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Optimization of Deep CNN Techniques to Classify Breast Cancer and Predict Relapse

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Abstract

Breast cancer is a fatal disease that has a high rate of morbidity and mortality. Finding the right diagnosis is one of the most crucial steps in breast cancer treatment. Doctors can use machine learning (ML) and deep learning techniques to aid with diagnosis. This work makes an effort to devise a methodology for the classification of Breast cancer into its molecular subtypes and prediction of relapse. The objective is to compare the performance of Deep CNN, Tuned CNN and Hypercomplex-Valued CNN, and infer the results, thus automating the classification process. The traditional method used by doctors to detect is tedious and time consuming. It employs multiple methods, including MRI, CT scanning, aspiration, and blood tests as well as image testing. The proposed approach uses image processing techniques to detect irregular breast tissues in the MRI. The survivors of Breast Cancer are still at risk for relapse after remission, and once the disease relapses, the survival rate is much lower. A thorough analysis of data can potentially identify risk factors and reduce the risk of relapse in the first place. A SVM (Support Vector Machine) module with GridSearchCV for hyperparameter tuning is used to identify patterns in those patients who experience a relapse, so that these patterns can be used to predict the relapse before it occurs. The traditional deep learning CNN model achieved an accuracy of 27%, the tuned CNN model achieved an accuracy of 92% and the hypercomplex-valued CNN achieved an accuracy of 98%. The SVM model achieved an accuracy of 89% and on tuning the hyperparameters by using GridSearchCV it achieved and accuracy of 98%.

Keywords: *Multiclass Classification, Tuned CNN, Hypercomplex Valued CNN, Relapse Prediction, Breast Cancer.*

1. Introduction

One of the most common malignant tumours in the world, breast cancer (BC) is responsible for 10.4% of all cancer-related deaths in women between the ages of 20 and 50. According to the World Health Organization figures, 2.3 million women were diagnosed with BC in 2020. There is an ongoing need for a reliable and accurate system that can be used to help in the early detection and diagnosis of Breast Cancer diseases to reduce the number of deaths. Early breast cancer discovery can lead to successful treatment.

In this research, a convolutional neural network (CNN) is proposed for classifying MRI scans of breasts. To achieve better results, it is necessary to tune CNN hyperparameters which is an NP-hard optimization problem. In this paper, the Pytorch Gradient Calculation framework is adjusted for tuning some of the CNN hyperparameters. On the other hand, breast cancer is classified into its molecular subtypes using a technique called Hypercomplex-Valued CNN (HvCNN), which is based on Clifford algebra processing of HSV-encoding. It is well known that the HvCNN has a substantially more straightforward design and fewer parameters than the real valued CNN. Hence performance of the two techniques is compared with traditional DL CNN and results are inferred. After remission, breast cancer survivors are still at risk for relapse, and the likelihood of survival is significantly lower. To find patterns in patients who have relapses, data mining and analysis can be performed. Potentially identifying risk factors and lowering the likelihood of relapse in the first place can come from a thorough study of data. Hence, an SVM (Support Vector Machine) module with GridSearchCV for hyperparameter tuning is

proposed for predicting relapse in a patient based on their history and other details.

2. Literature Review

Ahmad LG et al. [1] investigated three classification models, DT, SVM, and ANN, and found that SVM had the highest accuracy when used to create models to predict the recurrence of breast cancer.

Danish Vasan et al. [2] proposed the IMCFN (Image-based Malware Classification using Fine-tuned Convolutional Neural Network Architecture) classifier to identify variations of malware families and improve malware detection using CNN-based deep learning architecture. The unprocessed malware binaries are converted into coloured images using a method for multiclass classification issues that allows the optimised CNN architecture to use them to locate and categorise malware families.

Eva Tuba et. al [3] put forth a simple bare bones firework approach for fine-tuning a selection of CNN hyperparameters. On a common benchmark dataset for the detection of acute lymphoblastic leukaemia, the proposed technique was evaluated. It was compared to CNN without hyperparameter tuning and the optimised SVM method, and it outperformed the other two techniques in terms of accuracy.

Guilherme Vieira et al.[4] combined real-valued convolutional networks with eight hypercomplex-valued convolutional neural networks (HvCNNs) to perform the classification job. The outcomes demonstrated that HvCNNs outperform the real-valued model, displaying superior accuracy with a significantly fewer number of parameters.

Jesse C. Sealand et. al [5] proposed a study that utilised four machine learning gradient-boosting algorithms and five tree- based models to find patterns in ALL patients who experience relapses and use those patterns to predict relapses in advance.

J. Marget et al. [6] suggested a convolutional neural network-based technique to anticipate the five most typical heart views and automatically extract missing or noisy cardiac acquisition plane information from magnetic resonance imaging. The convolutional neural network (CNN) was initially trained on a sizable dataset for natural image identification (Imagenet ILSVRC2012) then fine-tuned before applying the learned feature representations to the recognition of cardiac views.

Jose M. Jerez-Aragones et al. [7] suggested a decision support tool for prediction of breast cancer recurrence that combines an innovative algorithm, TDIDT (control of induction by sample division method, CIDIM), to choose the most important prognostic factors for their precise prognosis of breast cancer, with a system composed of various neural network topologies that takes the selected variables as input in order to reach good correct classification probability.

Mandeep Rana et al. [8] proposed a study to determine if breast cancer is benign or malignant and to forecast the recurrence and non-recurrence of malignant cases after a specific time period. Support Vector Machine (SVM) was shown to be the most suitable for predictive analysis, and KNN outperformed Naive Bayes for the overall methodology. They have employed machine learning techniques such as Logistic Regression, Support Vector Machine, KNN, and Naive Bayes.

Marcos Eduardo Valle et al. [9] extended the bipolar RCNNs to handle hypercomplex-valued input. The stability of the novel hypercomplex-valued RCNNs employing synchronous and asynchronous update modes is then addressed after the mathematical foundation for a large class of hypercomplex-valued RCNNs is presented. The computational tests validate the potential use of hypercomplex-valued RCNNs as associative memories aimed at the storage and retrieval of grayscale images.

Mustafa Ghaderzadeh et al. [10] utilised a model based on deep convolutional neural networks to distinguish ALL instances from hematogone cases and then identify ALL subtypes. Ten well-known CNN architectures (EfficientNet, MobileNetV3, VGG-19, Xception, InceptionV3, ResNet50V2, VGG-16, NASNetLarge, InceptionResNetV2, and DenseNet201) were used for feature extraction of various data classes after colour thresholding-based segmentation in the HSV colour space by designing a two-channel network. Based on DenseNet201, a model was created and put forth that performed the best.

Richard Ha et al. [11] devised a system to identify the molecular subtype of a breast cancer based on MRI characteristics. Initially, 3D segmentation using a 3D slicer was performed on post-contrast MRI images. A 14-layer CNN architecture was created. In the early tiers, residual connections were utilised.Deeper in the network, Inception-style layers were used, along with significant regularisation that included dropout, L2, feature map dropout, and transition layers.

Srikanth Tammina [12] classified images using one of the pre-trained models, VGG-16 with Deep Convolutional Neural Network. In order to transfer low-level characteristics, such as edges, corners,

and rotation, and learn new level features related to the goal problem, which is to categorise the images, the pretrained VGG-16 model is utilised as leverage.

Sungmin Rhee et al. [13] used graph CNN to learn the expression patterns of cooperative gene communities, and RN is used to understand the relationships between the learnt patterns. The PAM50 breast cancer subtype classification task, the industry-standard classification of breast cancer subtypes with clinical relevance, is used to test the proposed model.

Tianwen Xie et al. [14] put out an innovative two-stage feature selection strategy combining conventional statistics and machine learning-based techniques. The reliability of the 4-IHC classification and the distinction between triple negative (TN) and non-TN tumours were evaluated.

Xiaoli Li et al. [15] proposed a system to construct a computer-aided diagnostic (CAD) system for classifying breast cancer molecular subtypes using deep learning characteristics. A pre-trained convolutional neural network (CNN) was utilized by the scientists to extract deep learning features from a dataset of breast cancer histopathology images. After that, a support vector machine (SVM) classifier was used to identify the molecular subtype of the breast cancer using these features.The findings demonstrated that the suggested CAD method, with an overall accuracy of 92.16 %, was very accurate in categorising breast cancer molecular subtypes.

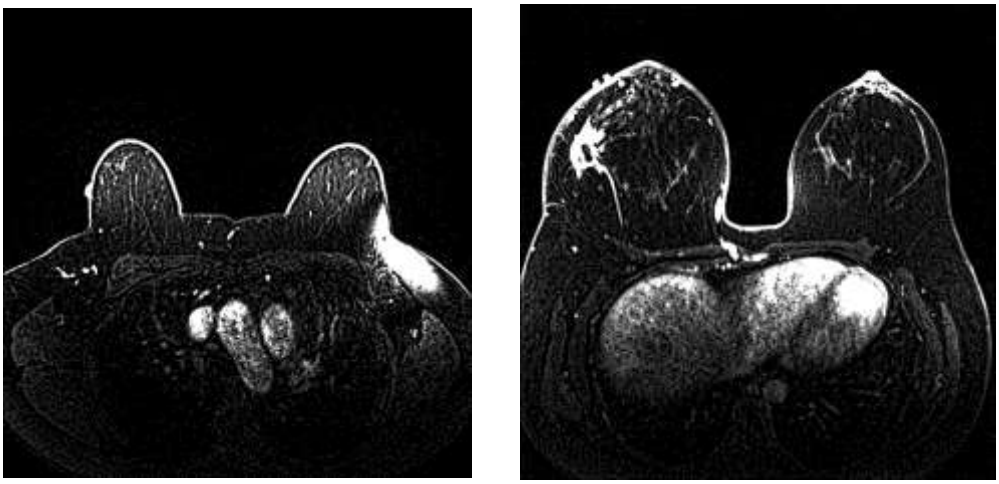
Yang Zhang et al. [16] proposed a system that used the smallest bounding box covering the tumour ROI as the input for deep learning to develop the model in the training dataset with the help of a conventional CNN, convolutional long short-term memory (CLSTM), and transfer learning. CNN and CLSTM both had higher mean accuracy when tested using 10-fold cross-validation.

Zhencun Jiang et al. [17] introduced the ViT-CNN ensemble model to aid in the diagnosis of acute lymphoblastic leukaemia by identifying cancer cells images and normal cells images. The vision transformer and convolutional neural network (CNN) models are combined to create the ViT-CNN ensemble model.The findings demonstrated that the model suggested in this article was more accurate than other models and had a balanced capacity for classification.

Mengwei Ma et al. [18] proposed to evaluate the performance of interpretable machine learning models in predicting breast cancer molecular subtypes. Shapley additive explanation (SHAP) technique is used to interpret the optimal model output. Optimal model is chosen as the assisted model to evaluate the prediction of the molecular subtype of breast cancer with or without model assistance, according to mammography and ultrasound images.

3. Materials And Methods

The breast MRI dataset includes 922 patients with invasive breast cancer who were treated at Duke Hospital between 1 January 2000 and 23 March 2014 and who had access to pre-operative MRI at Duke Hospital. The dataset [19] consists of MRI scans of 992 patients and their clinical data.



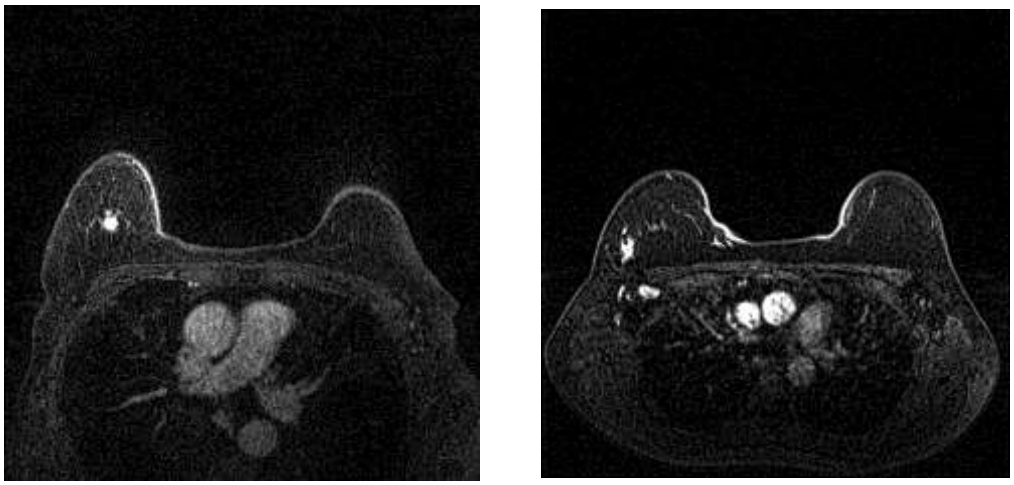


Figure 1: Molecular Subtypes of Breast Cancer - MRI

A. Clinical Features

Date of Birth (Days)	<= 26000 days
Menopause (at diagnosis)	0 = Pre , 1=Post
Metastatic at Presentation (Outside of Lymph Nodes)	0 = No, 1=Yes
ER	0 = Neg, 1=Pos
PR	0 = Neg, 1=Pos
HER2	0 = Neg, 1=Pos, 2 = Borderline
Mol Subtype	0 = luminal-like, 1 = ER/PR pos, HER2 pos, 2 = her2, 3 = trip neg
Oncotype score	<40
Staging(Tumor Size)# [T]	1-4
Staging(Nodes) #(Nx replaced by -1)[N]	1-4
Staging(Metastasis)#(Mx -replaced by -1)[M]	0, -1
Tumor Grade(T) (Tubule)	1=low 2=intermediate 3=high
Tumor Grade(N) (Nuclear)	1=low 2=intermediate 3=high
Tumor Grade(M)(Mitotic)	1=low 2=intermediate 3=high
Nottingham grade	1=low 2=intermediate 3=high
Histologic type	0=DCIS 1=ductal 2=lobular 3=metaplastic 4=LCIS 5=tubular 6=mixed 7=micropapillary 8=colloid 9=mucinous 10=medullary
Tumor Location	Side of cancer L=left R=right
Position	every bx positive for invasive
Bilateral Information	0 = No , 1=Yes
Multicentric/Multifocal	0 = No, 1=Yes
Contralateral Breast Involvement	0 = No, 1=Yes
Lymphadenopathy or Suspicious Nodes	0 = No, 1=Yes
Skin/Nipple Invovlement	0 = No, 1=Yes
Pec/Chest Involvement	0 = No, 1=Yes
Surgery	0 = No, 1=Yes
Days to Surgery (from the date of diagnosis)	<200
Definitive Surgery Type	{0=BCS, 1=mastectomy}
Neoadjuvant Radiation Therapy	0 = No , 1=Yes
Adjuvant Radiation Therapy	0 = No, 1=Yes
Clinical Response, Evaluated Through Imaging	1=complete response on imaging, 2=not complete response, 3=imaging to assess treatment response is unavailable, NA=no neoadjuvant therapy or not enough information to assess neoadjuvant therapy status
Pathologic Response to Neoadjuvant Therapy	1=complete response on imaging, 2=not complete response, 3=imaging to assess treatment response is unavailable, NA=no neoadjuvant therapy or not

	enough information to assess neoadjuvant therapy status
Recurrence event	0 = No, 1=Yes
Days to local recurrence (from the date of diagnosis)	<2000
Days to distant recurrence(from the date of diagnosis)	<2000
Days to death (from the date of diagnosis)	<2000
Days to last local recurrence free assessment (from the date of diagnosis)	<3500
Days to last distant recurrence free assemssment(from the date of diagnosis)	<3500
Age at last contact in EMR f/u(days)(from the date of diagnosis) , last time patient known to be alive, unless age of death is reported(in such case the age of death	<3500
Tumor Size (cm)	0-5
Neoadjuvant Chemotherapy	0 = No, 1=Yes
Adjuvant Chemotherapy	0 = No, 1=Yes
Neoadjuvant Endocrine Therapy Medications	0 = No, 1=Yes
Adjuvant Endocrine Therapy Medications	0 = No, 1=Yes
Known Ovarian Status	0 = No, 1=Yes
Number of Ovaries In Situ	0 = no ovaries intact, 1 = 1 ovary intact, 2 = 2 ovaries intact, NP = not pertinent to case
Therapeutic or Prophylactic Oophorectomy as part of Endocrine Therapy	0 = No, 1=Yes
Neoadjuvant Anti-Her2 Neu Therapy	0 = No, 1=Yes
Adjuvant Anti-Her2 Neu Therapy	0 = No, 1=Yes
Received Neoadjuvant Therapy or Not	0 = No, 1=Yes
Pathologic response to Neoadjuvant therapy: Pathologic stage (T) following neoadjuvant therapy	-1 = TX; 0 = T0; 1 = T1; 2 = T2; 3 = T3; 4 = T4; 5 = Tis (DCIS); NA = not applicable
Pathologic response to Neoadjuvant therapy: Pathologic stage (N) following neoadjuvant therapy	-1 = NX; 0 = N0; 1 = N1; 2 = N2; 3 = N3; NA = not applicable
Pathologic response to Neoadjuvant therapy: Pathologic stage (M) following neoadjuvant therapy	-1 = MX; 0 = M0; 1 = M1; NA = not applicable
Overall Near-complete Response: Stricter Definition	2 = Near complete (pathology report noted results constituted near-complete response to NAT) 3 = No residual disease, only atypical ductal hyperplasia 4 = No invasive carcinoma, DCIS only 5 = No invasive carcinoma, LCIS only 6 = 90% reduction in tumor volume 7 = 95% reduction

Table 1: Features of Clinical Data

	18 = 99% of tumor obliterated but extensive residual DCIS
Overall Near-complete Response: Looser Definition	2 = Near complete (pathology report noted results constituted near-complete response to NAT) 3 = No residual disease, only atypical ductal hyperplasia 4 = No invasive carcinoma, DCIS only 5 = No invasive carcinoma, LCIS only 6 = 90% reduction in tumor volume 7 = 95% reduction 8 = Near complete but DCIS 9 = 90% reduction with DCIS present 10 = No invasive disease but lymph nodes positive 11 = No residual disease, but positive LNs and DCIS 12 = Near complete response noted on path report, but positive LNs 13 = 98% reduction with positive LNs 14 = 95% fibrosis but positive lymph nodes 15 = 90% reduction with positive LNs 16 = > 95% reduction with only mucinous pools remaining 17 = 1mm residual invasive but extensive DCIS 18 = 99% of tumor obliterated but extensive residual DCIS
Near-complete Response (Graded Measure)	3 = No residual disease, only atypical ductal hyperplasia; 4 = No invasive carcinoma, DCIS only; 5 = No invasive carcinoma, LCIS only; 6 = 90% reduction in tumor volume; 7 = 95% reduction; 8 = Near complete but DCIS; 9 = 90% reduction with DCIS present; 10 = No invasive disease but lymph nodes positive; 11 = No residual disease, but positive LNs and DCIS; 12 = Near complete response noted on path report, but positive LNs; 13 = 98% reduction with positive

Proposed System

A. Architecture

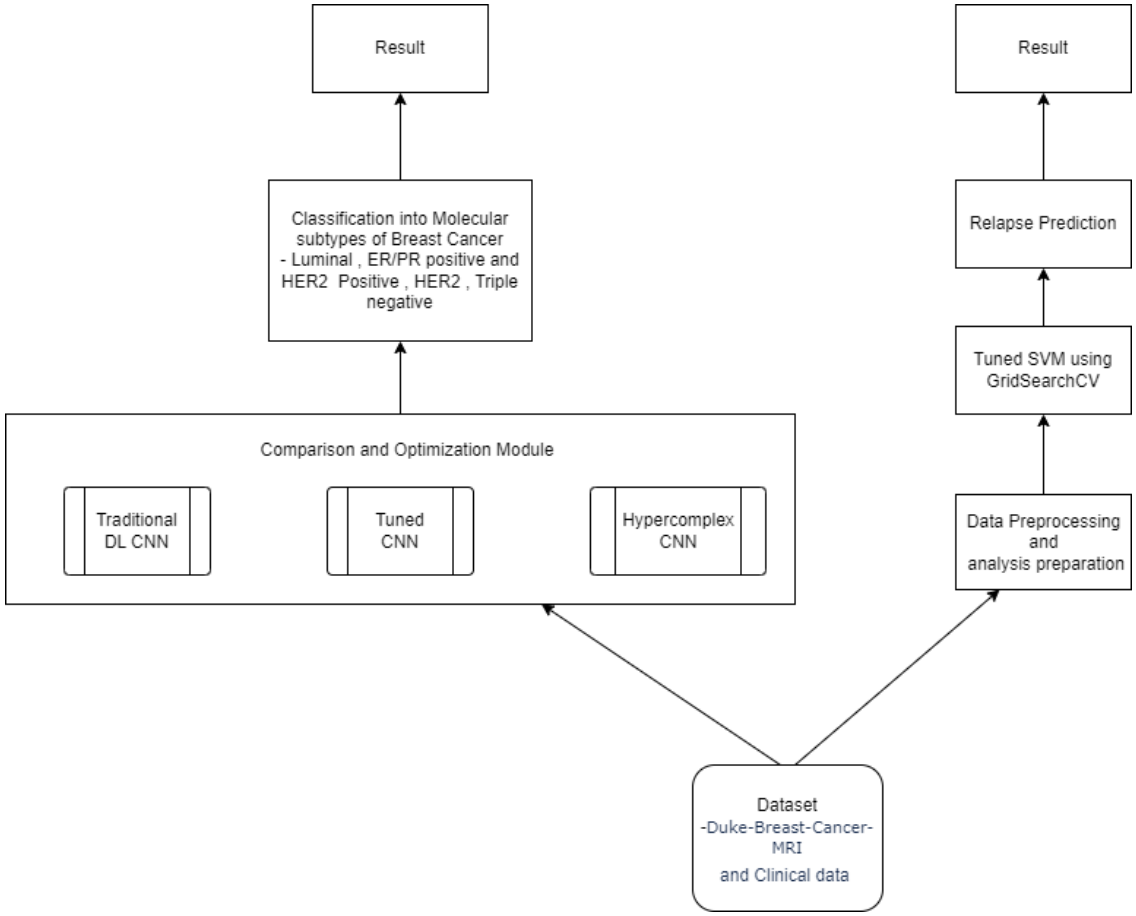


Figure 2: The architectural model of the system

B. Traditional Deep Learning CNN Model

Convolutional, pooling, and fully connected layers constitute the layers that make up the conventional deep learning Convolutional Neural Network (CNN) model. Learning hierarchical representations of the breast cancer MRI images is the aim of these layers. This model uses transfer learning using vgg16 and bottlenck features are obtained to classify the images into their molecular subtypes.

C. Tuned CNN Model

Tuned CNNs are CNN models that have several hyperparameters adjusted specifically for a given task or dataset. Hyper- parameters are configurations that the user selects rather than learning through training. A pre-trained VGG-16 model serves as the transfer learning model. When the transfer learning model is loaded, the initial classifier layers are swapped out for new ones for the improved model, and the model weights are locked to prevent further training. During training, only the weights of the newest neural network layers are modified. In order to facilitate the exploration, the model parameters are defined as a set. Finally, after fine-tuning the hyperparameters, the pictures are classified into their molecular subtypes using the CNN model with the best hyperparameter values.

D. Hypercomplex-valued CNN Model

Eight hypercomplex-valued convolutional neural networks (HvCNNs) are used for the categorization. Hv-CNNs can be used to analyze the images to classify Breast Cancer. Hypercomplex numbers provide a natural representation of orientation and rotation information, which can be useful for analyzing the structural and geometric features of breast cells in images. The input image would be represented as a hypercomplex-valued data tensor, and the convolutional layer performs convolution operations on the input data using hypercomplex-valued filters. The features extracted by the convolutional layer is then processed by fully connected layers, which will make the final classification decisions based on the learned features. The hypercomplex-valued model has a layer layout of convolutional layers followed by a max pooling layer with kernels, where each channel of the hypercomplex-valued corresponds to four real-valued feature channels, so that it uses much fewer filters per convolution layer. A quaternion numerical network constructed using quaternion algebra is used. Quaternions are the four-dimensional

extension of complex numbers.

A [-1, -1], A [-1, +1], A [+1, -1], and A[+1, +1]

B [-1, -1], B [-1, +1], B [+1, -1], B[+1, +1]

There are a total of eight 4-dimensional hypercomplex algebras. They are all associative, four anti-commutative and the rest commutative.

	i	j	k
i	s_{11}	$s_{12}k$	$s_{13}j$
j	$s_{21}k$	s_{22}	$s_{23}i$
k	$s_{31}j$	$s_{32}i$	s_{33}

Table 2: The multiplication table of the eight algebras

E. Relapse Prediction Module

Support Vector Machine (SVM), a component of the Scikit Learn package, is the algorithm employed. Support vector machines (SVMs), one of the most popular supervised learning techniques, are frequently used to solve machine learning regression problems. The goal of the SVM algorithm is to define an ideal boundary or decision line that can classify the n-dimensional space, making it straightforward to assign new data points to the proper category in the future. The hyperplane is the best-case decision boundary.

For fine-tuning the hyperparameters, we use GridSearchCV. By altering hyperparameters, GridSearchCV is a technique for determining the ideal settings for a specific model. The performance of a model is strongly influenced by the value of its hyperparameters. The optimal values for hyperparameters cannot be determined in advance, thus we need consider all possible values before choosing the best ones. As manual tuning could need a lot of time and resources, we use GridSearchCV to automate the process.

3. Results and Discussion

A. Traditional Deep Learning CNN

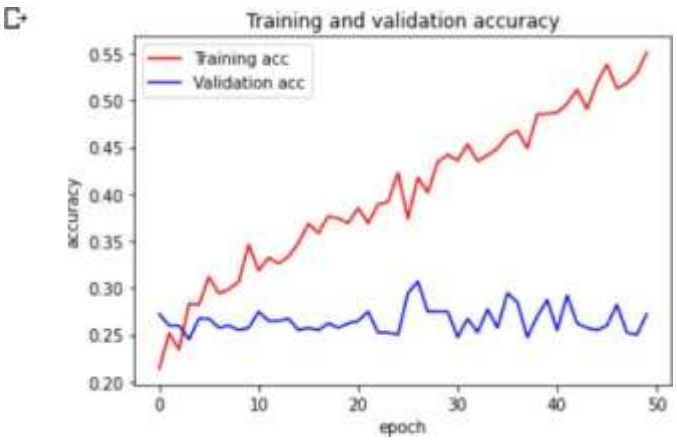


Figure 6: Graph depicting training and validation accuracy

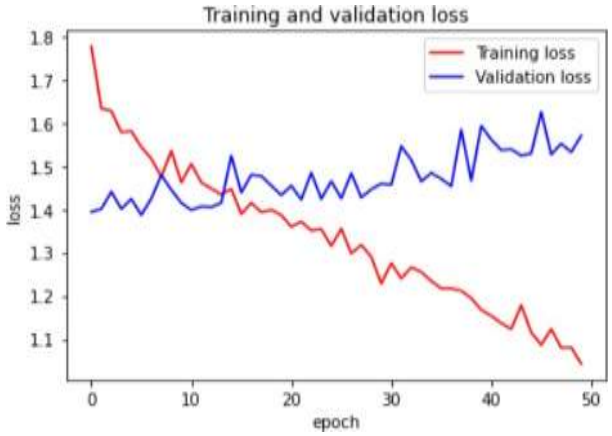


Figure 7: Graph depicting training and validation loss

```
[INFO] accuracy: 27.23%
[INFO] Loss: 1.570113182067871
Time:  0:01:23.710457
```

Figure 8: Results for the traditional CNN model

MRI images slides at different angles are repetitive and distorted.Accuracy and performance of the model can be considerably increased with improved preprocessing techniques and hyperparameters. At present an accuracy of 27.23% is achieved.

B. Tuned CNN Model

Figure 9: Graph depicting training and validation accuracy

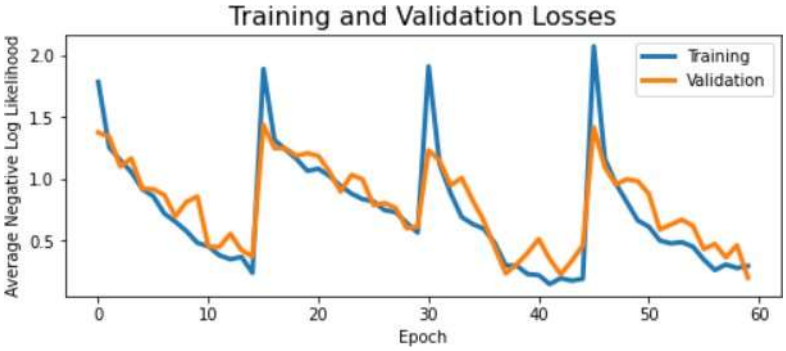


Figure 10: Graph depicting training and validation losses

	precision	recall	f1-score	support
HER2	0.97	0.94	0.95	201
Luminal	0.96	0.98	0.97	201
Triple	0.90	0.85	0.87	201
ER_PR_HER2	0.84	0.91	0.87	201
accuracy			0.92	804
macro avg	0.92	0.92	0.92	804
weighted avg	0.92	0.92	0.92	804

```
--Evaluation Metrics--
Test Accuracy:  0.9166666666666666
F1 Score:  0.9168057689293903
```

Figure 11: Classification report for the tuned CNN model

Tuning of cnn proved to be efficient. Increased number of epochs and different hyperparameter values will possibly increase the accuracy to great extent. Higher computation power is desirable. At present an accuracy of 91.6 % is obtained for the best hyperparameter set of droupout rate = 0.4, learning rate = 0.001, batch size = 25 and hidden units = 512.

C. Hypercomplex Valued CNN

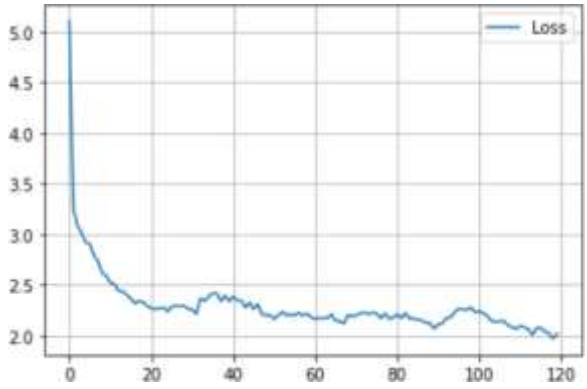


Figure 12: Graph depicting model loss

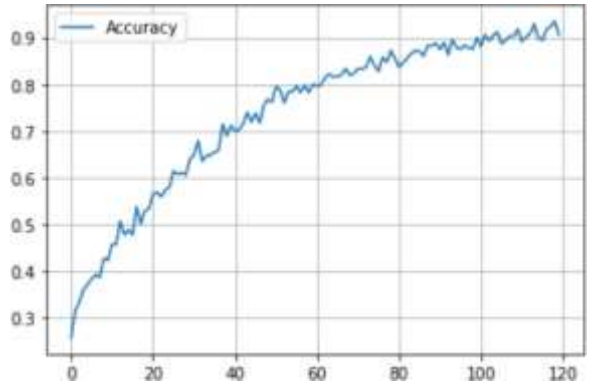


Figure 13: Graph depicting model accuracy

	precision	recall	f1-score	support
Luminal_like	0.92	1.00	0.96	24
HER2	1.00	1.00	1.00	29
ER/PR and HER	1.00	0.97	0.99	35
Triple negative	1.00	0.97	0.98	32
accuracy			0.98	120
macro avg	0.98	0.99	0.98	120
weighted avg	0.98	0.98	0.98	120

Figure 14: Classification report for the HvCNN model

HvCNN proved to be the better optimization technique providing an accuracy of 98% whereas hyperparamter tuned CNN provided an accuracy of 91.6%.

D. Relapse Prediction Model

```
SVC Accuracy : 89.73%
SVC Linear Accuracy : 89.19%
SVC RBF Accuracy : 89.73%
SVC Poly Accuracy : 89.73%
SVC Sigmoid Accuracy : 89.19%
```

Figure 15: Performance of the SVM model showing accuracies for different SVMs

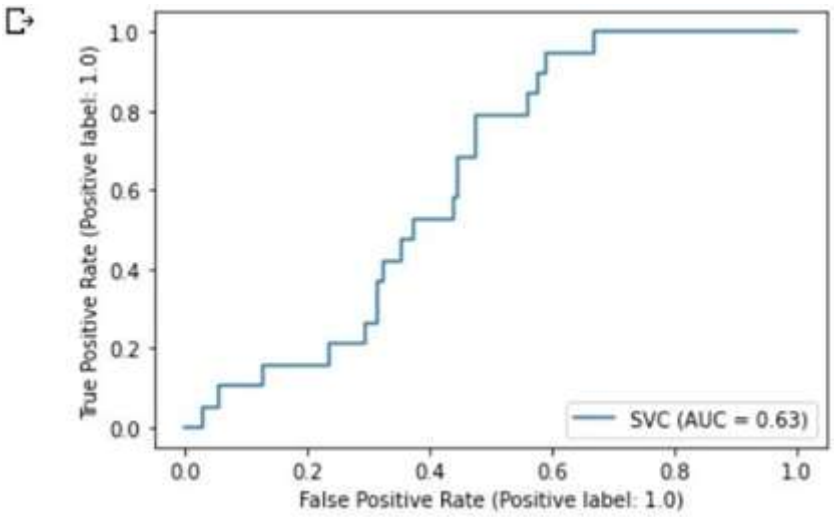


Figure 16: ROC curve for svm model

	precision	recall	f1-score	support
0.0	1.00	0.98	0.99	166
1.0	0.86	1.00	0.93	19
accuracy			0.98	185
macro avg	0.93	0.99	0.96	185
weighted avg	0.99	0.98	0.98	185

Figure 17: Classification report for relapse model with GridSearchCV used to optimize hyperparameters for SVM model performance

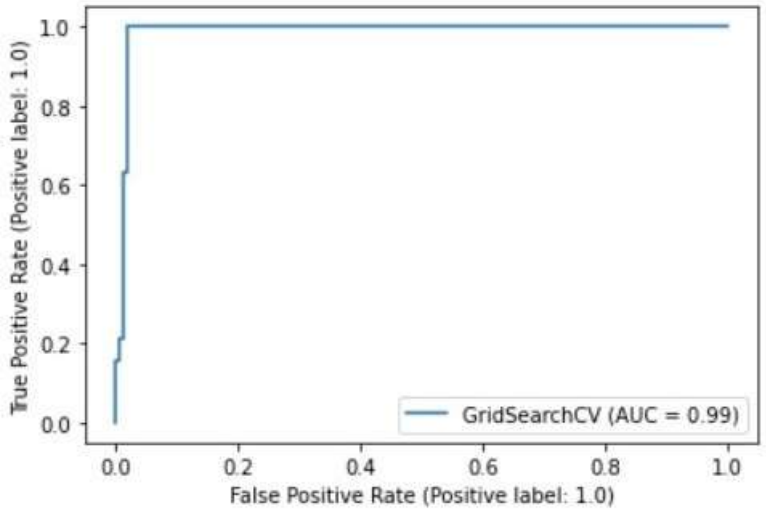


Figure 18: ROC curve for optimised model using GridSearchCV

The features of the clinical data have been reduced and an SVM model is applied on them to predict relapse which gave an accuracy of 89% and by optimizing the hyperparameters using GridSearchCV the accuracy has been considerably increased upto 98% .

E. Comparing Results with Previous Work

1) *Molecular Subtype classification: Predicting the molecular subtype of breast cancer and identifying interpretable imaging features using machine learning algorithms - Mengwei Ma et al. [18] used the decision tree (DT) model and found that it performed best in distinguishing triple-negative breast cancer (TNBC) from other breast cancer subtypes. We attained the best accuracy in classifying molecular subtypes using the HvCNN model.*

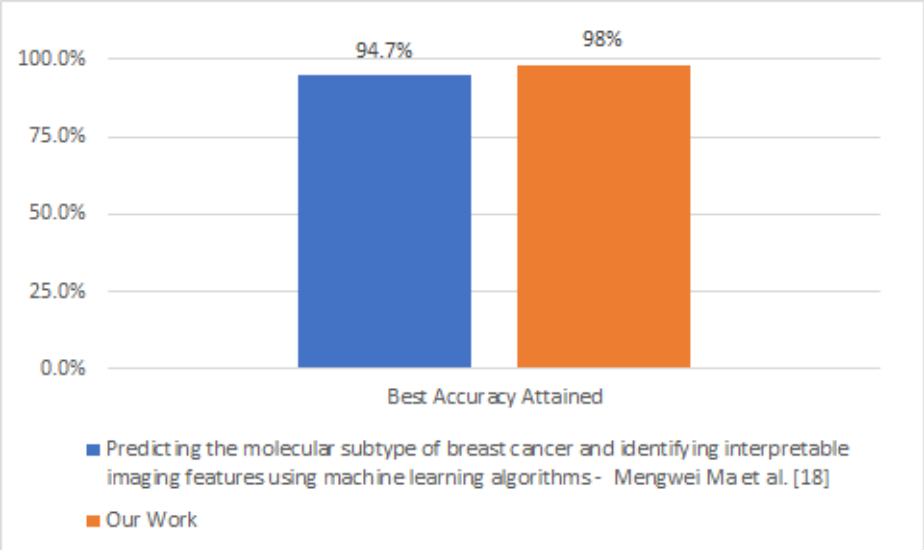


Figure 18: Comparing the results of two works

2) *Relapse Prediction: Results of* Breast cancer diagnosis and recurrence prediction using machine learning techniques - Mandeep Rana et al. [8] using SVM linear technique is compared with the techniques we used in relapse prediction.

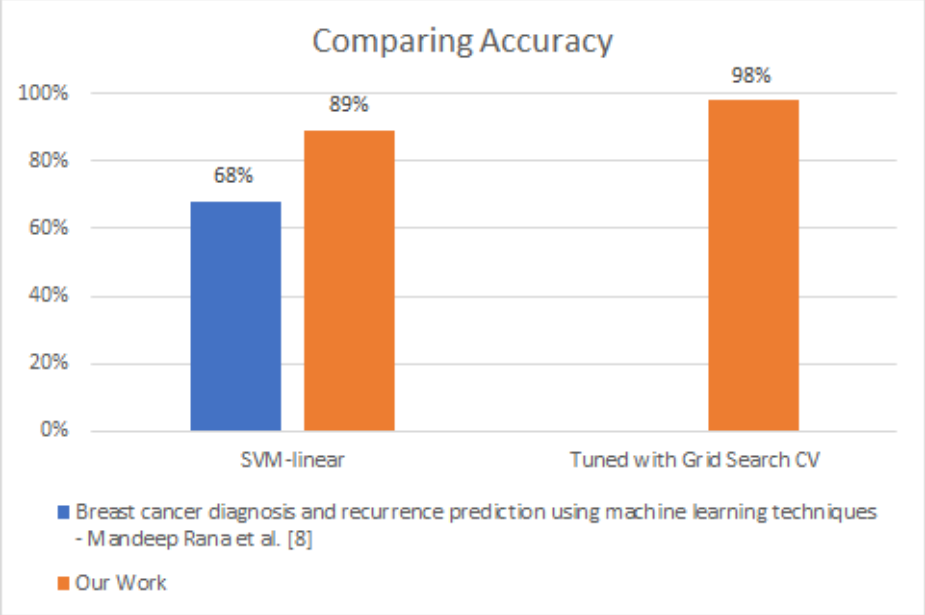


Figure 18: Comparing the results of two works

4. Conclusion

In this work, we have explored various CNN models to classify breast cancer into it's molecular subtypes based on MRI images. The traditional deep learning CNN model achieved an accuracy of 27% , the tuned CNN model achieved an accuracy of 92% and the hypercomplex-valued CNN achieved an accuracy of 98%. The authors found that the hypercomplex-valued CNN is the ost optimized model to classify breast cancer into it's molecular subtypes.Next, we have explored an SVM model to predict the relapse of breast cancer using clinical data of the patients.The SVM model achieved an accuracy of 89% and on tuning the hyperparameters by using GridSearchCV it achieved accuracy of 98%.To conclude, we have discussed, in this report, the detailed solution design for classifying breast cancer into their molecular subtypes using state-of-the-art CNN algorithm, the hypercomplex-valued CNN. We also compared the performance of Hyperparameter Tuned CNN with HvCNN. Relapse prediction was performed and accurate results were obtained.

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Consent to Participate: Informed consent is not necessary as this article does not involve human or animal participants.

Consent to Publish: All the authors agree to publish the manuscript in Journal of Medical and Biological Engineering.

Data Availability Statement: The Cancer Imaging Archive and the data set link is given in the reference no. 19.

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