

# Federated Learning Approach for Measuring the Response of Brain Tumors to Chemotherapy

Omneya Atef<sup>1</sup>, Mustafa Abdul Salam<sup>2</sup>, Hisham Abdelsalam<sup>3</sup>

Faculty of Computers and Information Technology, The Egyptian E-Learning University (EELU), Cairo, Egypt<sup>1,3</sup>

Faculty of Computers and Artificial Intelligence, Benha University, Benha, Egypt<sup>2</sup>

Faculty of Computer Studies, Arab open University, Cairo, Egypt<sup>2</sup>

Faculty of Computers and Artificial Intelligence, Cairo University, Egypt<sup>3</sup>

**Abstract**—Brain tumor is a fatal disease and one of the major causes of rising death rates in adults. Predicting methylation of the O6-Methylguanine-DNA Methyltransferase (MGMT) gene status utilizing Magnetic resonance imaging (MRI) imaging is highly important since it is a predictor of brain tumor responses to chemotherapy, which reduces the number of needed surgeries. Deep Learning (DL) approaches became powerful in extracting meaningful relationships and making accurate predictions. DL-based models require a large database and accessing or transferring patient data to train the model. Federated machine learning has recently gained popularity, as it offers practical solutions for data privacy, centralized computation, and high computing power. This study aims to investigate the feasibility of federated learning (FL) by developing a FL-based approach to predict MGMT promoter methylation status using the BraTS2021 dataset for the four sequence types, (Fluid Attenuated Inversion Recovery (FLAIR), T1-weighted (T1w), T1-weighted Gadolinium Post Contrast (T1wCE/T1Gd), and T2-weighted (T2w)) MRI images. The FL model compared to the DL-based and the experimental results show that even with imbalanced and heterogeneous datasets, the FL approach reached the training model to 99.99% of the model quality achieved with centralized data after 300 communication rounds between 10 institutions using OpenFl framework and the improved EfficientNet-B3 neural network architecture.

**Keywords**—Federated Learning (FL); BraTS2021; Data Privacy; O6-Methylguanine-DNA Methyltransferase (MGMT); OpenFl; EfficientNet-B3; brain tumors; Deep Learning (DL)

## I. INTRODUCTION

Brain tumors are a grave problem that threatens human life and leads to death if not diagnosed and treated early. Especially, Glioblastoma (GBM) and astrocytic glioma with molecular features of GBM (WHO Grade 4 astrocytoma). The glioblastoma multiform tumor is a highly malignant brain tumor. Most of these brain tumors occur in adults, and they are characterized by a wide range of symptoms. It has a poor prognosis with a median survival of about ten months in most cases [1]. Recently been discovered that, the presence of a specific genetic sequence in the tumor known as MGMT (o6-methylguanine-DNA methyltransferase) promoter methylation during GBM patient's chemotherapy is a significant and independent predictive factor of favorable survival in glioblastoma patients undergoing the treatment.

MGMT is a protein that repairs damage to the DNA of human body cells. The chemotherapy drugs cause damage to

tumor cells. Thus, the more MGMT protein the tumor produces, the less effective the chemotherapy drug is expected to be, as the protein will repair the damage to the tumor. The detection of MGMT requires the performance of a biopsy (removing tissue from the tumor and analyzing it) and can take several weeks depending on the results and the types of treatments initially implemented, subsequent surgery may be necessary [2]. The development of an efficient method of detection utilizing medical imaging (i.e., MRI, radio genomics) could potentially minimize the number of surgeries.

Deep learning (DL) based applications have shown promising results in this area but to cover all medical questions that can be applied to a vast patient population and ensure high and accurate performance, DL-based applications rely on large, diverse datasets from different health institutions [3]. This is particularly challenging due to the natural sensitivity of healthcare informatics, legal and cultural challenges. Each health institution (e.g., hospital, clinic, lab, etc.) is often resistant to sharing patient data. Moreover, the available data in a single institution is not adequate for the training due to the low incidence rate of brain tumor pathologies and limited patient numbers. These limitations raise the need to seek alternative approaches [4-6].

A recent surge in popularity has been witnessed by federated learning, a paradigm that offers great promise for learning with fragmented, sensitive data. By allowing training a global model through a central server while keeping the data in local institutions where they originated, rather than aggregating data from different places altogether or using the traditional discovery and replication approach, a shared global model can be trained [7-9]. The main idea is moving computations to data, where a globally shared model is brought to where the data is.

## II. MOTIVATION AND CONTRIBUTION

In this study, a set of contributions are achieved using the proposed study:

- 1) Development of an improved EfficientNetB3 model relying on the combination of convolution neural network (CNN) and Recurrent neural network (RNN) architectures.
- 2) Four types of Scans are used in this study, while other related work depended on only one or two scans.
- 3) Two approaches are applied based on classical and federated learning.

4) The federated learning showed the ability to deal with data privacy, diversity, real time continuous learning, and hardware efficiency.

### III. RELATED WORK

Recently, machine learning and deep learning techniques have been used to predict MGMT status, and it achieved satisfactory results. Korfiatis et al. in 2017 trained three residual deep neural network architectures, ResNet18, ResNet34, and ResNet50 in order to predict MGMT methylation status based on MRI scans with T2 and T1 weighted post-contrast images obtained from Mayo Clinic. [10]. in another work by Yogananda et al., 2021, Based on 3D-Dense-UNets, they developed a T2WI-only network (MGMT-net) to detect MGMT methylation status and segment tumors. Using MRI scans from The Cancer Imaging Archive (TCIA) and The Cancer Genome Atlas (TCGA) datasets [11]. The deep-learning approach developed by Chen et al., 2022 for MGMT promoter methylation using MRI scans of 111 patients was based on ResNet18 with fivefold cross-validation. Four sequences were analyzed for radiomics features for two regions of interest (the whole tumor area and the tumor core area), including T1 weighted images (T1WI), T2 weighted images (T2WI), apparent diffusion coefficient maps (ADC), and T1 contrast-enhanced images (T1CE) [12].

Despite the efficiency of the mentioned works but all of them depended on the classical way of learning, That Lacked patient privacy protection. Even removing metadata such as names or dates of birth is insufficient to protect privacy because it is possible to reconstruct a patient's face from MRI data. This sensitivity of healthcare informatics directed the researchers toward using federated learning in the healthcare applications such as federated medical imaging, federated remote health monitoring, and federated EHRs management applications [13, 14]. Due to the novelty of the approach, there are a few articles on Brain tumor diagnosis using federated learning, and almost all of these articles focus on brain tumor segmentation only.

The first use of federated learning in a multi-institutional collaboration was presented by Sheller et al. in 2019, allowing deep learning modeling without sharing patient data. They used the Brats dataset and achieved 99% of the model performance with a data-sharing model. They compared federated learning with two alternative collaborative learning methods, Cyclic Institutional Incremental Learning (CIIL) and Institutional Incremental Learning (IIL). The comparison shows that these two methods failed to match the performance of federated learning. Even though CIIL may seem like a simpler option, full validation should be carried out periodically, such as at the end of a cycle, which will help in selecting a good model. The validation process would need the same synchronization and aggregation steps as FL and would even add communication costs over FL. in addition, a large number of institutions with small amounts of data do not scale well with IIL and CIIL [15].

Using a deep neural network, Li et al. applied federated learning for the segmentation of brain tumors using the BraTS dataset as a part of the NVIDIA Clara Train SDK. They

studied various practical aspects of the federated model sharing with an emphasis on preserving patient data privacy. While a strong differential privacy guarantee. The experimental results show that the FL training was done at twice the number of epochs in the data centralized training to reach the same result [16].

An FL-based cross-site modeling platform has been proposed by Guo et al. in 2021 for the reconstruction of MRI images collected from a variety of institutions with different scanners and acquisition protocols. The experiments were conducted on a variety of datasets with promising results. Hidden features were aligned with hidden features extracted from various sub-sites [17]. Table I summarizes the effective methods for predicting the MGMT methylation status based on the Classical and the recent federated learning approaches for brain tumor diagnosis.

TABLE I. METHODS FOR BRAIN TUMOR DIAGNOSIS

| Related Work         | Methods for Brain Tumor |                                  |  | Limitations   |
|----------------------|-------------------------|----------------------------------|--|---|
|                      | Architecture            | Algorithm                        | Dataset                                      |   |
| Korfiatis et al [10] | DCNN                    | ResNet18<br>ResNet34<br>ResNet50 | MRI from Mayo Clinic                         | Only two type of scans are used, Following classical learning |
| Yogananda et al [11] | CNN                     | 3D-Dense-UNets,                  | TCIA and TCGA datasets                       | Only one type of scans are used, Following classical learning |
| Chen et al [12]      | DCNN                    | ResNet18                         | MRI Scans for 111 patients                   | Following classical learning                                  |
| Sheller et al [15]   | FL , CLL ,IIL           | DNN                              | Different Institutions, collaborated dataset | Brain tumor segmentation model                                |
| Li et al [16]        | FL                      | DNN                              | BraTS 2018                                   | Brain tumor segmentation model                                |
| Guo et al [17]       | FL                      | DNN                              | Multiple Datasets                            | Model for reconstructing MRI scans                            |

### IV. MATERIALS AND METHODS

#### A. Training Model

The training model is based on an improved EfficientNet-B3 architecture relying on RNN layers. The EfficientNet-B3 was released by Google in 2019. It is a convolutional neural network architecture and scaling technique that uses the compound coefficient technique to uniformly scale depth, width, and resolution in a simple and efficient manner. Which make it is better at analyzing images than the existing Artificial intelligence models such as ResNet, inception and DenseNet [18]. The EfficientNet-B3 is a part of the EfficientNet family, which ranges from B0 to B7. B3 was selected among this family because it offers a good compromise between computational resources and accuracy. The compound scaling method uniformly scales each

dimension with a certain fixed set of scaling coefficients. Instead of randomly scaling up width, depth, or resolution. Equation (1) show how it is achieved mathematically.

Fig. 1 illustrate the architecture of the proposed model. The fully connected features extracted from the EfficientNetB3 are input to a proposed RNN architecture based on a long short term memory (LSTM) layers. The fully connected layer output is input to a sequence input layer, 2 LSTM layers, 2 dropout layers, 1 fully connected layer, and a Softmax layer.

$$S.t. \alpha \cdot \beta^2 \cdot \gamma^2 \approx 2 \quad (1)$$

$$\alpha \geq 1, \beta \geq 1, \gamma \geq 1$$

compound coefficient:  $\phi$

depth:  $d = \alpha^\phi$

width:  $w = \beta^\phi$

resolution:  $r = \gamma^\phi$

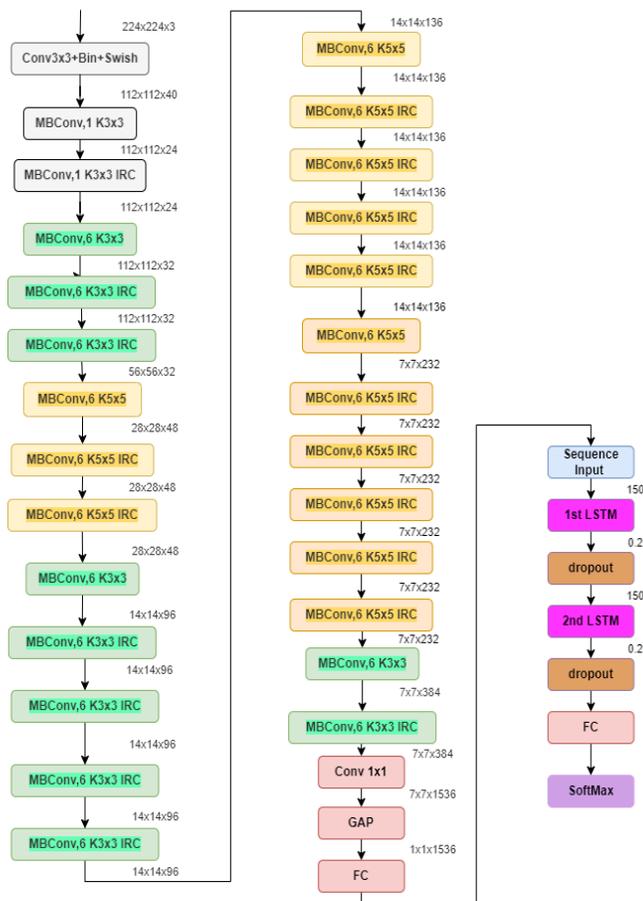


Fig. 1. The Improved EfficientNet-B3 Model Architecture.

The training process carried out on four distinct models based on the scan type FLAIR, T1w, T1wCE, and T2w respectively. Each model calculates a probability that the model belongs to class 0 (no presence of MGMT) or class 1 (present presence of MGMT).

Algorithm 1 shows how the final score per patient is obtained. Although the training model works on each scan

type separately, each scan type has the same pre-processing and training steps. All the resulted predictions are aggregated to finally predict the MGMT value of each patient. The results of the prediction are aggregated together for each patient in order to get the most confident result reached out of all predictions. The aggregation process is applied by obtaining the mean of the four types of scans for each patient individually. Moreover, the maximum and the minimum are also calculated. Then, the difference between the mean and the maximum, and also the variance between the mean and the minimum is compared. Finally, the nearest difference to the mean is the optimal value (maximum or minimum).

**Algorithm 1** Predicting MGMT Value

**Start**

Predicted\_MGMT\_Value: List

**For each scan type** ['flair', 't1w', 't1wce', 't2w']:

T\_df, V\_df, ← training and validation sets data frames

Ts\_df ← testing set data frame

T\_g, V\_g, Ts\_g ← Augmentation (T\_df, V\_df, Ts\_df)

Best\_model ← train\_model (MRI, T\_g, V\_g, E=20)

Ts\_pred ← best\_model.Prediction (Ts\_g)

Ts\_df [Pred\_y] ← Ts\_pred

M\_pred ← Ts\_pred.mean ()

Ts\_pred\_agg ← Aggregate the predictions results on

all MRI types for each patient

**For each patient\_id:**

Ts\_pred\_agg ← Max (Ts\_df [Pred\_y])

**If** Max (Ts\_df [Pred\_y]) – M\_pred > M\_pred – Min (Ts\_df [Pred\_y])

**Else if** Min (Ts\_df [Pred\_y])

**End if**

**End**

Predicted\_MGMT\_Value ← Ts\_pred\_agg

**End**

**End**

Data augmentation is performed on the images and the type of augmentation applied was based on geometric techniques. The augmentation step aims to balance the number of images in each class before training. The model takes the whole training and validation data (Original and augmented) as an input. The epochs of the model are defined with 20 (E=20), whereas the number of iterations for each epoch is equal to 58. This forms a total of 1160 iterations for the entire model.

**B. Federated Learning**

To preserve patient data privacy, we need to eliminate the existence of a centralized dataset to prevent data movement and share it with others. On the other hand, the single medical site has its data only, which is a bit amount of data and insufficient to train the model. Federated learning (FL) is a data-private collaborative learning approach that enables multiple health institutions to parallel train a machine learning model at the same time using their own data [19].

The general architecture of federated learning consists of four main components. Fig. 2 illustrates the architecture of the federated learning approach. The training model learned using the local dataset and sends the results to the central server (Aggregator), the server sends these results to the global

model to learn from it. After that, the global model sends back the updated results to all the local models. The whole training process is done through several communication rounds between the aggregator and the collaborators.

- **Aggregator:** is the responsible for the aggregation process, receives updates and results from each local model, and feeds them with the updates.
- **Collaborator(s):** represent the medical institutions.
- **Local Model:** learn from the local data.
- **Global Model:** learn from the local model gradients.

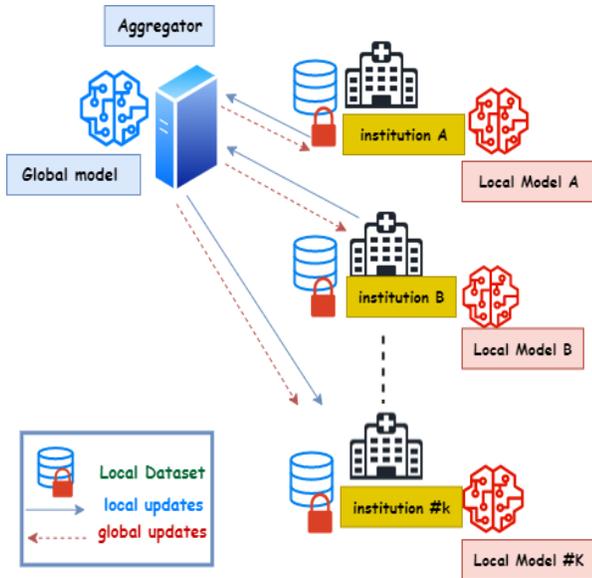


Fig. 2. The Architecture of the Federated Learning Approach – Hospitals Represents the Medical Institution.

In this way, FL enables connecting data from different institutions while not requiring any movement of patient data. Furthermore, FL solves insufficient data volume problem in a single institution.

## V. EXPERIMENTAL RESULTS

### A. Experimental Setup

1) **BraTS Dataset:** collaboration with the MICCAI Society (the Medical Image Computing and Computer-Assisted Intervention Society), the Radiological Society of North America (RSNA) provided a massive dataset of MRI scans from patients diagnosed with gliomas (BraTS2021) [20]. These scans were obtained from various institutions under standard clinical conditions, and various imaging equipment and protocols were used to produce a heterogeneous image quality reflecting the diverse clinical practices at different institutions. Four different sequence types of images are collected for each patient (Fluid Attenuated Inversion Recovery (FLAIR), T1-weighted (T1w), T1-weighted Gadolinium Post Contrast (T1wCE/T1Gd), and T2-weighted (T2w)). A total of 585 scans were collected for the training set and 87 scans were collected for the testing are sorted by the

patient ID. A binary label is used to describe the methylation status of the MGMT promoter (0: unmethylated, 1: methylated). Fig. 3 shows four types of scans for two patients with various MGMT\_value.

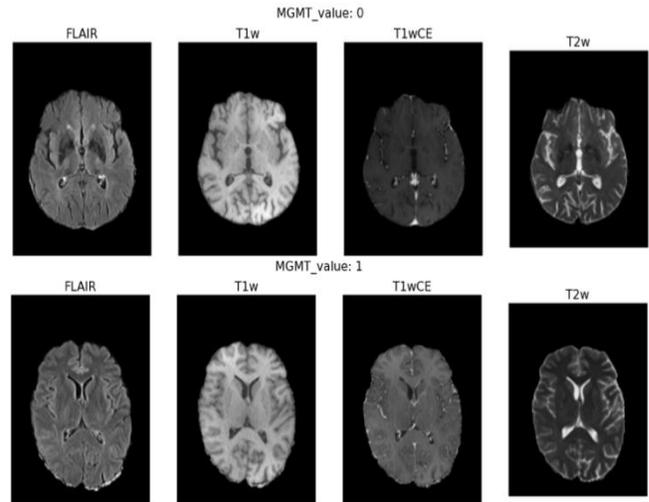


Fig. 3. Sample from the Dataset Includes Two Patients with two different MGMT\_Value.

2) **Data Pre-Processing:** This dataset is presented in DICOM (Digital Imaging and Communications in Medicine) format, which is extremely complex and inefficient for image processing and analysis. DICOM has the drawback that a single volume is stored as a series of 2D slices. The FLAIR sequence of patient #00014 is 74 slices as shown in Fig. 4, while the FLAIR sequence of patient #00000 contains 400 slices, making it extremely challenging to analyze.

To facilitate the data handling, the DICOM sequences were converted to the NIfTi (Neuroimaging Informatics Technology Initiative) format.

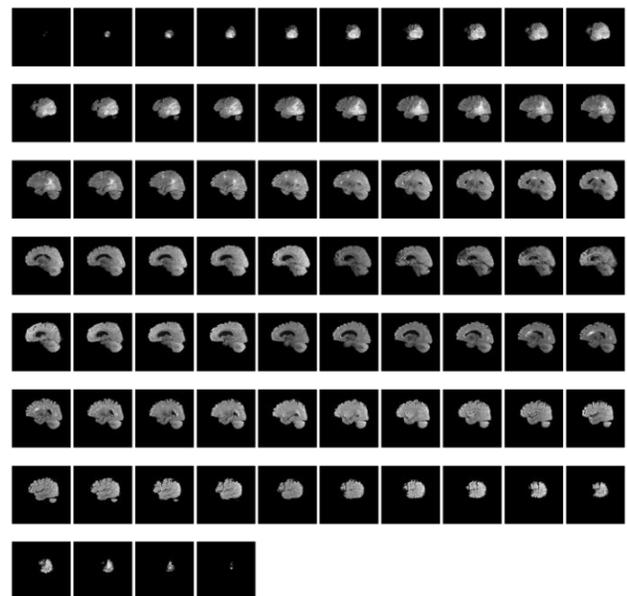


Fig. 4. The FLAIR Sequence of Patient with ID #00014.

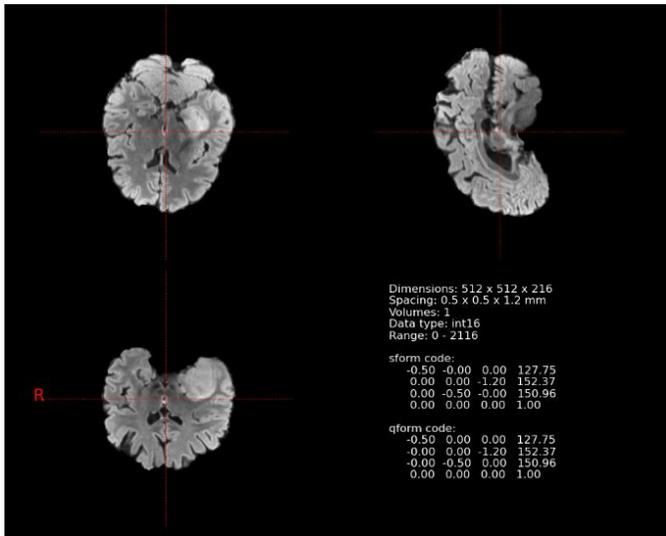


Fig. 5. FLAIR Sequence of Patient 00014 after converting it to the nii Format.

Fig. 5 shows the FLAIR sequence of patient #00014 that was displayed before in Fig. 5 after converting it to NIfTi format. The generated NIfTi file has 512 x 512 x 216 dimensions in x, y, and z. In both x and y dimensions, the spacing between slices is 0.5 mm, and in z dimensions, it is 1.2 mm.

In each NIfTi file, the header file contains sform and qform code matrices, which are always related to the input image. These code matrixes are appropriately remapped when padding, cropping, or applying affine spatial transformations. Whenever the sform is set in processing operations that deal with a single image, it is transformed in the same manner as qform. These matrices displayed in detail with Fig. 6.

Some simple preprocessing transformations applied to the NIfTi files. They normalized, resized and rotated to be easier in loading and processing Fig. 7 displays the nii file for the same patient after applying those preprocessing steps. After resizing the NIfTi files, they have x, y, and z dimensions of 128 x 128 x 64, with a spacing value of 1.0 millimeters between slices. After normalization, the range is reduced from 0-2116 to -1.0-1.0. Furthermore, sform and qform code matrix values have been changed.

3) *Data partitioning*: The host of the provided dataset has confirmed that these three cases have some issues in the training dataset. For the two patients with ID #00109 and #00709, the FLAIR sequences are blank, and for the patient with ID #00123, the TW1 sequence is blank. As a result, 582 patient’s cases were successfully trained. We shared the two training and testing datasets with 10 collaborators, corresponding to the 10 institutions that exist in real life. The resulting patient counts for each of the institutions, which we will refer to as collaborators (C) 1–10 are given randomly with high variations. A local validation set, consisting of 10% of training data of each institution, is also held out as a validation set. The actual numbers of patients at each institution in the training, validation, and testing datasets illustrated in Table II.

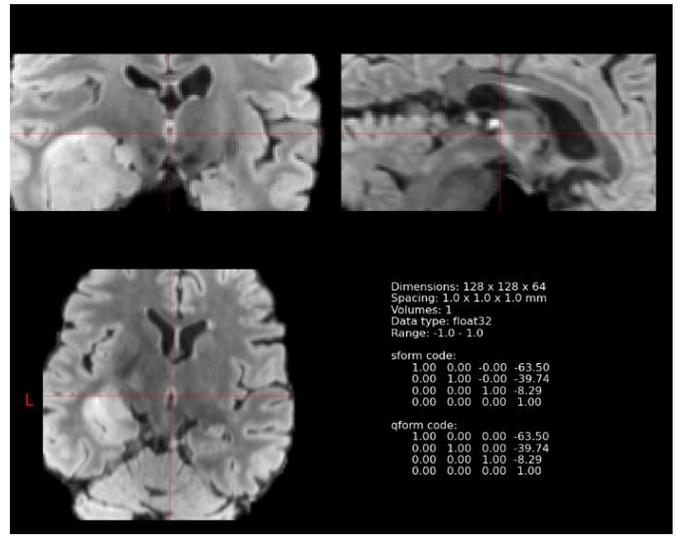


Fig. 6. The FLAIR Sequence of Patient 00014 after the Normalization Process.

TABLE II. PATIENTS DISTRIBUTION FOR EACH COLLABORATOR

| Collaborator #Number | Number of Patients |            |         |
|----------------------|--------------------|------------|---------|
|                      | Training           | Validation | Testing |
| C1                   | 72                 | 8          | 10      |
| C2                   | 63                 | 7          | 9       |
| C3                   | 67                 | 8          | 9       |
| C4                   | 54                 | 6          | 8       |
| C5                   | 31                 | 4          | 8       |
| C6                   | 58                 | 7          | 8       |
| C7                   | 45                 | 5          | 9       |
| C8                   | 36                 | 4          | 8       |
| C9                   | 32                 | 4          | 8       |
| C10                  | 63                 | 7          | 10      |

The data partitioning process followed the Horizontal partitioning (sharding) strategy which partitioned the dataset into multiple different datasets. The partitions all share the same features but have entirely different patients. Similarly, each partition has its own set of data.

4) *Work flow*: Federated Learning projects require a trusted execution environment to support the development process and facilitate the implementation of all necessary features in a secure manner. OpenFL is an open-source Python 3 framework for federated learning developed by Intel Labs in collaboration with the Internet of Things Group. Through a plugin mechanism, ML models and neural network training frameworks such as Tensor Flow and PyTorch can be used to train models. Communication between participants is secured by certificates [21].

OpenFL can be used to establish and run experiments with federations in two different ways: via Director-based workflows and Aggregator-based workflows. Fig. 7 illustrates the Aggregator-based workflow in OpenFL framework, which

is the chosen workflow in the conducted experiment. The federation runs between the aggregator node which owns the learning model and an arbitrary number of collaborators. This workflow is based on creating a workspace at the aggregator node and sending this workspace to each collaborator individually.

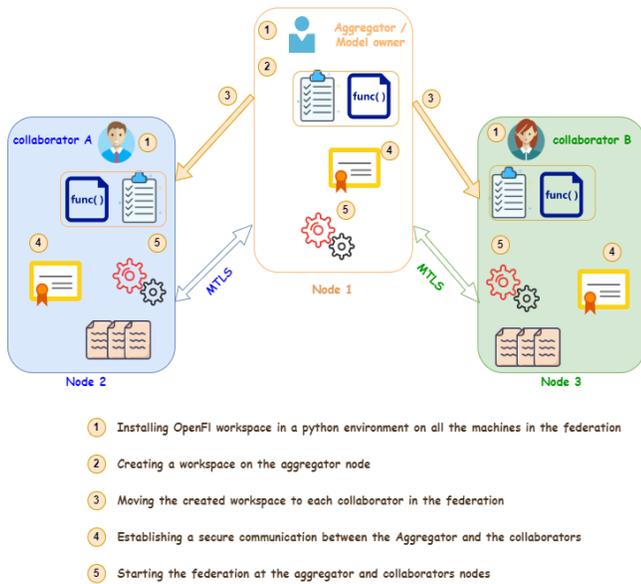


Fig. 7. The Architecture of the Aggregator-based Workflow.

This workspace consists of the plan and the learning model. The plan is a YAML file where the experiment settings are defined and is used to modify the workspace to the needed requirements such as the address of the aggregator, the global model that will be sent to collaborators, the number of federation rounds, and the encryption for network connections. Other parameters describing the model training process can be included as well.

To establish the connection, all participants must provide a valid public key infrastructure certificate signed by a trusted certificate authority (CA). OpenFL uses mutually authenticated transport layer security (TLS) connections. It is possible to create a certificate authority and generate X.509 certificates with OpenFL, but it is intended only for non-production testing. Once the connection is established, the federation starts with the aggregator and the collaborators.

### B. Practical Considerations

1) *Training parameters:* Several parameters are adjusted to the EfficientNetB3 architecture to achieve high accuracy performance. The first parameter is the optimizer, and it is selected to be adaptive moment estimation (Adam). The second parameter is the learning rate, and it is set to 0.001. The third parameter is the number of epochs of the model, and it is defined with 20, whereas the number of iterations for each epoch is equal to 58. In order to prevent overfitting, batch normalization is added and a 40% dropout is added before each fully connected layer. A sigmoid activation function is used on the last layer to resolve the two-class classification problem. A binary-crossentropy function is used for the cost

function to solve the two-class classification problem. Also, some parameters are adjusted to the proposed RNN architecture. The number of neurons of each LSTM layer is 150, and the dropout layer has a probability value of 0.2.

2) *Plan parameters:* The experiment conducted with 10 collaborators represent the 10 institutions and lasted for 300 communication rounds to achieve the same results. OpenFL framework supports four aggregation algorithms in this experiment the FedOpt algorithm is used with the Adam optimizer.

### C. Experimental Results

We conducted two experiments the first, followed the classical way of learning, the training model use a centralized dataset to predict the MGMT value. In the second, we use the same data set and the same Learning model but with the federated learning approach. The main goal is to show that the developed FL-based model can perform the same as the DL-based model in addition to persevering the patient's privacy, preventing data transferring and aggregation from data owners, and using less computational power, which makes it better for healthcare applications. The two developed model were evaluated according to the performance of the model and the resulting values of the MGMT promoter methylation.

1) *Model performance:* To test the performance of the machine learning model, 10% of the dataset has been allocated for testing the model and it achieved accuracy with a score 96.21% and with 3.783 loss.

The following line charts Fig. 8 illustrate the classical model performance over the twenty epochs for each scan type. a and b represent the training accuracy and Loss of the four scan types and each scan type is colored by a specific color. The first two scan types are colored in yellow and black for Flair and T1w respectively, while the last two scan types are colored in red and blue for T1wce and T2w, respectively. The validation accuracy and loss represented in c and d, respectively.

The Federated learning model was also tested on 10% of the dataset and achieved an accuracy of 96.713% and a loss of 3.287. Fig. 9 shows the performance of the same previous model but as the global model in the FL experiment in terms of training and validation. a and c manifest the validation and training accuracy curve in the yellow and blue colors over 300 rounds and b and c manifest the validation and training loss.

2) *Predicted MGMT\_value:* The presence of the MGMT protein is the main desired results of the proposed approach and the most important factor to measure the effectiveness of Federated Learning approach. The results of the two models are shown In Table III and Table IV. Using both federated and classical learning respectively. Each table consists of three columns. The first column represents the records of the patients, while the second column describes the patient ID and it was provided with the dataset, whereas the last column presents the predicted MGMT value. The predicted MGMT value for each patient in the two models are the same, which ensures the efficiencies of the federated

model to work as the classical one and produce the same results.

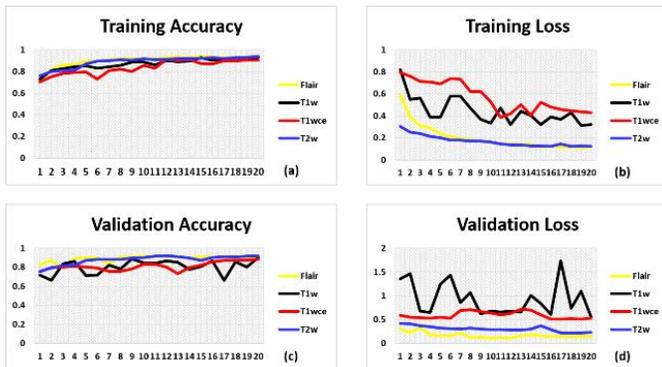


Fig. 8. (a) and (b) Represent the Training Accuracy and Loss for Four Scan Types and (c) and (d) Illustrates the Validation Accuracy and Loss for the Same MRI Scan Types.

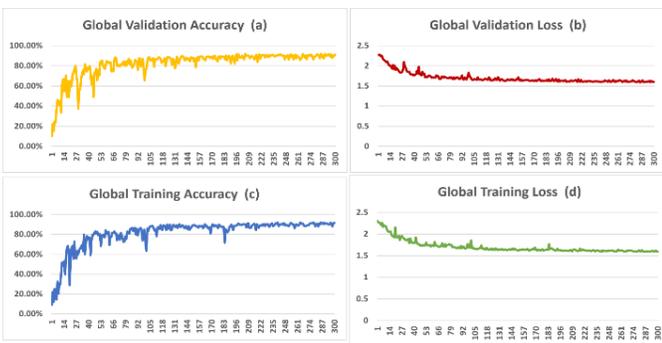


Fig. 9. (a and c) Represent the Global Accuracy Curves on the Training and Validation Data (b and d) Represent the Loss Obtain from the Training and Validation Data.

TABLE III. RESULTS OF THE FEDERATED LEARNING MODEL

| Federated Learning Results |           |            |
|----------------------------|-----------|------------|
| Record                     | BraTS21ID | MGMT_value |
| 0                          | 1         | 0.6135     |
| 1                          | 13        | 0.4693     |
| 2                          | 15        | 0.4871     |
| 3                          | 27        | 0.6152     |
| 4                          | 37        | 0.4731     |
| ----                       | -----     | -----      |
| 80                         | 826       | 0.5684     |
| 81                         | 829       | 0.5231     |
| 82                         | 833       | 0.4285     |
| 83                         | 997       | 0.5021     |
| 84                         | 1006      | 0.5481     |

Several trials were applied using different values for the round number. The trials started from 10 rounds till reached 500, and at 300 rounds the performance of the federated and the classical learning was approximately identical. The MGMT values from both models show a 99.99% similarity degree.

TABLE IV. RESULTS OF THE CLASSICAL LEARNING MODEL

| Federated Learning Results |           |            |
|----------------------------|-----------|------------|
| Record                     | BraTS21ID | MGMT_value |
| 0                          | 1         | 0.6135     |
| 1                          | 13        | 0.4693     |
| 2                          | 15        | 0.4871     |
| 3                          | 27        | 0.6152     |
| 4                          | 37        | 0.4732     |
| ----                       | -----     | -----      |
| 80                         | 826       | 0.5684     |
| 81                         | 829       | 0.5231     |
| 82                         | 833       | 0.4285     |
| 83                         | 997       | 0.5021     |
| 84                         | 1006      | 0.5481     |

A sample of 87 patients was used in the experiment for testing and obtaining their MGMT values. Fig. 10(a) and (b) visualize the probability distribution of the patients using federated and classical learning respectively. Each class in federated learning is exactly equal in the number of patients to its corresponding class in classical learning.

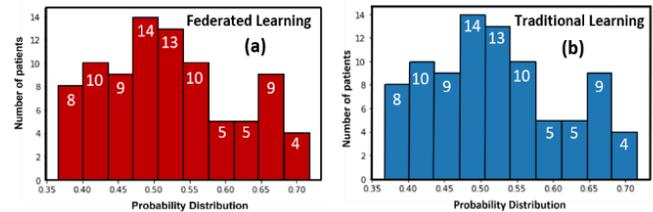


Fig. 10. (a) MGMT Probability Distribution using Federated Learning (b) MGMT Probability Distribution using Classical Learning.

## VI. DISCUSSION

The study proposed a methodology based on an improved efficientNetB3 model for the predicating the MGMT promoter methylation of GBM brain tumor with the aim of measuring the response of the tumor to the chemotherapy. At the beginning the data were obtained from the BraTS2021 dataset entirely. The next step is converting the images from the DICOM to NIFTI format. The reason for this conversion is to enhance the performance and it can be easy and simple in the processing. Then, the images in the NIFT format are normalized to be ready for feature extraction using the improved efficientNetB3. The features are extracted using the improved efficientNetB3 based on the combination of the CNN and RNN architectures. The entire methodology ran using two different approaches. The first approach is based on classical or conventional learning, while the second approach relies on the federated learning. The illustrated results in Table III, Table IV and Fig. 10, show that the proposed federated model architecture using the OpenFl framework and the BraTS2021 dataset through 300 communication rounds between the aggregator and 10 collaborators managed to surpass the limitation of the classic training model in the following points:

1) *Data privacy*: Each one of the ten collaborators participates in the training process while, keeping its data private, only sharing results and its model gradients.

2) *Data diversity*: Federated learning facilitates training the machine learning model with various and diverse datasets from different institutions, eliminating the need for a centralized data center while making the local data of each collaborator sufficient for the training process as the local training model utilizes its local data and the gradients of the other collaborators.

3) *Real-time continual learning*: Continual learning is done by using client data instead of aggregated data to improve models.

4) *Hardware efficiency*: Since federated learning models operate without a central server, less complex hardware is needed.

## VII. CONCLUSION AND FUTURE WORK

Our study explores various practical aspects of the federated model sharing with an emphasis on protecting the privacy of patient data in order to predict the MGMT promoter value of brain tumors. We demonstrate how clinical institutions can train their models without sharing their data by using federated learning. Our FL experiments shows that even with imbalanced datasets, such as the BraTS institutional distribution the FL approach among 10 institutions reached the training model to 99.99% of the model quality achieved with centralized data.

Incorporating such an FL system into a clinical setting for multi-institutional collaboration, which produces computer-aided analytics and assistive diagnostics, is expected to contribute to precision medicine at a catalytic level. Integrating knowledge from another institution into the trained models would be particularly beneficial since patient data wouldn't have to be shared, thereby removing concerns about privacy and data ownership. As a result, the final accuracy achieved a value of 96% on both classical and federated learning. This proves that the federated learning is more efficient in all terms as an environment than the classical learning.

We are striving to improve the performance of the FL model to achieve the results with a smaller number of communication rounds and reduce time consumption in addition to increasing the number of collaborated institutions and exploring different workflows using swarm intelligence.

## REFERENCES

- [1] M. L. Goodenberger and R. B. Jenkins, "Genetics of adult glioma," *Cancer Genet.*, vol. 205, no. 12, pp. 613–621, 2012.
- [2] N. Thon, S. Kreth, and F.-W. Kreth, "Personalized treatment strategies in glioblastoma: MGMT promoter methylation status," *Oncotargets Ther.*, vol. 6, pp. 1363–1372, 2013.
- [3] F. Wang, L. P. Casalino, and D. Khullar, "Deep learning in medicine: promise, progress, and challenges," *JAMA Intern. Med.*, vol. 179, no. 3, pp. 293–294, 2019.
- [4] G. Chartrand, P. Cheng, E. Vorontsov, M. Drozdal, S. Turcotte, C. Pal and Samuel Kadoury, "Deep learning: A primer for radiologists," *Radiographics*, vol. 37, no. 7, pp. 2113–2131, 2017.
- [5] J. De Fauw, "Clinically applicable deep learning for diagnosis and referral in retinal disease," *Nat. Med.*, vol. 24, 2018. R. Nicole, "Title of paper with only first word capitalized," *J. Name Stand. Abbrev.*, in press.
- [6] C. Sun, A. Shrivastava, S. Singh, and A. Gupta, "Revisiting unreasonable effectiveness of data in deep learning era," arXiv [cs.CV], 2017.
- [7] N. Rieke, J. Hancox, W. Li, F. Milletari, H. Roth, S. Albarqouni, S. Bakas, M. Galtier, B. Landman, K. Maier-Hein, S. Ourselin, M. Sheller, R. Summers, A. Trask, D. Xu, M. Baust and M. Cardoso, "The future of digital health with federated learning," *NPJ Digit. Med.*, vol. 3, no. 1, p. 119, 2020.
- [8] J. Xu, B. S. Glicksberg, C. Su, P. Walker, J. Bian, and F. Wang, "Federated learning for healthcare informatics," *J. Healthc. Inform. Res.*, vol. 5, no. 1, pp. 1–19, 2021.
- [9] G. Long, T. Shen, Y. Tan, L. Gerrard, A. Clarke, and J. Jiang, "Federated learning for privacy-preserving open innovation future on digital health," in *Humanity Driven AI*, Cham: Springer International Publishing, 2022, pp. 113–133.
- [10] P. Korfiatis, T. L. Kline, D. H. Lachance, I. F. Parney, J. C. Buckner, and B. J. Erickson, "Residual deep convolutional neural network predicts MGMT methylation status," *J. Digit. Imaging*, vol. 30, no. 5, pp. 622–628, 2017.
- [11] C.G.B. Yogananda, a B.R. Shah, a S.S. Nalawade, a G.K. Murugesan, a F.F. Yu, a M.C. Pinho, a B.C. Wagner, a B. Mickey, b T.R. Patel, b Fei, c A.J. Madhuranthakam, a and J.A. Maldjian, "MRI-based deep-learning method for determining glioma MGMT promoter methylation status," *AJNR Am. J. Neuroradiol.*, vol. 42, no. 5, pp. 845–852, 2021.
- [12] S. Chen, Y. Xu, M. Ye, Y. Li, Y. Sun, J. Liang, J. Lu, Z. Wang, Z. Zhu, X. Zhang, and B. Zhang, "Predicting MGMT promoter methylation in diffuse gliomas using deep learning with radiomics," *J. Clin. Med.*, vol. 11, no. 12, p. 3445, 2022.
- [13] D. C. Nguyen, Q. Pham, P. Pathirana and M. Ding, "Federated Learning for smart healthcare: A survey," *ACM Comput. Surv.*, vol. 55, no. 3, pp. 1–37, 2021.
- [14] A. Rauniyar, Desta. Hagos, D. Jha, Jan. Hakegard, U. Bagci, D.B. Rawat and V. Vlassov, "Federated learning for medical applications: A taxonomy, current trends, challenges, and future research directions," arXiv [cs.LG], 2022.
- [15] M. J. Sheller, G. A. Reina, B. Edwards, J. Martin, and S. Bakas, "Multi-institutional deep learning modeling without sharing patient data: A feasibility study on brain tumor segmentation," *Brainlesion*, vol. 11383, pp. 92–104, 2019.
- [16] W. Li, F. Milletari, D. Xu and N. Rieke, "Privacy-preserving federated brain tumour segmentation," arXiv [cs.CV], 2019.
- [17] P. Guo, P. Wang, J. Zhou, S. Jiang, and V. M. Patel, "Multi-institutional collaborations for improving deep learning-based magnetic resonance image reconstruction using federated learning," *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.*, vol. 2021, pp. 2423–2432, 2021.
- [18] M. Tan and Q. V. Le, "EfficientNet: Rethinking model scaling for convolutional Neural Networks," arXiv [cs.LG], 2019.
- [19] H. Zhang, J. Bosch, and H. H. Olsson, "Federated learning systems: Architecture alternatives," in *2020 27th Asia-Pacific Software Engineering Conference (APSEC)*, 2020.
- [20] U. Baid, S. Ghodasara, S. Mohan, M. Bilello, E. Calabrese, E. Colak, K. Farahani, J. Kalpathy-Cramer, F.C. Kitamura, S. Pati, L.M. Prevedello, J.D. Rudie, C. Sako, R.T. Shinohara, T. Bergquist, R. Chai, J. Eddy, J. Elliott, W. Reade, T. Schaffter, T. Yu, J. Zheng, BraTS Annotators, C. Davatzikos, J. Mongan, C. Hess, S. Cha, J. Villanueva-Meyer, J. B. Freymann, J. S. Kirby, B. Wiestler, P. Crivellaro, R. R. Colen, A. Kotrotsou, D. Marcus, M. Milchenko, A. Nazeri, H. Shaykh, R. Wiest, A. Jakab, Marc. Weber, A. Mahajan, B. Menze, A. E. Flanders, and S. Bakas, "The RSNA-ASNR-MICCAI BraTS 2021 benchmark on brain tumor segmentation and radiogenomic classification," arXiv [cs.CV], 2021.
- [21] G Anthony Reina, Alexey Gruzdev, Patrick Foley, Olga Perepelkina, Mansi Sharma, Igor Davidyuk, Ilya Trushkin, Maksim Radionov, Aleksandr Mokrov, Dmitry Agapov, Jason Martin, Brandon Edwards, Micah J. Sheller, Sarthak Pati, Prakash Narayana Moorthy, Shih-han Wang, Prashant Shah and Spyridon Bakas, "OpenFL: An open-source framework for Federated Learning," Arxiv.org. [Online]. Available: <https://arxiv.org/pdf/2105.06413.pdf>. [Accessed: 30-Sep-2022].