PROBLEM STATEMENT OF PHASE 1:

Structural magnetic resonance imaging (sMRI) is widely used for the brain neurological disease diagnosis, which could reflect the variations of brain. However, due to the local brain atrophy, only a few regions in sMRI scans have obvious structural changes, which are highly correlative with pathological features.Hence, the key challenge of sMRI-based brain disease diagnosis is to enhance the identification of discriminative features. To address this issue, a dual attention multi-instance deep learning network (DA-MIDL) is proposed for the diagnosis of Alzheimer's disease (AD) and its prodromal stage mild cognitive impairment (MCI). Specifically, DA-MIDL consists of three primary components: 1) the Patch-Nets with spatial attention blocks for extracting discriminative features within each sMRI patch whilst enhancing the features of abnormally changed micro-structures in the cerebrum, 2) an attention multi-instance learning (MIL) pooling operation for balancing the relative contribution of each patch and yield a global different weighted representation for the whole brain structure, and 3) an attention-aware global classifier for further learning the integral features and making the AD-related classification decisions.

- **Discriminant patch selection** using Genetic Algorithm

PROBLEM STATEMENT OF PHASE 2:

Federated learning (FL) is a learning paradigm seeking to address the problem of data governance and privacy by training algorithms collaboratively without exchanging the data itself. Originally developed for different domains, such as mobile and edge device use cases, it recently gained traction for healthcare applications. FL enables gaining insights collaboratively, e.g., in the form of a consensus model, without moving patient data beyond the firewalls of the institutions in which they reside. Instead, the ML process occurs locally at each participating institution and only model characteristics (e.g., parameters, gradients) are transferred. Recent research has shown that models trained by FL can achieve performance levels comparable to ones trained on centrally hosted data sets and superior to models that only see isolated single-institutional data.

UNet++ is an architecture for semantic segmentation based on the U-Net. Through the use of densely connected nested decoder sub-networks, it enhances extracted feature processing and was reported by its authors to outperform the U-Net in Electron Microscopy (EM), Cell, Nuclei, Brain Tumor, Liver and Lung Nodule medical image segmentation tasks.

INTRODUCTION:

ALZHEIMER'S DISEASE:

Alzheimer's disease is a progressive neurologic disorder that causes the brain to shrink (atrophy) and brain cells to die. Alzheimer's disease is the most common cause of dementia — a continuous decline in thinking, behavioral and social skills that affects a person's ability to function independently.

Atrophy:the medical condition of losing flesh, muscle, strength, etc. in a part of the body because it does not have enough blood.

Dementia is a term used to describe a group of symptoms affecting memory, thinking and social abilities severely enough to interfere with your daily life. It isn't a specific disease, but several diseases can cause dementia. Though dementia generally involves memory loss, memory loss has different causes.

The early signs of the disease include forgetting recent events or conversations. As the disease progresses, a person with Alzheimer's disease will develop severe memory impairment and lose the ability to carry out everyday tasks.

SYMPTOMS:

1.Difficulty in

1)Thinking and reasoning
2)Making judgments and decisions
3)Planning and performing
1.Memory loss is the key familiar tasks

2.Changes in personality and behavior Depression

- Apathy
- Social withdrawal
- Mood swings
- Distrust in others
- Irritability and aggressiveness
- Changes in sleeping habits
- Wandering
- Loss of inhibitions
- Delusions, such as believing something has been stolen

PRESERVED SKILLS:

Many important skills are preserved for longer periods even while symptoms worsen. Preserved skills may include reading or listening to books, telling stories and reminiscing, singing, listening to music, dancing, drawing, or doing crafts.
These skills may be preserved longer because they are controlled by parts of the brain affected later in the course of the disease.

REMEDIES:

1.There is no treatment that cures Alzheimer's disease or alters the disease process in the brain.In advanced stages of the disease, complications from severe loss of brain function — such as dehydration, malnutrition or infection — result in death.
2.Medications may temporarily improve or slow progression of symptoms.These treatments can sometimes help people with Alzheimer's disease maximize function and maintain independence for a time.

CAUSES:

1.The exact causes of Alzheimer's disease aren't fully understood.
2.But at a basic level, brain proteins fail to function normally, which disrupts the work of brain cells (neurons) and triggers a series of toxic events. Neurons are damaged, lose connections to each other and eventually die.

Scientists believe that for most people, Alzheimer's disease is caused by a combination of genetic, lifestyle and environmental factors that affect the brain over time.

Researchers trying to understand the cause of Alzheimer's disease are focused on the role of two proteins:
Plaques. Beta-amyloid is a fragment of a larger protein. When these fragments cluster together, they appear to have a toxic effect on neurons and to disrupt cell-to-cell communication. These clusters form larger deposits called amyloid plaques, which also include other cellular debris.
Tangles. Tau proteins play a part in a neuron's internal support and transport system to carry nutrients and other essential materials. In Alzheimer's disease, tau proteins change shape and organize themselves into structures called neurofibrillary tangles. The tangles disrupt the transport system and are toxic to cells.

Research has shown that the same risk factors associated with heart disease may also increase the risk of Alzheimer's disease. These include:
• Lack of exercise
• Obesity
• Smoking or exposure to secondhand smoke
• High blood pressure

TESTS:

1.Physical and neurological exam

2.Lab tests:
1)Blood tests may help your doctor rule out other potential causes of memory loss and confusion, such as a thyroid disorder or vitamin deficiencies.
2)Mental status and neuropsychological testing
3)Brain imaging
1.Magnetic resonance imaging (MRI)
2.Computerized tomography (CT)

Imaging of disease processes can be performed with positron emission tomography (PET). During a scan, a low-level radioactive tracer is injected into the blood to reveal a particular feature in the brain. imaging may include the following:
• Fluorodeoxyglucose (FDG) scans show areas of the brain in which nutrients are poorly metabolized. Identifying patterns of degeneration — areas of low metabolism — can help distinguish between Alzheimer's disease and other types of dementia.
• Amyloid imaging can measure the burden of amyloid deposits in the brain. This imaging is primarily used in research but may be used if a person has unusual or very early onset of dementia symptoms.
• Tau imaging, which measures the burden of neurofibrillary tangles in the brain, is generally used in the research setting.

OUTLOOK:

People with Alzheimer's disease can live for several years after they start to develop symptoms. But this can vary considerably from person to person.

Alzheimer's disease is a life-limiting illness, although many people diagnosed with the condition will die from another cause.

As Alzheimer's disease is a progressive neurological condition, it can cause problems with swallowing.

This can lead to aspiration (food being inhaled into the lungs), which can cause frequent chest infections.

It's also common for people with Alzheimer's disease to eventually have difficulty eating and have a reduced appetite.

There's increasing awareness that people with Alzheimer's disease need palliative care.

This includes support for families, as well as the person with Alzheimer's.

BRIEF SUMMARY OF RELATED WORKS:

1. EEG-Based Graph Neural Network Classification of Alzheimer's Disease: An Empirical Evaluation of Functional Connectivity Methods

METHODS:

1)EEG-Based Graph Neural Network Classification of Alzheimer's Disease.

2)Functional Connectivity model.

DATA:

The EEG dataset consists of 20 AD patients and 20 healthy control participants (HC) below 70 years.

MAJOR FINDINGS:

GNN models perform significantly better than the other baseline models.Moreover,using FC measures to estimate brain graphs improves the performance of GNN compared to models trained using a fixed graph based on the spatial distance between the EEG sensors.The best GNN reaches 0.984 area under sensitivity-specificity curve (AUC) and 92% accuracy, whereas the best baseline model, a convolutional neural network, has 0.924 AUC and 84.7% accuracy.

CONCLUSION:

GNN models are superior to classical machine learning and CNN models for brain graph classification.

FUTURE WORK:

The utilised GNN architecture is a black-box model. Thus, future work should focus on implementing interpretable GNN architectures that achieve similar performance but additionally offer interpretability, such as which nodes, i.e. brain regions, drive the prediction.

2. Alzheimer's Disease Detection Using Comprehensive Analysis of Timed Up and Go Test via Kinect V.2 Camera and Machine Learning

METHODS:

1.Timed Up and Go Test 2.Machine Learning(SVM)

DATA:

A total of 42 AD and 50 HC subjects were recruited in this study. The AD subjects were recruited from the patients of Iran Dementia and Alzheimer's Association (IDAA) who under-went comprehensive diagnostic processes and assessments of psychological tests, MRI, and EEG.

COMPONENT:

1.Kinect V.2 Camera
"The Kinect v2 face recognition, motion tracking, and resolution are much more precise than the Kinect v1. Kinect v2 uses "time of flight" technology to determine the features and motion of certain objects.

MAJOR FINDINGS:

The model classified the two groups(AD vs HC-Healthy isControl) with an average accuracy of 97.75% and an F-score of 97.67% for five-fold cross-validation and 98.68% and 98.67% for leave-one-subject out cross-validation.

FUTURE WORK:

Future work extends the method to a larger cohort which includes individuals with MCI(Mild cognitive impairment) and other related disorders.

3. Adaptive 3DCNN-Based Interpretable Ensemble Model for Early Diagnosis of Alzheimer's Disease

METHOD:

3-D convolutional neural network (3DCNN) and genetic algorithm (GA)

DATASETS USED:

1)Data partially used in this article were obtained from the ADNI database.
2)MRI datasets.

CONCLUSIONS:

1) More accurate disease classification (AD versus NC, MCIc versus NC, and MCIc versus MCInc),Alzheimer's Disease (AD),Mild Cognitive Impairment (MCI),Normal Control (NC).

2) The identification of discriminative brain regions that could be the biomarkers for early detection in AD progression.

FUTURE WORK:

Since some brain regions are too small to effectively train corresponding base classifiers, they could be inevitably excluded by the proposed method here. This could result in the loss of important features for the classification to some degree. The possible solution to this problem warrants further investigation.

4. Extracting ROI-Based Contourlet Subband EnergyFeature From the sMRI Image for Alzheimer's Disease Classification

METHOD:

1.Structural magnetic resonance imaging (sMRI)-based Alzheimer's disease (AD) classification.
2.Regions Of Interest-based contourlet subband energy (ROICSE) feature.
3.SVM Classifier.

DATASET USED:

Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu).

MAJOR FINDINGS:

Instead of extracting features from the brain ROIs in the spatial domain, the contourlet transform is performed on these ROIs to obtain their subbands, and then subband energy feature vectors of different brain ROIs are concatenated to form the ROICSE feature for representing the sMRI image.Finally, results of SVM-based AD classification on six data sets show that the ROICSE approach outperforms six other state-of-the-art methods.

FUTURE WORK:
However, experiments to find brain ROIs related to AD indicate that not all brain ROIs are important for classifying subjects with AD, MCI, and HC.In our future work, we will model associations between different brain regions in frequency domain so that those brain ROIs mostly related to AD can be selected for AD classification.

5.Dual Attention Multi-Instance Deep Learning for Alzheimer's Disease Diagnosis With Structural MRI

METHOD:

Dual attention multi-instance deep learning network (DA-MIDL) for the early diagnosis of Alzheimer's disease (AD) and its prodromal stage mild cognitive impairment (MCI).

DATASETS USED:

Two datasets (i.e., ADNI and AIBL) used in our study are acquired from the public Alzheimer's Disease Neuroimaging Initiative (ADNI) database (http://adni.loni.usc.edu) and Aus-tralian Imaging, Biomarker and Lifestyle Flagship Study ofAgeing (AIBL) database (https://aibl.csiro.au).

CONCLUSION:

Performance improvement.

FUTURE WORK:

1) The size of input patches is fixed and equivalent.However, the structural changes in the cerebrum caused by brain atrophy may occur across multiple regions with different scales. Using the fixed size could not represent various local features. It's more reasonable to use multi-scale patches as inputs, while it may increase the difficulty of constructing the networks. In addition, ROI pooling may be adopted for settling the inputs with non-uniform sizes.
2)The patch location proposals based on the group comparison are isolated from the subsequent network. This means that the proposed method is not strictly an end-to-end analysis procedure, which may affect the optimal performance of the model. Therefore, it is important to combine the generator of patch location proposals and the network into a unified framework.

6."Federated Learning of Generative Image Priors for MRI Reconstruction",in IEEE Transactions on Medical Imaging, 2022.

APPROACHES AND TECHNIQUES:

Federated learning of Generative Image Priors, MRI reconstruction.

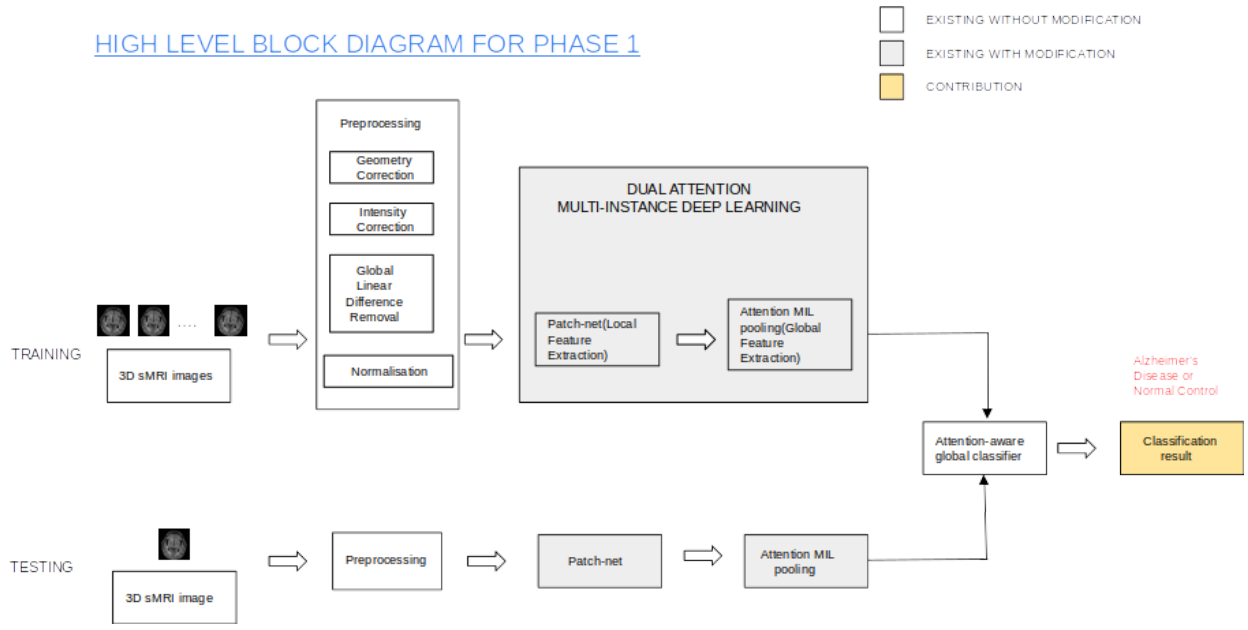
ADVANTAGES:

Benefits over state-of-the-art federated and traditional methods were demonstrated in multi-site MRI datasets.

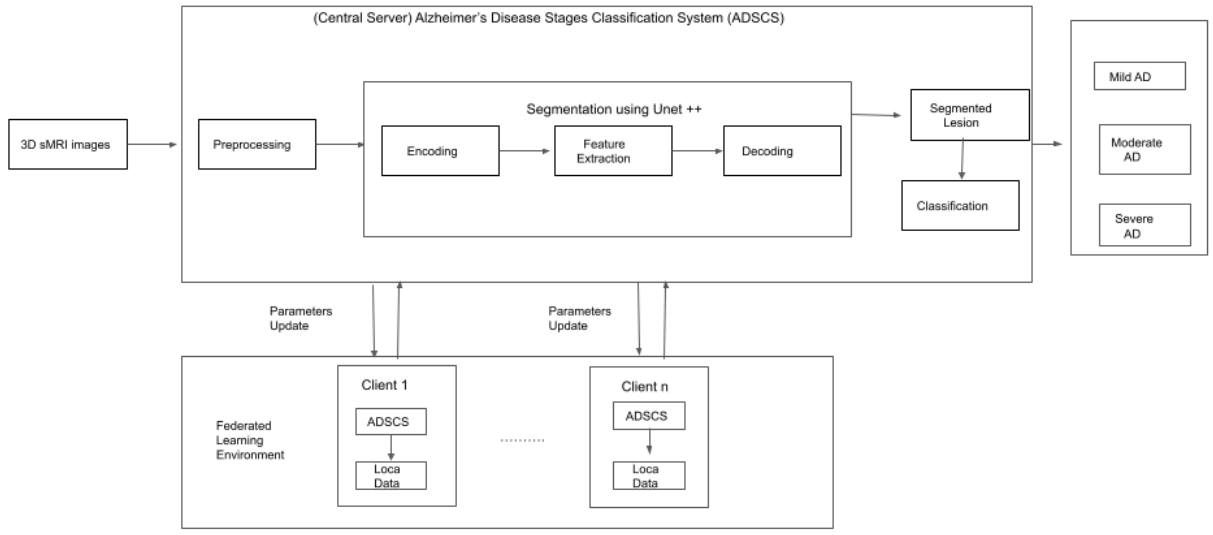
Improved generalization against domain shifts renders FedGIMP a promising candidate for multi-site collaborations in accelerated MRI.

FedGIMP might also be used for physics-based reconstruction in other modalities such as CT, PET, or ultrasound by modifying its imaging operator.Improved generalization against domain shifts renders FedGIMP a promising candidate for multi-site collaborations in accelerated MRI. FedGIMP might also be used for physics-based reconstruction in other modalities such as CT, PET, or ultrasound by modifying its imaging operator.

HIGH LEVEL BLOCK DIAGRAM FOR PHASE 1



HIGH LEVEL BLOCK DIAGRAM FOR PHASE 2



PROPOSED SYSTEM:

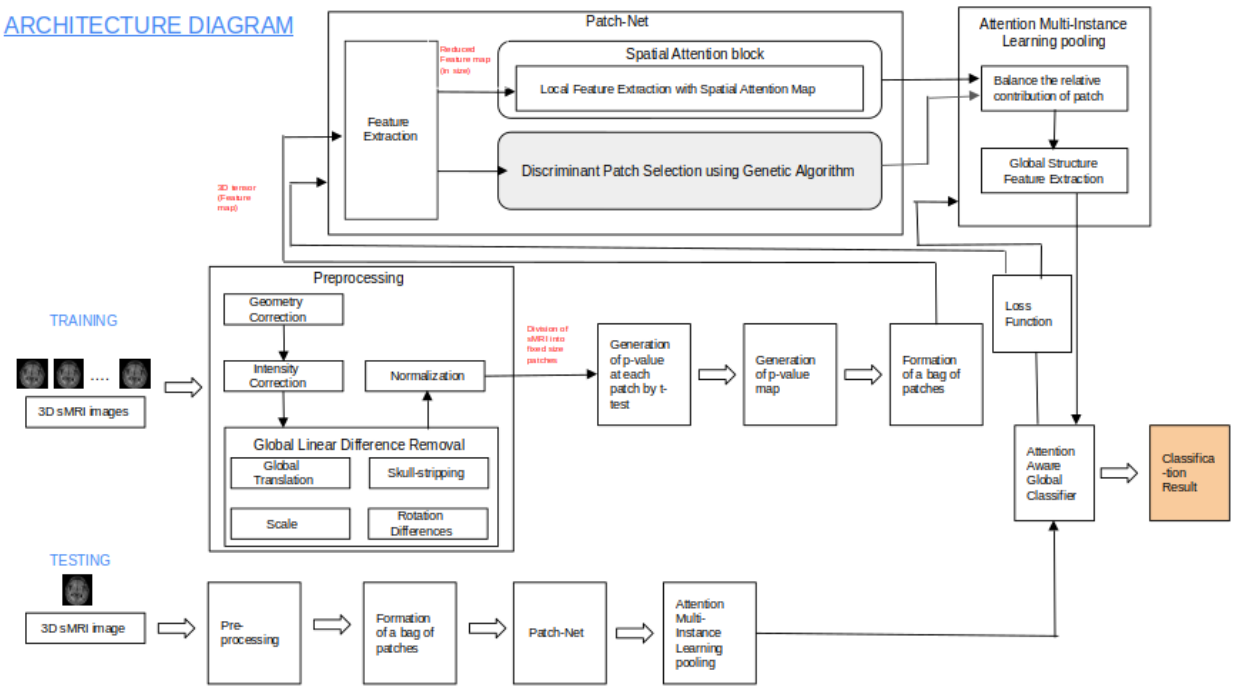
Structural magnetic resonance imaging(sMRI) is widely used for the brain neurological disease diagnosis, which could reflect the variations of brain.However, due to the local brain atrophy, only a few regions in sMRI scans have obvious structural changes, which are highly correlative with pathological features.Hence, the key challenge of sMRI-based brain disease diagnosis is to enhance the identification of discriminative features. To address this issue, a dual attention multi-instance deep learning network (DA-MIDL) for the early diagnosis of Alzheimer's disease (AD) and its prodromal stage mild cognitive impairment(MCI is proposed). Specifically, DA-MIDL consists of three primary components: 1) the Patch-Nets with spatial attention blocks for extracting discriminative features within each sMRI patch whilst enhancing the features of abnormally changed micro-structures in the cerebrum, 2) an attention multi-instance learning (MIL) pooling operation for balancing the relative contribution of each patch and yield a global different weighted representation for the whole brain structure, and 3) an attention-aware global classifier for further learning the integral features and making the AD-related classification decisions.The proposed DA-MIDL model is evaluated on the baseline sMRI scans of 1689 subjects from two independent datasets (i.e., ADNI and AIBL).

Phase1 : To design and develop Alzheimer's disease diagnosis system **using Dual Attention Multi-Instance Learning** with three components,

1) **Patch-Nets** with spatial attention blocks for extracting discriminative features from local patches and genetic algorithm.
2) An Attention MIL pooling operation for balancing the relative contribution of each patch and yield a global feature representation for the whole brain.
3) An Attention-aware global classifier for making the AD-related diagnosis decisions based on the combined feature representation for the whole brain structure.
    - Discriminant patch selection using Genetic Algorithm.

Phase2 : To diagnose the different stages of Alzheimer's disease using **Segmentation with Classification**,

- To resolve the issues with the privacy of models and to distribute the heavy computing process, usage of Federated Learning of Generative Image Priors for MRI Reconstruction.
- To handle the segmentation with classification to identify the stages,
    1) Mild Dementia.
    2) Moderate Dementia.
    3) Severe Dementia.



DATASET DESCRIPTION:

Two datasets (i.e., ADNI and AIBL) used in our study are acquired from the public Alzheimer's Disease Neuroimaging Initiative (ADNI) database (http://adni.loni.usc.edu) and Australian Imaging, Biomarker and Lifestyle Flagship Study of Ageing (AIBL) database (https://aibl.csiro.au). In the ADNI dataset, there are totally 1193 1.5T/3T T1-weighted structural MRI (sMRI) scans from subjects at their own base-line/screening visit (i.e., the first examination) across three ADNI phases (i.e., ADNI-1, ADNI-2 and ADNI-3). These subjects can be divided into three categories: AD (Alzheimer's disease), MCI (mild cognitive impairment) and NC (normal control) in accordance with the standard clinic criteria, such as Mini-Mental State Examination (MMSE) scores and Clinical Dementia Rating (CDR). For MCI conversion prediction, MCI subjects can be further categorized into two classes: pMCI (progressive MCI subjects who had converted to AD within 36 months after baseline visit) and sMCI (stable MCI subjects who were continuously diagnosed as MCI for 36 months after baseline visit). The studied ADNI dataset contains 389 AD, 172 pMCI, 232 sMCI and 400 NC subjects. The AIBL dataset consists of baseline sMRI scans from 496 different subjects, including 79 AD, 17 pMCI,93 sMCI and 307 NC subjects.

The original structural MRI data downloaded from ADNI are pre-processed for subsequent better feature learning and classification. First, the original images in 3D Neuroimaging Informatics Technology Initiative (NIfTI) format are standardized through

geometry correction for gradient nonlinearity by 3D gradwarp correction and intensity correction for non-uniformity by B1 non-uniformity correction. Then,we perform linear registration to the Colin27 template to remove global linear differences (including global translation,scale, and rotation differences) and skull-stripping on all the structural MR images respectively using ‘flirt’ instruction with default parameters (e.g., DOF (degrees of freedom) as 12 and Correlation Ratio as cost function) and ‘bet’ instruction with default fractional intensity threshold (0.5) in FSL toolbox.After image normalization to the Colin27 standard space, MR images have a size of 181 × 217 × 181 voxels.

PERFORMANCE MEASURE:

1. Usage of four metrics to evaluate the classification performance, including-

Accuracy (ACC) - the measure of overall effectiveness of the classifier,
Sensitivity (SEN) - the percentage of correctly classified positive classes among the total actual positive classes,
Specificity (SPE) - the measure of effectiveness of a classifier to identify negative instances,
The area under receiver operating characteristic curve (AUC) - the aggregate measure of performance across all possible classification thresholds.

2. These metrics are defined as: ACC = (TP+TN)/(TP+TN+FP+FN), SEN = TP/(TP+FN), SPE = TN/(TN+FP),where TP, TN, FP and FN are denoted as true positive, true negative, false positive and false negative value respectively.

3. AUC is calculated on all possible pairs of true positive rate (TPR = SEN) and false positive rate (FPR = 1−SPE) by changing the thresholds performed on the prediction results from our trained network.

DELIVERABLES TO BE DEMONSTRATED AT THE END OF PHASE 1 AND PHASE 2:

Phase1 :

Input - 3D sMRI images.
Output - Decision Support System to classify Alzheimer’s Disease (AD) and Normal Control (NC).

Phase2 :

Input -3D sMRI images.
Output -The different stages of Alzheimer’s Disease -
1) Mild Dementia.
2) Moderate Dementia.
3) Severe Dementia.

REFERENCES:

[1] Dan Pan, Genqiang Luo, An Zeng, Chao Zou, Haolin Liang, Jianbin Wang, Tong Zhang, Baoyao Yang, and for the Alzheimer's Disease Neuroimaging Initiative, "Adaptive 3DCNN-Based Interpretable Ensemble Model for Early Diagnosis of Alzheimer's Disease," in IEEE Transactions on Computational Social Systems, 2022, pp. 1-20.

[2] Jinwang Feng, Shao-Wu Zhang, Luonan Chen, and Alzheimer's Disease Neuroimaging Initiative, "Extracting ROI-Based Contourlet Subband Energy Feature From the sMRI Image for Alzheimer's Disease Classification," in IEEE/ACM Transactions on Computational Biology and Bioinformatics, 2022, vol. 19, no. 3, pp. 1627-1639.

[3] Wenyong Zhu, Liang Sun, Jiashuang Huang, Liangxiu Han, and Daoqiang Zhang, "Dual Attention Multi-Instance Deep Learning for Alzheimer's Disease Diagnosis With Structural MRI," in IEEE Transactions on Medical Imaging, 2021, vol.40, pp. 2354-2366.

[4] Mahmoud Seifallahi, Afsoon Mehraban, James E. Galvin, and Behnaz Ghoraani, "Alzheimer's Disease Detection Using Comprehensive Analysis of Timed Up and Go Test via Kinect V.2 Camera and Machine Learning," in IEEE Transactions on Neural Systems and Rehabilitation Engineering, 2022, vol. 30, pp. 1589-1600.

[5] Zhenyuan Ning, Qing Xiao, Qianjin Feng, Wufan Chen, and Yu Zhang, "Relation-Induced Multi-Modal Shared Representation Learning for Alzheimer's Disease Diagnosis," in IEEE Transactions on Medical Imaging, 2021, vol. 40, no. 6, pp. 1632-1645.

[6] Gokberk Elmas, Salman UH Dar, Yilmaz Korkmaz, Emir Ceyani, Burak Susam, Muzaffer Ozbey, Salman Avestimehr,Fellow and Tolga Çukur, "Federated Learning of Generative Image Priors for MRI Reconstruction," in IEEE Transactionson Medical Imaging, 2022, pp. 1-13.