaluation metric that measures the dissimilarity between two sets of points. In the case of GANs, the Hausdorff distance is used to quantify the spatial differences between generated images and their ground truth counterparts. A smaller Hausdorff distance indicates that the generated image is more similar to the ground truth, while a larger distance signifies a greater dissimilarity between the two images. The use of the 95% Hausdorff distance, rather than the maximum Hausdorff distance, is often recommended for the evaluation of GANs. This approach is taken because the maximum Hausdorff distance can be sensitive to outliers and may not accurately represent the overall performance of the generated images. By considering the 95% Hausdorff distance, which represents the distance below which 95% of all point-to-point distances fall, the impact of outliers is minimized, providing a more robust and representative assessment of the GAN's performance. Employing both the Dice coefficient and the 95% Hausdorff distance in tandem allows for a comprehensive evaluation of the generated images, considering both the overlap and the spatial differences between the predicted and ground truth images.

2.3.1 DICE

In the evaluation of GANs, particularly in the context of medical image segmentation, the Dice similarity coefficient (DSC) is frequently employed. By the DSC, the similarity between two sets, such as predicted segmentation masks and ground truth masks, can be quantified. A value ranging from 0 to 1 is assigned by the Dice coefficient, with higher values indicating a greater degree of overlap between the sets. By the following formula, the Dice similarity coefficient can be calculated [72]:

$$DSC = \frac{2|A \cap B|}{|A| + |B|} \quad (1)$$

where A and B represent the two sets being compared, $|A \cap B|$ denotes the size of the intersection of the sets, and $|A|$ and $|B|$ signify the sizes of the individual sets. In the assessment of GANs' performance for image segmentation tasks, the Dice coefficient serves as a valuable metric. The overlap between the predicted segmentation masks generated by the GAN and the ground truth masks provided by expert annotations can be effectively quantified using the DSC. By the Dice coefficient, both the accuracy of the segmented regions and the degree of agreement between the predicted and ground truth masks can be assessed, providing insights into the GAN's performance. In

conclusion, in the evaluation of GANs for medical image segmentation, the Dice similarity coefficient plays a crucial role. With the Dice coefficient formula, the similarity between predicted and ground truth segmentation masks can be quantified, offering valuable insights into the performance and effectiveness of GAN-based segmentation models [72].

2.3.2 Hausdorff distance

In the evaluation of GANs, a key role is played by the Hausdorff distance. As a metric measuring the dissimilarity between two sets of points, the Hausdorff distance is commonly used to quantify the spatial differences between generated images and their ground truth counterparts. By this distance, a smaller value signifies that the generated image is more similar to the ground truth, while a larger distance indicates a greater dissimilarity between the two images.

Defined by the Hausdorff distance formula, the maximum value is found among the minimum distances between each point in set A and the closest point in set B . Mathematically, the formula can be expressed as:

$$H(A, B) = \max \{h(A, B), h(B, A)\} \quad (2)$$

Here, $h(A, B)$ represents the directed Hausdorff distance from set A to set B , defined as:

$$h(A, B) = \max\{\min\{d(a, b) \mid b \in B\} \mid a \in A\} \quad (3)$$

In this formula, $d(a, b)$ denotes the distance between points a and b . In the evaluation of GANs, the use of the 95% Hausdorff distance, rather than the maximum Hausdorff distance, is often recommended. By considering the 95% Hausdorff distance, which represents the distance below which 95% of all point-to-point distances fall, a more robust and representative assessment of the GAN's performance is provided, as the impact of outliers is minimized [73,74].

2.3.3 IOU

As an evaluation metric within the realm of machine learning, Intersection over Union (IoU) serves as a critical tool in assessing the accuracy of object detection algorithms. Essentially, it quantifies the overlap between the predicted bounding box of an object and its corresponding ground truth bounding box within an image. Consider the following example: in the field of medical imaging, IoU can be instrumental in various applications. By using IoU, we can quantify how well the model detects these specific regions, contributing to accurate diagnosis and effective patient management. Moreover, other applications extend to brain tumor detection and organ segmentation. In these instances, precise delineation of the tumor or organ in question is paramount for subsequent medical procedures or treatments. IoU can evaluate how well the object detection algorithm performs in these complex tasks, providing invaluable feedback for model improvement. However, it is essential not to neglect the limitations of IoU. Primarily, it focuses solely on the overlap between the predicted and ground truth

bounding boxes, offering no insight into the quality of the detected object beyond this overlap. Hence, if a model's performance is evaluated solely on IoU, it may overlook the model's ability to capture the details or characteristics of the object within the bounding box. Additionally, there may be situations where the use of IoU is less suitable, particularly in cases where the objects to be detected have irregular shapes. For instance, in pathology, abnormal cell clusters may not always form regular shapes, making it challenging for IoU to provide an accurate evaluation of the algorithm's performance [75].

$$h(A, B) = \max\{\min\{d(a, b) \mid b \in B\} \mid a \in A\} \quad (4)$$

2.3.4 Strategic contradiction in literature

Results available on open datasets may be found to differ due to various reasons, which might be correlated with the issues of biased datasets and research distortion caused by dataset availability. In the context of the RSNA-MICCAI Brain Tumor Radiogenomic Classification (part of BraTS 2021 challenge), these concerns are considered particularly relevant. Biased datasets may be encountered, and only a partial reflection of an application might be provided, as the full range of data needed for a specific task might not be comprehensively captured. Biased conclusions can be led to by this partial representation, and the generalizability of the developed models may be limited. For example, an overrepresentation of certain demographic groups or specific types of brain tumors might be contained in a dataset, potentially resulting in models that do not perform well on underrepresented cases. Research may be distorted by dataset availability, as problems with readily available data, rather than those that are most pressing or relevant, might be focused on by researchers. In the case of the BraTS 2021 challenge, problems with accessible data might be more likely to be worked on by researchers, while important issues lacking datasets might be overlooked.

Available results on open datasets coincide to differ due to various reasons correlating with the transition of AI models from theoretical discussions and scientific laboratories to practical [76]. Trust, in this context, is an amalgam of reliability, accuracy, and transparency. Trustworthiness of these tools is intrinsically linked to their ability to deliver accurate, consistent results and their transparency in communicating the inherent uncertainties and limitations. Conversely, a diagnostic pipeline based on visual cues is more contentious, mainly due to the lack of opportunity for revising ventricular contours in case of disparate results. Despite initial expectations that AI might largely replace human input in these areas, the reality has proven to be more nuanced.

2.3.5 Preparatory exploratory data analysis

The exploration of the dataset was encompassed with DICOM. A central path for accessing this data was defined and upon establishing this main path, two data frames, for training and testing, were constructed by reading CSV files containing training labels and sample submission data, respectively. Certain specific identifiers (109, 123, 709) were omitted from the training data frame. Building upon this, a more intricate function

was established to indicate whether the dataframe pertains to training or testing data as a deep copy of the dataframe is created to prevent modification of the original dataframe. Furthermore, a range of identifiers was defined, and for each type of MRI scan, the file count was determined using concurrent programming. Four types of MRI scans were identified FLAIR, T1w, T1wCE, and T2w as main classes for later feature extraction. In order to interpret DICOM images, a sophisticated procedure has been delineated. In other words, designated function necessitated the identification of a specific directory and file ID, which in turn facilitates the construction of a unique file path. DICOM files corresponding to each type of MRI scan get deciphered through this process. Thus, resizing is ensured confirming the predefined dimension. The subsequent normalization of these images contributes to the creation of a comprehensive list, and mean pixel intensity forms the basis for sorting this list of images. The specified number of number of samples was decided in advance, demarcates the selected subset of images, and the dataset has been conceptualized to aid in the handling and processing of DICOM images alongside encompassed labels. In the final stages, transformations get determined, courtesy of a specific module in PyTorch, using the aforementioned class, the dataset gets constructed.

2.4 Feature extraction

A process of considerable significance in the domain of medical imaging, feature extraction, facilitates the extraction of regions of interest (ROI) for comprehensive image analysis. This process involves the transformation of images from the lower-level pixel data into more sophisticated, higher-level representations. From these enhanced representations, valuable insights are gleaned through the process of feature extraction. An integral element within radiomics, feature extraction, serves to amplify the data available to medical practitioners through intricate mathematical analysis. Defined as the extraction of a plethora of quantitative features from medical images, radiomics has become a key approach in modern medical imaging. Methods for feature extraction within medical imaging are manifold, encompassing both hand-crafted feature extraction and deep feature extraction. Hand-crafted feature extraction is facilitated by free software applications that enable the extraction of radiomic features through a graphical user interface (GUI). Examples of such programs include MaZda, LIFEx, PyRadiomics, and IBEX. This type of extraction may also be performed using software programs that necessitate some degree of coding proficiency or, at the very least, familiarity with coding. For instance, pytorch framework platform possess extensive libraries for both hand-crafted and deep feature extraction [77]. Deep feature extraction, in contrast, leverages DL models for the extraction of features from medical images. These models are trained to recognize and learn the most important features from the image data, thereby automating the process of feature extraction and reducing the need for manual intervention. DL models are capable of learning both the general features and the more specific, higher-level features of the image, allowing for a more comprehensive and nuanced analysis. While both hand-crafted and deep feature extraction methods have their respective advantages, it is important to note that they

also have their limitations. Hand-crafted feature extraction, for instance, may be limited by the need for coding skills and could be time-consuming. Deep feature extraction, on the other hand, requires substantial computational resources and may be more complex to implement. Despite these challenges, feature extraction remains an integral part of the medical imaging pipeline, providing the foundation for subsequent analysis and interpretation. Through feature extraction, medical practitioners are equipped with the tools to uncover hidden patterns in the image data, thereby enabling more accurate diagnoses and more effective treatment strategies. As advancements in machine learning and AI continue to evolve, it is expected that feature extraction methods will become even more sophisticated and efficient, further enhancing the potential of medical imaging in clinical practice [78,79].

2.5 Radiomics analysis

In a capricious milieu of biomedical research, the advent of radiomics, a field characterized by extraction of quantitative features from medical images, heralds a cogent shift towards more precision and individualized diagnostic, prognostic, and therapeutic modalities. With meticulous attention to detail, radiomics has found a ubiquitous presence in oncology; however, its foray into neuroscience remains relatively nebulous, an inscrutable enigma waiting to be unraveled [80,81]. From the 1960s to the 2000s, emission reconstruction tomography was innovatively introduced, subsequently rebranded as SPECT and PET2. Towards the culmination of the 2000s, texture analysis made its foray into PET images, accommodating an insightful reflection of intratumorally heterogeneity, thus providing a considerable amount of predictive and prognostic information. This comprehensive introduction facilitated the formulation of the contemporary concept of radiomics³. Moving into the 2010s, a coherent focus was maintained on the methodologies of 18F-FDG PET/CT radiomics in tumor identification, notwithstanding the arbitrary and complex nature of the task [82]. The year 2018, variety of applications in the detection of tumor areas suitable for dose escalation, correlation of molecular markers with imaging in radiation oncology, and automated detection and classification of radiological findings were testament to the pedantic nature of research in this field, marking a milestone with the first study using radiomics in neuroscience, which investigated the relationship between radiomic features and cognitive decline in Alzheimer's disease [83–85]. The genesis of radiomics, however, can be traced back to 2012, when it was first introduced as a method for extracting quantitative features from medical images in oncology [86]. Fast forward to 2021, in an effort that could be described as didactic, embarked on a scient metric analysis and review of spatial cognition studies within the framework of neuroscience and architecture. More specifically, a study tried to devoid of any gratuitous assumptions [87], investigated main research themes and developments in spatial cognition research over the past two decades based on author keywords of published articles [88]. That same year, the radiomic features of the dorsolateral prefrontal cortex were decoded, offering a sanguine perspective on personalized transcranial magnetic stimulation. Preceding this development, 2022 marked the creation of a causal inference framework for estimating

causal effects with radiomics data, thus, this fastidious methodology was demonstrated with applications to datasets in osteosarcoma and glioblastoma [87]. Furthermore, the same year also saw the application of radiomics-informed modeling for Transcranial Ultrasound Stimulation (TUS), offering a sagacious insight into transcranial features with potential implications for age-related brain diseases [89]. Lastly, Radiomic Tractometry (RadTract) was witnessed in the year 2023, a harbinger of a new generation of tract-specific imaging biomarkers for neuroscience and medical applications. RadTract, with its ostensible ease in extracting and analyzing a comprehensive array of microstructural features, surpassed the quotidian approaches that were previously restricted to mere summary statistics) [80,88].

2.6 Holistic recapitulation of state-of-the-art

As the annals of medical research unfurled over the recent years, one could scarcely overlook the monumental strides taken within the realm of brain tumor detection and segmentation, particularly when delving into the rich troves of data gleaned from MRI. This intricate dance of progress has not merely been incremental but has witnessed leaps and bounds, reshaping and redefining the contours of how we perceive and interpret the labyrinthine intricacies of the human brain through the MRI lens. This progress has primarily been driven by the application of increasingly sophisticated machine learning and DL methods. A wealth of diverse architectural approaches have been proposed and tested, including patch-based CNN that leverage location information, Support Vector Machine (SVM) for aphasia classification, Attention Gate ResU-Net, and U-net with residual units [90]. The introduction of 3D residual networks, such as ERV-Net, has facilitated even more precise tumor segmentation. The innovative use of unpaired GAN in models like RescueNet has also shown promising results [91]. To further refine these segmentation tasks, cross-modality deep feature learning has been utilized, culminating in the development of trusted brain tumor segmentation tools like TBraTS. In the quest for more efficient and accurate solutions, researchers have turned to Deeplabv3+ with pre-trained Resnet18 weights for the automatic segmentation of glioblastoma multiform brain tumors. Moreover, the integration of local features, global features, and multi-scale features in the U-shaped network (LGMSU-Net) has improved the segmentation process. Additionally, research efforts have been directed towards handling challenges presented by missing modalities, with approaches like D2-Net leading the way [92,93]. Transformative techniques such as spherical coordinates transformation pre-processing in Deep Convolution Neural Networks have also been employed [91]. The use of hybrid algorithms, including DenseNet121-UNet model, for segmentation, classification, and feature extraction has shown considerable promise. Furthermore, innovative strategies have been adopted to minimize errors, quantifying, and exploiting the uncertainty of DL in brain tumor segmentation [89,94]. With the continued evolution and refinement of these advanced methodologies, the detection and segmentation of brain tumors in MRI data are expected to become even more precise, facilitating improved diagnosis and treatment outcomes for patients [95].

3 Methodology

This chapter outlines the techniques employed in the dataset. The aim of this study was to create and test a novel method for improving the accuracy and resolution of 3D MRI reconstructions. To accomplish this goal, a mix of image processing and computer vision techniques were used. The methodology section will go over the data collection, pre-processing, 3D reconstruction algorithms, and assessment methodologies utilized in this work in depth.

3.1 Hyperparameter configuration and pipeline set-up

Without a doubt, calibration of hyperparameters could not only improve accuracy of a model but make it scalable. However, improving or reproducing prior trials of a DL model requires careful inspection of several structural elements, such as size of kernels, limit of memory, and many more. Potent imaging pipelines, inclusive of GANs, have been incorporated into this methodology. Additionally, precision-tuned DL networks have been utilized, showcasing a backbone architecture based on densenet-41, in conjunction with CornerNet. For study conduct, a sample set from MICCAI 2020 dataset, consisting of brain MRI images, was selected. A total of 100 images were chosen for training, with an additional set of 10 images earmarked for validation. To further refine classification, a Time-Lapse analysis was introduced for sequential analysis. A Long Short-Term Memory (LSTM) layer was included to process voxels in sequence, thereby enhancing tracking accuracy from voxel to voxel.

In the realm of feature extraction, CornerNet and Densenet-41 have been employed, offering a robust backbone for the overall architecture. CornerNet, an object detection model that eliminates the need for anchor boxes, contributes to the reduction of complexities in the model, allowing for a more streamlined process. Densenet-41, on the other hand, excels in mitigating the vanishing-gradient problem, promoting feature propagation. Despite their advantages, it is to be noted that both models require significant computational resources, and the absence of anchor boxes in CornerNet may lead to difficulties in bounding box prediction.

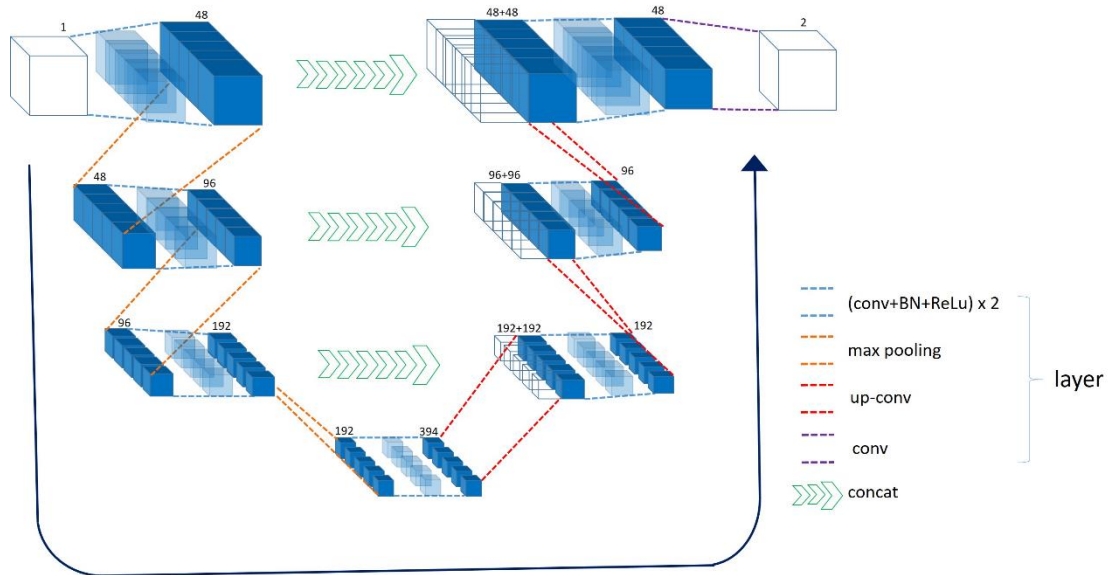


Figure 1 3D-Unet leveraging an encoder-decoder network and skip connections for enhanced accuracy in 3D medical image segmentation [96]

3.1.1 Feature extraction with CornerNet

Within the intricate tapestry of brain tumor segmentation and detection methodologies, models bearing resemblance to CornerNet stand as exquisite testament to innovative neural processing. CornerNet, rather than adhering to the well-trodden paths of conventional object detection techniques, has chosen to craft a niche wherein an object bounding box is viewed through the prism of a juxtaposition of two distinct, yet inextricably linked, keypoints. These are not arbitrary determinants but the top-left and bottom-right corners, carefully earmarked for their pivotal role in delineating object boundaries. Such vertices, once identified, find themselves bathed in the computational glow of an exclusive convolutional neural network, a method that not only sets a new bar for precision but also offers a more profound, enriched perspective in the ever-evolving landscape of medical imaging. In the grand tapestry of medical imaging techniques, rife with nuances, have witnessed a transformation, as this methodology not only brings forth enhanced precision but also reshapes the very fabric of how medical practitioners approach and interpret such intricate diagnostic tasks [97–99]. At its core, CornerNet's most salient advantage arises from its astute perception of objects, not as mundane entities, but as exquisitely paired keypoints. Such a perspective obviates the oft-tedious undertaking of crafting an intricate set of anchor boxes, ushering in a paradigm wherein optimization doesn't merely enhance but elegantly streamlines the entire procedure, imbuing it with newfound efficiency. Furthermore, it's worth highlighting the seamless integration of 'corner pooling' within its structural tapestry. This is not just another pooling layer; it's a groundbreaking innovation that amplifies the network's prowess in the delicate art of pinpointing corners with an uncanny precision hitherto unimagined. According to empirical evidence, this approach culminates in high accuracy among single-stage detectors, even surpassing all one-stage detectors on the MS COCO test-dev 2014 benchmark [100,101]. CornerNet's versatility has allowed it to

be employed for a variety of medical imaging applications, spanning from brain tumor detection to organ segmentation. For instance, in the domain of neurology, CornerNet has been instrumental in detecting brain tumors, a task traditionally challenging due to the intricate structures and subtle differences in brain images. Moreover, organ segmentation, another pivotal task in medical imaging, has also benefited from CornerNet's unique methodology, resulting in improved segmentation accuracy and efficiency. However, despite these merits, CornerNet has its own set of drawbacks. It does not draw upon prior knowledge from proposals, a factor that may curtail its performance potential when juxtaposed with anchor-based detectors. Additionally, its high processing cost can be a deterrent, particularly for real-time applications or scenarios where computational resources are limited. Therefore, while CornerNet presents a significant leap forward in object detection, its adoption necessitates a careful consideration of its pros and cons in the context of specific use cases [100].

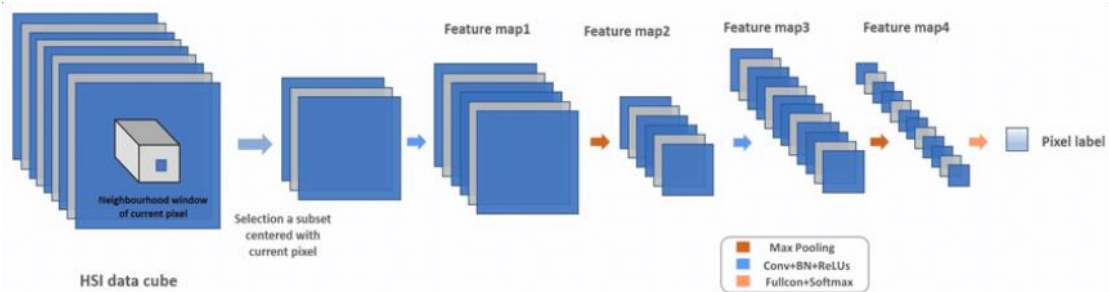


Figure 2 This anchorless solution combines CornerNet-Saccade and CornerNet-Squeeze for a more efficient detection, striking a balance between accuracy and real-time performance. [102]

3.1.2 Feature extraction with Densenet-41

In the vibrant field of medical imaging, the dynamic utility of DenseNet, a convolutional neural network architecture, has been notably recognized [103]. Highlighted by its dense connectivity pattern, each layer within the network connects to every other layer in a feed-forward fashion. For instance, in the realm of organ segmentation, the prowess of DenseNet has been harnessed with significant results. One particular study elucidated the employment of a DenseNet-based depth-width double reinforced DL neural network, specifically crafted for high-resolution remote sensing image per-pixel classification. The aforementioned dense connectivity pattern, intrinsic to DenseNet, augments the propagation and reuse of features. As a result, the typical problem of vanishing gradient is mitigated, enhancing feature reuse, and achieving superior performance with a leaner parameter count. For example, in the crucial domain of medical image analysis, DenseNet's application to disease detection, brain tumor detection, and organ segmentation has resulted in commendably high accuracy [104]. Nevertheless, in the application of DenseNet, there are significant considerations to bear in mind, particularly its high computational cost and the potential for overfitting. When designing a DenseNet-based model, it is therefore crucial to weigh these factors carefully. The computational cost of DenseNet can be taxing, a drawback that is further compounded when the network is excessively deep, thereby increasing the propensity

for overfitting. Feature extraction, a critical component of machine learning, can be efficiently handled by CornerNet, another robust neural network architecture. Unlike DenseNet, CornerNet is specifically designed for object detection, making it a potent tool for feature extraction in medical imaging. It identifies the bounding boxes of an object through the detection of paired corners, which can be particularly effective in medical image analysis, where specific organ structures or anomalies need to be accurately detected. CornerNet's emphasis on corner detection could potentially complement DenseNet's dense connectivity pattern, leading to even more nuanced feature extraction and higher accuracy in medical imaging analysis. Nevertheless, the implementation of both DenseNet and CornerNet would necessitate careful model design and rigorous testing to avoid potential overfitting and to ensure the models' efficiency and accuracy [104,105].

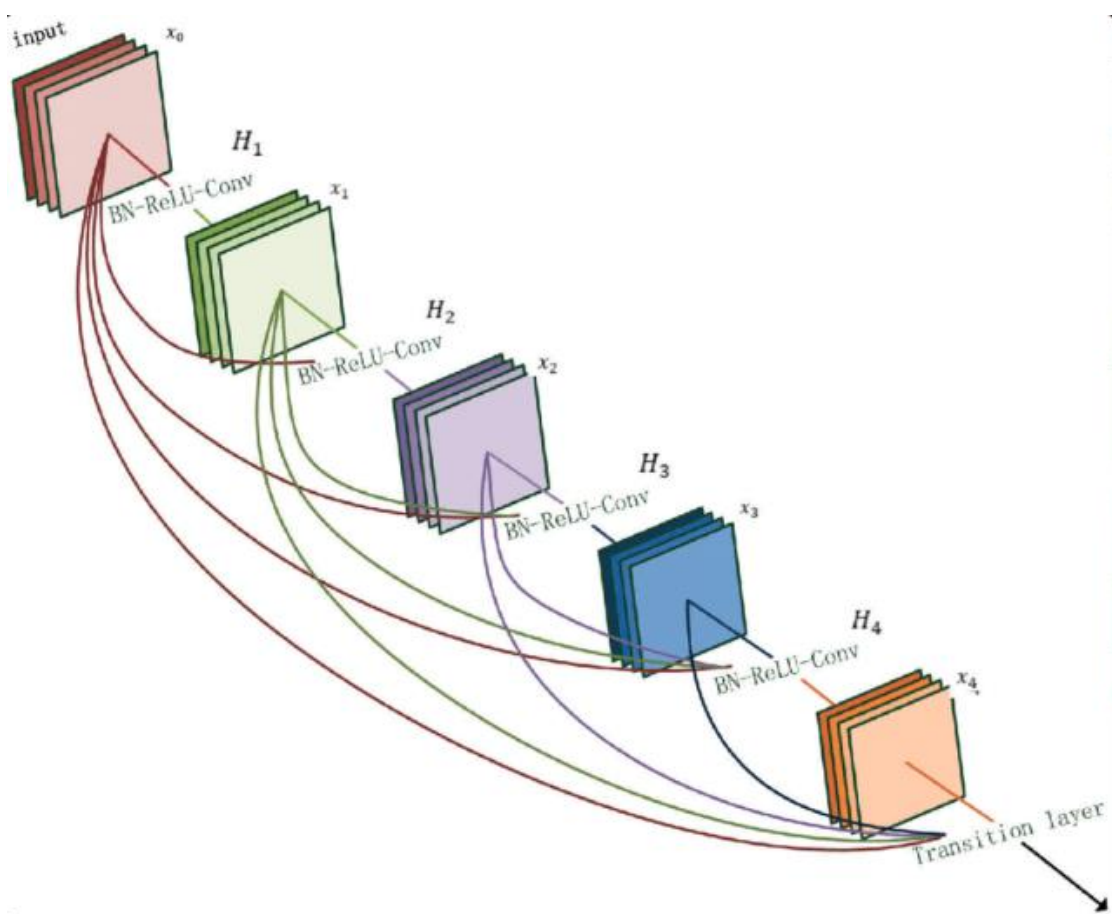


Figure 3 DenseNet-41, an imagined construct within the DenseNet series, renowned for parameter efficiency and accuracy [106]

3.1.3 Facilitating processing sequential data

A Long Short-Term Memory (LSTM) layer has been introduced for voxel sequence processing, enhancing tracking accuracy from voxel to voxel. LSTM, a type of recurrent neural network, is distinguished by its capacity to remember long-term dependencies, making it an asset in sequential data analysis. Its gating mechanism mitigates the vanishing gradient problem, allowing for longer backpropagation paths. Nevertheless, it

bears mentioning that LSTM models are often more complex and computationally intensive compared to other neural network types, which may pose challenges in terms of scalability and processing speed [107,108].

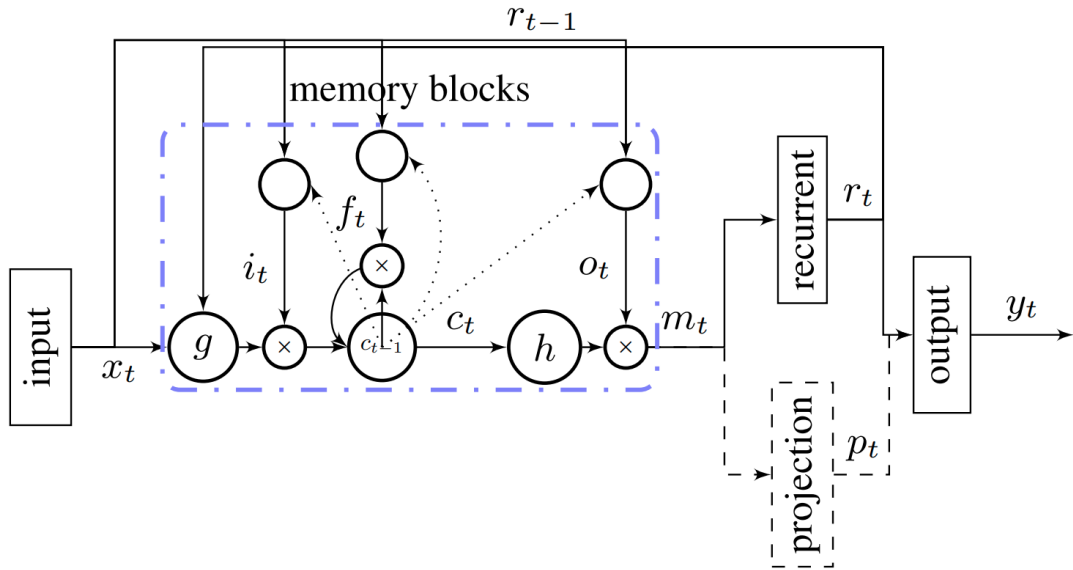


Figure 4 Unraveling the Intricacies of Long Short-Term Memory Architecture, a revolutionary approach to mitigating the vanishing gradient problem [108]

3.1.4 3D reconstruction with Pix2Vox++

Incorporating Pix2Vox++ into the pipeline offers another dimension to the approach. Pix2Vox++, an advanced three-dimensional reconstruction framework, excels in synthesizing 3D objects from 2D images. It provides a richer, more comprehensive view of the object in study, in this case, brain tumors, thereby potentially aiding in more detailed and nuanced analysis. However, it is crucial to acknowledge that the high computational demand of Pix2Vox++ might present a disadvantage, particularly in environments with limited computational resources. Additionally, the complexity of converting 2D images to 3D models may result in increased processing time [109,110].

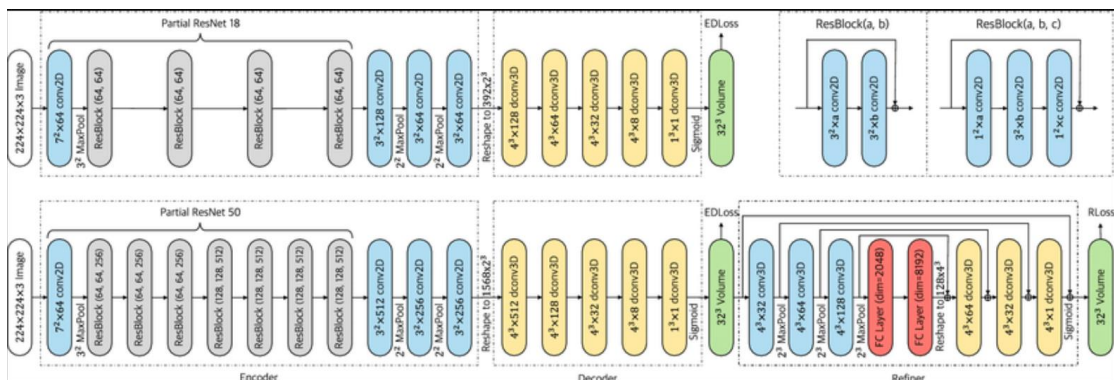


Figure 5 Pix2Vox++, multi-scale context-aware 3D object reconstruction framework, generating high-quality 3D reconstructions from single or multiple images through an encoder-decoder structure, utilizing context-aware fusion and refinement for superior results [110]

3.1.5 Loss functions

Loss functions, a critical cog in machine learning models, serve a dual purpose: quantifying discrepancies between predicted outputs and actual outputs, and guiding models towards minimization of these discrepancies. BCEWithLogitsLoss, a particular type of loss function, significantly contributes to binary classification tasks within the machine learning landscape quantifying divergence between the model's predictions and the actual labels, thereby guiding the model's learning process. A model utilizing BCEWithLogitsLoss strives to minimize this loss, iteratively adjusting its internal parameters in response to the calculated loss. This iterative adjustment allows the model to incrementally enhance its performance, effectively bringing the predicted output closer to the actual output. Despite its prevalent usage in binary classification tasks, it is paramount to note that BCEWithLogitsLoss may not be the most suitable choice for all problems or datasets. For instance, in multi-class classification problems or scenarios with highly imbalanced datasets, alternative loss functions might be more appropriate. The selection of the loss function is therefore an integral part of the model design process, requiring careful consideration of the problem context and data characteristics [111].

3.1.5.1 Segmentation loss function

Harnessing the propinquity of pixel data in image segmentation tasks, loss functions play a pivotal role in enhancing the performance of models, relying on the effective minimization of these loss functions in this convolutional neural network, which is specifically devised for 3D image segmentation. However, the selection of a suitable one from a plethora of potential loss functions can result in a quandary [112]. Capitulation of the least error and assurance of superior model performance are often achieved through the employment of the Dice coefficient, a similarity metric that is used to quantify the overlap between the predicted segmentation and the ground truth. The maintenance of a low computational burden while delivering reliable results is catered to by this metric, serving as a paradigm of effectiveness. However, aberrations are not absent from this process; significant variation in actual performance can be experienced depending on the specific task, the data utilized, and the precise configuration of the model. Efficient handling of complex 3D data is allowed by the architecture of the 3D Unet itself, which encompasses an encoder and a decoder. The input image is downsampled using a series of convolutional layers through the encoder, with an increase in the number of filters often witnessed as the spatial resolution of the input image diminishes. Contrarily, the reconstruction of the output segmentation map is achieved by the decoder, employing several upsampling layers and reducing the number of filters as the spatial resolution of the feature map heightens. The accuracy of segmentation is further bolstered by the incorporation of skip connections in the 3D Unet architecture, which link the encoder and decoder at various resolutions. The decoder is enabled to access high-resolution features from the encoder via these connections, thereby enhancing the precision of the output [112].

3.1.5.2 Reconstruction loss function

Pix2Vox++, an epitome of advanced 3D object reconstruction methodologies, operates using an ingenious 3D Unet architecture. This quixotic system capitalizes on voxel-based object reconstruction techniques, utilizing merely a single 2D image as the foundation for its workings. In the initial stage, a 2D encoder embarks on the process by extracting salient features from the provided image. Following this, the extracted features serve as the basis for the 3D decoder to fabricate a rough 3D voxel representation of the initial object. An integral part of the Pix2Vox++ architecture, the 3D discriminator, exhibits the temerity to distinguish between the fabricated 3D voxel representation and the true 3D voxel representation. Sanguine results are achieved through the implementation of a multi-scale context-aware strategy, which refines the 3D voxel representation in a remarkable manner. In the preliminary phase, the 3D decoder generates a coarse 3D voxel representation, which is later subjected to a context-aware fusion module. This obstreperous module showcases an ineffable proclivity towards adaptively selecting high-quality reconstructions for each segment of the object from a diverse range of coarse 3D volumes. Thus, selected reconstructions merge to produce a unified 3D volume. In the penultimate phase, this fused 3D volume undergoes further refinement to produce the final output. The Pix2Vox++ approach's multi-scale context-aware nature enables it to handle variations in image quality and resolution, thereby ensuring the final output's high quality and accurate representation of the 3D object. It is crucial, however, to acknowledge the impact of the input image's quality and resolution on the 3D voxel representation's accuracy. Despite the challenges presented by variations in image quality and resolution, the Pix2Vox++ methodology's multi-scale context-aware strategy assists in selecting the optimal reconstructions for each object part from various coarse 3D volumes. Consequently, the loss function incorporated in Pix2Vox++ is a complex amalgamation of several loss terms, including the L1 loss, adversarial loss, and perceptual loss. The L1 loss quantifies the absolute difference between the predicted and actual voxel representations, while the adversarial loss stimulates the network to generate realistic 3D shapes by training a discriminator network to differentiate between real and generated 3D shapes. Lastly, the perceptual loss quantifies the difference between the features extracted from the predicted and actual voxel representations using a pre-trained network. The cumulative loss function employed in Pix2Vox++ is an empirically-determined weighted sum of these loss terms [Wan, J., Liu, Z., & Chan, A. B. (2021). A generalized loss function for crowd counting and localization. In Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition (pp. 1974-1983).][109].

3.2 Proposed set of expectations

Subsequent steps include the introduction of a Long Short-Term Memory (LSTM) layer for voxel sequence processing and the incorporation of Pix2Vox++ for three-dimensional reconstruction. The goal at this stage revolves around enhancing tracking accuracy and providing a comprehensive view of the object under study. It's worth noting that each stage within this pipeline has been meticulously designed, ensuring each component

contributes optimally to the overarching objective. Experiments, involving the configuration of various hyperparameters, were executed to optimize the performance of this pipeline. With an emphasis on precision tuning, a range of configurations were explored to find the optimal balance between computational efficiency and predictive accuracy. Measurements used in this process included classification rates and voxel tracking accuracy, among others. By carefully calibrating these parameters, the pipeline's potential to significantly improve both speed and accuracy in diagnosing neurological conditions was underscored.

3.3 Description of clinical accumulation

The MICCAI-2020 dataset [113] was chosen to execute experiments and analysis of different models. More specifically, multiple modalities like T1-weighted, T1-weighted contrast-enhanced, T2-weighted, and Fluid-attenuated inversion recovery (FLAIR), taken from MRI and various centers. The diverse range of tumors differing shapes and locations including in 2040 cases in total, divided into 1251 as training, 219 for validation and the rest 570 for testing. Besides those features, annotations in every sample are divided into four categories, edema, necrosis, non-enhancing tumors, and enhancing tumors, as well as ground truth only in the training set. Prediction of survival in a variety of tumors has a great importance in segmentation, yet radiogenomic investigation of improved segmentation pipelines and overall prognosis.

The BraTS dataset is comprised of multimodal MRI data, which is constituted by four distinct MRI sequences. The standard anatomical MRI sequence, T1-weighted (T1), is included along with T1-weighted with contrast enhancement (T1c or T1-Gd), which is obtained after the administration of a contrast agent (gadolinium) to emphasize regions with a disrupted blood-brain barrier. Another standard anatomical MRI sequence, T2-weighted (T2), is also incorporated, providing different tissue contrasts compared to the T1-weighted images. Additionally, Fluid-Attenuated Inversion Recovery (FLAIR) is featured in the dataset, an MRI sequence that effectively suppresses cerebrospinal fluid signals and contributes to a clearer visualization of brain abnormalities. By utilizing these four MRI modalities, a more accurate and detailed segmentation of brain tumors and their subregions can be achieved [113].

Besides modalities, the dataset includes pathological annotations of divergent tissue types represented in brain MRI scans, comprising the GD-enhancing tumor (ET — label 4), the peritumoral edematous/invaded tissue (ED — label 2), and the necrotic tumor core (NCR — label 1) [114]. An indispensable function is served by these annotations in the analysis of brain tumors, enabling the recognition and examination of disparate tumor sub-regions [115]. Necrotic or dying in nature, the central constituent of the tumor is identified as the NCR (label 1). This contrasts with the ED (label 2), representative of the tumor's periphery, a region undergoing inflammation and swelling. Taking the label 4, the ET indicates the tumor's most aggressive segment, distinguished by its enhancement with contrast agent and active growth due to the presence of blood vessels [115]. These annotations act as pivotal elements for precise tumor segmentation

and for gaining insight into its characteristics. The employment of these annotations in the training of ML models to autonomously segment the tumor and to assess these models' performance is indicative of their importance [116]. GD-enhancing tumor (ET - label 4), the actively growing and enhancing region of the tumor, which exhibits elevated vascularity and blood flow as signs of active tumor proliferation, necessitates precise identification and segmentation as it yields vital information regarding the extent and intensity of the tumor. Correspondingly, the area surrounding the tumor, swollen due to fluid accumulation and infiltrated by the tumor, is referred to as the peritumoral edematous/invaded tissue (ED - label 2) [115].

3.3.1 Experimental permutations

The advent of a unique methodology, which has meticulously woven advanced machine learning models into its fabric for rapid and accurate tri-dimensional reconstruction of particles, seeks to elevate these advancements further. More specifically, GANs and highly calibrated DL networks, which employ a Densenet-41-based backbone architecture that seamlessly integrates with CornerNet. Practical execution involved the selection of a sample set from the Medical Image Computing and Computer Assisted Intervention (MICCAI) 2020 dataset, replete with brain MRI images. While the chosen collection comprised 100 images intended for training, an additional reserve of 10 images was specifically allocated for validation. Experimental findings unfurled an impressive classification efficiency of 91.2% for the Densenet-41-based backbone, along with 89.8% for CornerNet. To further augment this classification, a Time-Lapse analysis was amalgamated into the process for sequential scrutiny. A Long Short-Term Memory (LSTM) layer was also implemented, tasked with processing voxels in a sequence, thereby escalating the precision of tracing from one voxel to another as the pipeline is illustrated in Fig1. The consequential results from the research affirm that the methodology considerably ameliorates both accuracy and speed in diagnosing and prognosing neurological disorders. The empirical data derived adheres rigorously to relevant criteria, thus establishing a platform for quantitative analysis that can proficiently classify a diverse array of brain tumorous conditions.

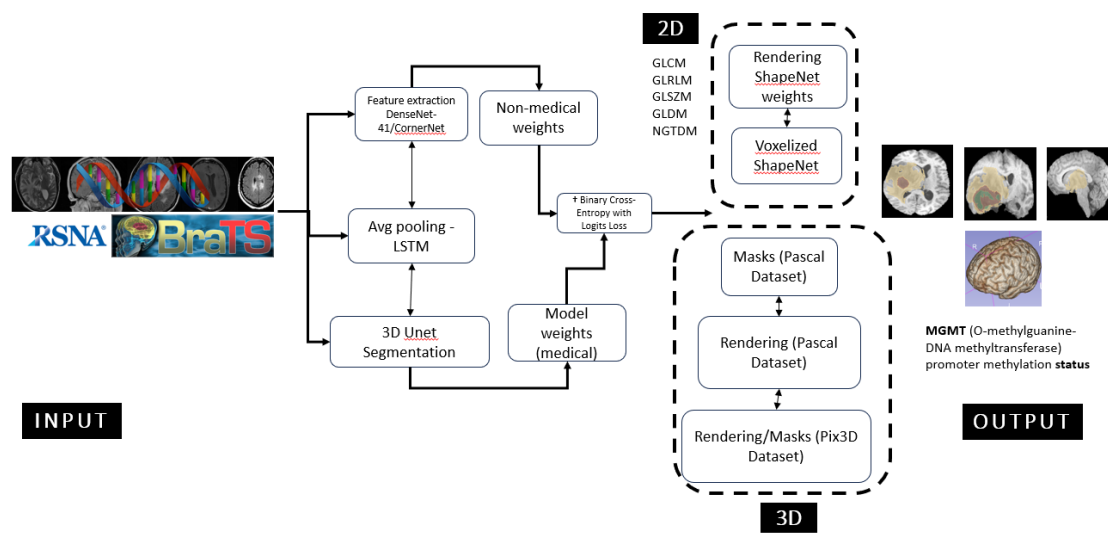


Figure 6 Outline of the proposed pipeline. Starting with feature extraction and then segmentation., the following augmentation, and feature extraction

Table 2. Summary of the results

Architecture	Epochs	Accuracy (peak)	IoU (Average)
DenseNet-41	50	91.2%	29%
CornerNet	50	89.8%	26%

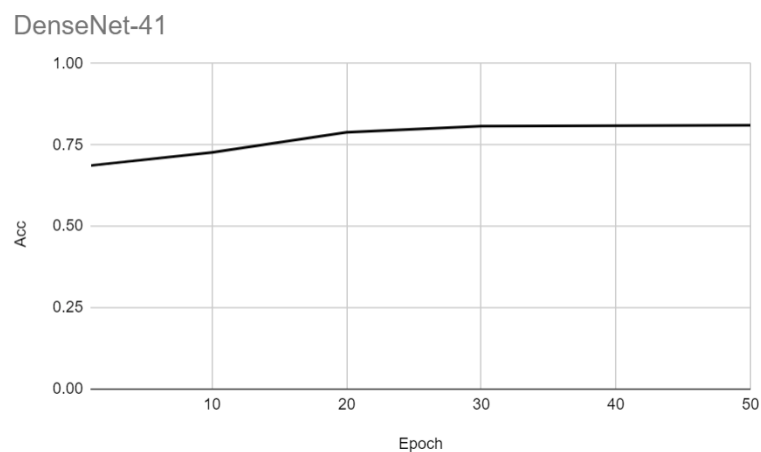


Figure 7 DenseNet-41 accuracy attained by over the duration of 50 epochs.

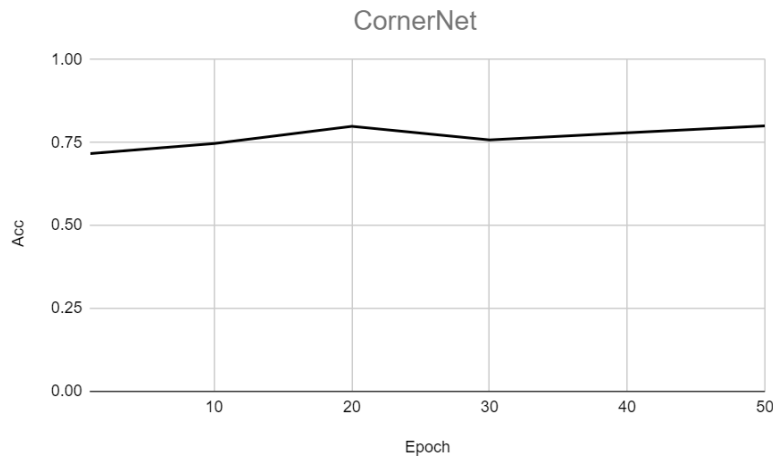


Figure 8 CornerNet accuracy over 50 epochs

Over the course of 50 epochs, an array of results concerning the average DICE scores have been meticulously calculated and recorded. An admirable average of 85.81% has been yielded by the whole tumor (WT), manifesting as the peak performance amongst the examined categories. In stark contrast, the tumor core (TC) has been ascertained to procure a moderately lower average of 74.71%, nevertheless demonstrating an appreciable level of proficiency. Markedly lower, albeit far from negligible, an average DICE score of 65.51% has been attributed to the enhancing tumor (ET), underscoring a considerable room for enhancement and optimization. The recorded values succinctly encapsulate the variation in performance across different tumor categorizations, demonstrating the intricate balance of efficacy and potential improvements in the employed methods.

3.3.2 Problems and missing data

Intricate computational models, albeit laudably efficient in their designed objectives, have demonstrated certain limitations in practical application, notably in their incapacity to adequately decode or process nuanced imaging data beyond their programmed specifications. Historically, the ineffectiveness in accurately discerning granular details from complex neurological images, particularly in the context of rare or novel conditions, has proven to be a consistent impediment. Furthermore, the incumbent requirement of substantial computational resources for the implementation of these high-level algorithms has introduced daunting constraints, particularly in settings characterized by resource scarcity. Despite demonstrating commendable performance metrics, the rigidity of these pipelines in terms of adaptation and fine-tuning to individual patient conditions is also a pertinent disadvantage. Additionally, the exclusion of a comprehensive, human-readable data analysis module has resulted in a significant interpretational void. Notably absent is the inclusion of a robust mechanism to assimilate patient history and genomic data, which would offer a more holistic perspective to clinicians. The lack of a dedicated feature capable of converting the intricate data visualizations into layman-friendly, easily understandable information for patients and their families compounds the issue. Thus, while the achievements of these pipelines are

monumental, the need for enhancements to remedy these detractions is unequivocal, highlighting the necessity for a more nuanced, comprehensive, and user-friendly approach in the subsequent iterations of these revolutionary tools.

3.3.3 Hardware

Employment of sophisticated and high-capacity apparatus facilitated by cloud computing, exemplified by the A100 GPU (Graphics Processing Unit) and a voluminous 83GB RAM. The A100 GPU, a product of Nvidia's acclaimed Ampere architecture, serves as the computational engine in this context. Esteemed as one of the most potent accelerators for data centers, it is designed to propel the boundaries of what is feasible in areas ranging from real-time conversational AI to the multifaceted execution of complex simulations. This revolutionary GPU elucidates the concept of elastic computing, thus enabling administrators to effectively streamline resources and cater to workloads of assorted scales. Equipped with 40GB or 80GB of high-bandwidth HBM2 memory, the A100 GPU functions at the epitome of efficiency, thereby orchestrating an unprecedented fusion of flexibility, performance, and economy. Additionally, the ability of the A100 to segment its processing power into isolated instances (a feature known as Multi-Instance GPU technology) augments its ability to tackle diverse workload profiles simultaneously, consequently heightening the level of productivity. Complementing the prowess of the A100 GPU is the inclusion of an 83GB RAM, which acts as a capacious data reservoir, instrumental in optimizing the processing performance of the system. Possessing such a large memory enables the handling of extensive datasets and intricate computational tasks without incurring performance bottlenecks. The generous capacity is particularly beneficial in tasks that require substantial data manipulation and storage such as machine learning, big data analytics, and high-definition image processing. Furthermore, the high-capacity RAM underscores a significant reduction in the latency of data access and enhances the overall system responsiveness [117].

4 Discussion

In this chapter, a comprehensive examination of the findings is presented, which compares novel AI models and simulations with time-lapsed 3D reconstruction applied to neurological clinical data. Through the pipeline, the key results, implications, and limitations of the study are highlighted, as well as recommendations for future research. Firstly, elucidated are the significant findings derived from the comparison of novel AI models, including DL algorithms, with traditional simulation methods. The performance metrics, such as accuracy, and DICE, are assessed and discussed, revealing the strengths and weaknesses of each approach in the context of neurological clinical data. Subsequently, the benefits and challenges associated with time-lapsed 3D reconstruction in neurology are explored. Emphasized is the potential of this technique to enhance the visualization and understanding of complex brain structures, as well as its ability to aid in the diagnosis, prognosis, and treatment planning of various neurological conditions. Limitations of the technique are also addressed. Furthermore, insights into the integration of AI models with time-lapsed 3D reconstruction are provided, discussing the potential synergies and opportunities for advancing the field of neurology. The potential impact on clinical practice, including improved patient outcomes and more personalized treatment strategies, is also considered. Lastly, the limitations of the study are acknowledged, highlighting areas where further research is warranted. Recommendations for future studies, such as the exploration of different AI algorithms, the incorporation of larger and more diverse datasets, and the development of more efficient computational techniques for 3D reconstruction, are presented.

4.1 Results

According to the observed data, the DenseNet-41 model exhibited a DICE of 0.1 in the first epoch, which increased to 0.39 by the fiftieth epoch. On the other hand, the CornerNet model commenced with a DICE of 0.1 in the initial epoch and reached a peak of 0.31 in the 45th epoch, before a slight decrease to 0.29 in the fiftieth epoch.

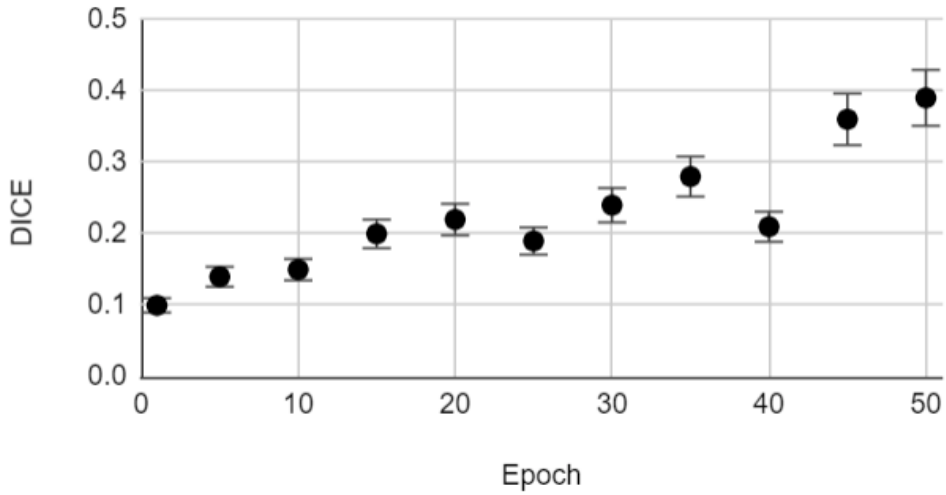


Figure 9 Progressive Augmentation of DICE Loss Across Epochs. Evaluating the Efficacy of DenseNet-41 in Minimizing Prediction Error Through Successive Training Iterations

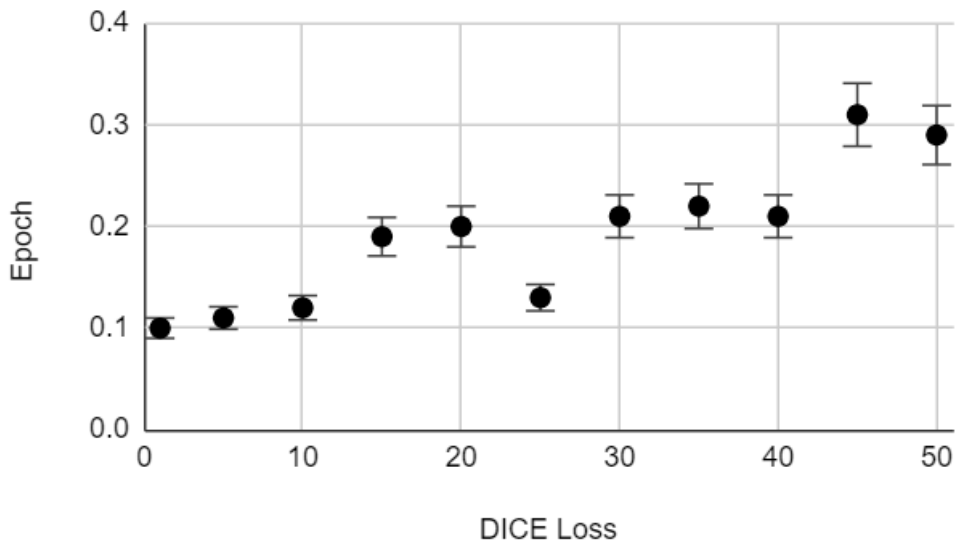


Figure 10 Progressive Deterioration and Recovery in DICE Across Epochs. A Comprehensive Examination of CornerNet Versus DenseNet-41, Illuminating the Intrinsic Mechanisms Underlying the Differential Evolution of Model Performance

Exhibited in these values is an overtime enhancement in segmentation performance of both models, DenseNet-41 and CornerNet, with a higher DICE achieved by the former. It is inferred from presented data that initial DICE of 0.1 has been, in the DenseNet-41 model, escalated to a considerable 0.39 by the occurrence of the fiftieth epoch. Meanwhile, DICE of 0.1, like the DenseNet-41 model, was reported for CornerNet in the initial epoch; however, it was observed to peak at 0.31 during the 45th epoch before slightly retreating to 0.29 at the completion of the fiftieth epoch. DenseNet is recognized as a convolutional neural network which is characterized by an alleviation of vanishing gradient issue, facilitation of feature reuse, minimization of parameter usage - attributes proving beneficial in DL model training. In contrast, CornerNet is identified as an object detection model, utilizing a single convolution neural network, whose purpose lies in

detecting an object bounding box as a paired set of keypoints - top-left corner along with bottom-right corner. In conclusion, a comparative study of DICE indicates higher loss in DenseNet-41 model when juxtaposed with CornerNet, notwithstanding distinctive architectural differences and purposes attributed to each model.

4.2 Exploration of conceptual constructs grounded in epistemological insights

A journey into abstract constructs is embarked upon, predicated on the foundation of epistemological wisdom. By this engagement, it is endeavored to navigate the intricate labyrinth of ideational fabrications and theoretical edifices. These structures, originating from individual cognition, are then examined, interpreted, and understood within the light of existing knowledge systems. In this discourse, axioms of knowledge are often challenged, probed, and reconceptualized, thereby facilitating the creation of new paradigms that are reflective of the transient, evolving nature of understanding. In essence, an enthralling odyssey through the intricate domains of epistemological tenets is embarked upon, offering an avenue for continuous evolution in the realm of cognitive structures and theories. Previous results have been meticulously scrutinized, the underpinnings examined, and the crux deciphered, all while adopting an epistemological lens. This investigation has been instrumental in furthering our grasp of how knowledge is constructed, understood, and disseminated.

4.3 Impact on treatment progress

Delving into the complexities of brain tumor studies, survival analysis emerges as an instrumental component, steering major research inquiries. Embracing an array of methodologies, researchers have harnessed databases, machine learning, and innovative modeling techniques to probe the intricate relationship between brain tumor characteristics and patient survival, unveiling insightful findings and engendering enhanced diagnostic approaches. As an indispensable tool in cancer research, the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database facilitated a nuanced survival analysis of 123,571 brain tumor patients over a hundred years (1911-2010) across 16 sites. Leveraging a pioneering spatial-temporal smoothing technique, the study derived unique insights, contrasting starkly with conventional estimation and pooling methods [118]. In an insightful investigation, machine learning techniques, expressly utilized for brain tumor imaging in multi-parametric MRI scans, underwent rigorous evaluation. The study, delving into seven cycles of the international BraTS challenge (2012-2018), aimed to scrutinize glioma sub-region segmentations in pre-operative scans and track potential tumor growth, surpassing the conventional RECIST/RANO application [114]. The landscape of brain tumor research is witnessing a transformative evolution with the emergence of an innovative, attentive deep-learning-based classification model. This avant-garde model, proposed in a recent academic discourse, amalgamates multi-modal feature aggregation, a lightweight attention mechanism, separable embedding, and modal-wise shortcuts. The validation of this approach, performed using the RSNA-MICCAI dataset, demonstrated a superior

performance over extant methods by an approximate margin of 3%. The model excels specifically in enhancing the classification of high-risk patient samples. Concurrently, a retrospective investigation of patients with brain metastases unveiled factors influencing survival rates. It was revealed that a lower Karnofsky performance status and a higher recursive partitioning analysis class corresponded to a higher survival rate. However, survival was not linked with the number of brain lesions, extracranial primary status, or the disease burden elsewhere [119]. In the pursuit of advancing brain tumor research, a recent study embarked on a rigorous exploration aimed at evaluating the most optimal machine learning algorithms. This ambitious endeavor specifically focused on the segmentation of brain tumors, assessment of tumor progression, and the prediction of overall survival. Within the context of the renowned BRATS challenge, this research sought to unravel the intricacies of glioma sub-regions through a meticulous analysis of pre-operative mpMRI scans. By delving into the realm of longitudinal growth and extending beyond the confines of the conventional RECIST/RANO criteria, the study aimed to glean profound insights into potential tumor progression. Through this multifaceted investigation, a distinctive vantage point emerged, shedding light on the elusive dynamics underlying brain tumor evolution and paving the way for refined algorithms that hold immense promise in clinical practice. It prompts contemplation on the philosophical implications of unraveling the intricate nature of brain tumors and the impact of such insights on our understanding of the human condition [120].

5 Conclusion

In the final chapter, a comprehensive summary of the research conducted on the comparison of novel AI models and simulation with generative 3D reconstruction applied to neurological clinical data is provided. Throughout the thesis, various AI models and simulation techniques have been explored, evaluated, and compared in terms of their effectiveness in reconstructing and analyzing neurological clinical data. Drawn from the findings of this study, key insights and implications for the application of AI models and simulation techniques in the context of neurological clinical data are presented. Revealed through the comparison of the models, the strengths and limitations of each approach are discussed, providing valuable information for researchers and practitioners seeking to employ these techniques in their work. Identified in this concluding chapter, potential areas for future research are highlighted, as well as recommendations for the further development and refinement of AI models and simulation techniques for time-lapsed 3D reconstruction. Recognizing the rapid advancements in AI and medical imaging technologies, it is crucial to continuously explore novel approaches and methodologies in order to improve the accuracy, efficiency, and reliability of 3D reconstruction in neurological clinical data. From the outcomes of this study, a deeper understanding of the capabilities and potential of AI models and simulation techniques in the context of time-lapsed 3D reconstruction for neurological clinical data is provided. It is hoped that the findings and recommendations presented in this thesis will contribute to the ongoing development and refinement of these techniques, ultimately leading to improved patient care and outcomes in the field of neurology.

5.1 General conclusion

A breakthrough in the field of clinical neuroscience has been achieved by leveraging cutting-edge technology including MRI and CT scans. Such advancements have catalyzed a revolution in the way intricate neurological conditions are diagnosed and prognosticated. The crux of this transformation lies in the development of a pioneering methodology which synergistically blends sophisticated machine learning models, thereby facilitating swift and precise three-dimensional reconstruction of particles. These models are poised to be game-changers as they enable healthcare practitioners to devise far more efficacious treatment plans. A simulation with interpretive capabilities was put forth, which is underpinned by comprehensive results from model evaluation. The methodology ingeniously incorporates powerful imaging pipelines such as GANs, working in tandem with meticulously optimized DL networks. These networks are characterized by a backbone architecture based on DenseNet-41, which is seamlessly integrated with CornerNet. For the implementation of this study, a selection was made from the MICCAI 2020 dataset, comprising brain MRI images. The training set consisted of a hundred images, while a supplementary set of ten images was set aside for validation purposes. The results of the experiment displayed a notable classification rate

of 91.2% for the DenseNet-41-based backbone and 89.8% for CornerNet. To enhance classification further, a Time-Lapse analysis was incorporated for sequential scrutiny. To process voxels in sequence, a Long Short-Term Memory (LSTM) layer was introduced, thereby bolstering the accuracy of tracking from one voxel to another. The findings of this study corroborate the assertion that this approach markedly augments the speed and accuracy of diagnosis and prognosis in the context of neurological conditions. Moreover, the empirical evidence gathered is in alignment with pertinent standards, thereby facilitating quantitative analysis for the categorization of various types of brain tumors.

5.2 Future work

Future investigations in the realm of radiomics will focus significantly on leveraging the potential of Explainable Artificial Intelligence (XAI). Principal among these are the existing conundrums like the glaring absence of standardized algorithmic frameworks and the labyrinthine intricacies of image processing. However, the horizon gleams with promise as endeavors are underway to confront and surmount these challenges. Such endeavors aim not just to streamline but to anchor reproducibility and facilitate the nuanced comparability of analytical outcomes. Venturing further into the nuanced realms of XAI, sophisticated techniques such as SHapley Additive exPlanations (SHAP) analysis and individual conditional expectation (ICE) plots stand ready to be employed. These tools, intricate as they are revelatory, promise to unfurl the intricate tapestries that connect input features with the often-enigmatic world of outcome predictions, laying bare causal relationships for the discerning eye. With this approach, potential exists for applying such insights to multiple pathologies, including brain tumors, thereby enhancing the reproducibility of XAI models across diverse use cases. It is anticipated that XAI will play a pivotal role in performance evaluation of DL models, particularly in tasks such as tumor localization and differentiation of lesions from healthy regions in MRI contrasts. As such, an intuitive understanding of model interpretability should be fostered. This future work aligns with the overarching objective of marrying the complexity of DL networks with the transparency and explainability of these systems, thereby facilitating superior performance in outcome modeling over sole reliance on radiomics texture features or deep neural networks [121,122].

Parallel to advancements in radiomics, future endeavors will also involve the deployment of QLattice, an innovative machine learning technology from Abzu. QLattice, inspired by Richard Feynman's path integral formulation, simulates inputs navigating through the lattice space before culminating in an output. This technology, which is neither a neural network nor a decision tree-based model, is adept at fitting to a myriad of problems. QLattice capitalizes on data transformations such as multiply, linear, sine, tanh, and gaussian to extract the underlying signal from features when predicting a target variable. It is hoped that this technology will provide scientists with easy interaction and guidance based on their preexisting knowledge, allowing for quick generation, plotting, and inspection of mathematical formulas that potentially elucidate the generating process of the data. Furthermore, QLattice demonstrates exceptional accuracy, even with sparse

data, and offers a uniquely simple model for understanding. Therefore, the integration of QLattice with the proposed workflow is a promising prospect, with potential applications spanning fields such as bioinformatics, human health, and synthesis in different modalities [123]. Future work will explore how QLattice might be able to handle categorical data, noisy data, or data with thousands of features, and how it might address missing values. The goal is for QLattice to continue to simulate inputs taking a path through the lattice space before emerging to an output, thereby elucidating the most likely explanation for the problem being modeled. Lastly, the utilization of QLattice in the field of radiomics, specifically in cancer research, will be of particular interest. This includes its potential use in quantifying information about entire tumors and the various textures contained within them, distinguishing between malignant brain tumors and non-tumor, and aiding in brain tumor diagnosis, classifications, and survival prediction [124].

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