May 2022

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The University of Texas at Austin

Multimodal Learning for Breast Tumor Molecular Subtype Diagnosis

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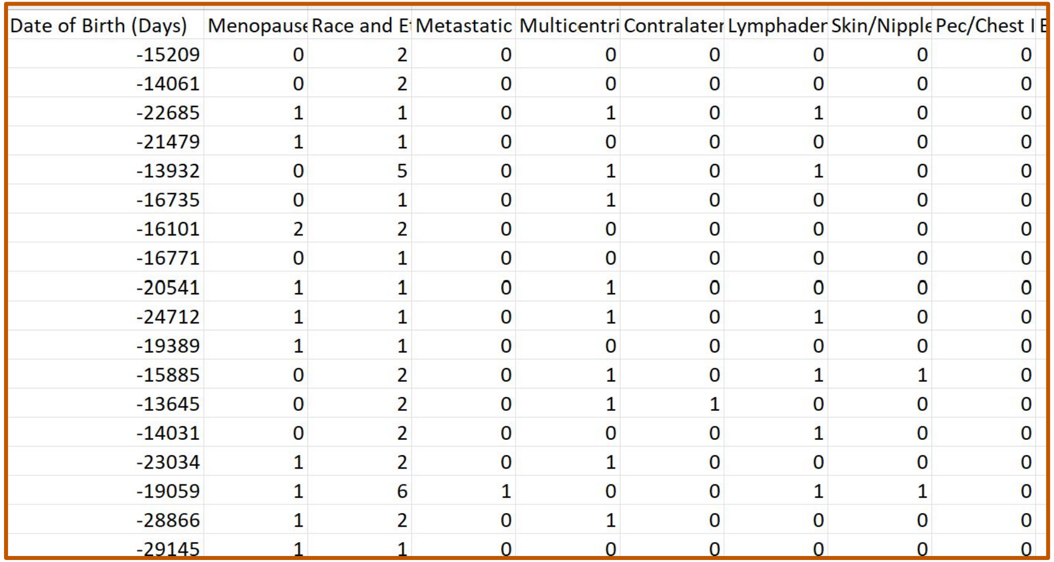
Our Dataset

Duke Breast MRI Data

- 922 cases:
    - Images
    - 7 important Clinical Characteristics
    - Radiomics Data



Date of Birth (Days)	Menopause	Race and E	Metastatic	Multicentri	Contralater	Lymphader	Skin/Nipple	Pec/Chest I	E
-15209	0	2	0	0	0	0	0	0	
-14061	0	2	0	0	0	0	0	0	
-22685	1	1	0	1	0	1	0	0	
-21479	1	1	0	0	0	0	0	0	
-13932	0	5	0	1	0	1	0	0	
-16735	0	1	0	1	0	0	0	0	
-16101	2	2	0	0	0	0	0	0	
-16771	0	1	0	0	0	0	0	0	
-20541	1	1	0	1	0	0	0	0	
-24712	1	1	0	1	0	1	0	0	
-19389	1	1	0	0	0	0	0	0	
-15885	0	2	0	1	0	1	1	0	
-13645	0	2	0	1	1	0	0	0	
-14031	0	2	0	0	0	1	0	0	
-23034	1	2	0	1	0	0	0	0	
-19059	1	6	1	0	0	1	1	0	
-28866	1	2	0	1	0	0	0	0	
-29145	1	1	0	0	0	0	0	0	

Preprocessing & Task

Goal: Predict “luminal-like” molecular subtype of patient tumor

Data Split: 70% train | 10% val | 20% test

Image Data: 64x64 tumor images

- Maximum intensity projection of (3D) MRI scan

Clinical Data: 7 patient features

- Ex: age, race/ethnicity, menopause status

Radiomics Data: 530 “radiomics” features

- Handcrafted local descriptors of tumor image

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Analysis 1: Clinical Characteristics

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Clinical Data Analysis- Logistic Regression Model

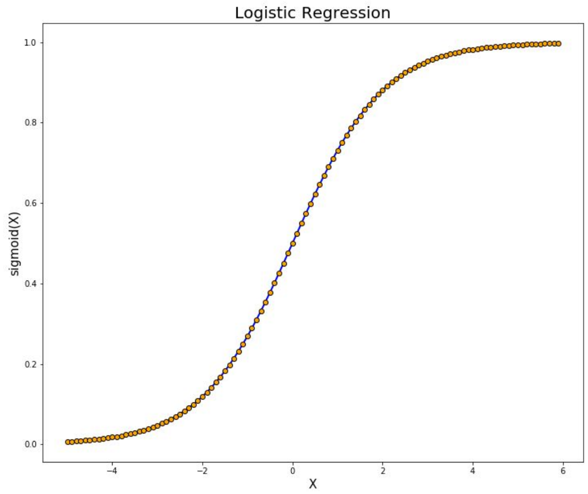
Purpose: Determining a baseline accuracy using given clinical data.

Data input:

- Demographics: race, ethnicity etc.
- Menopause status
- Tumor characteristics: metastatic, multicentric etc.

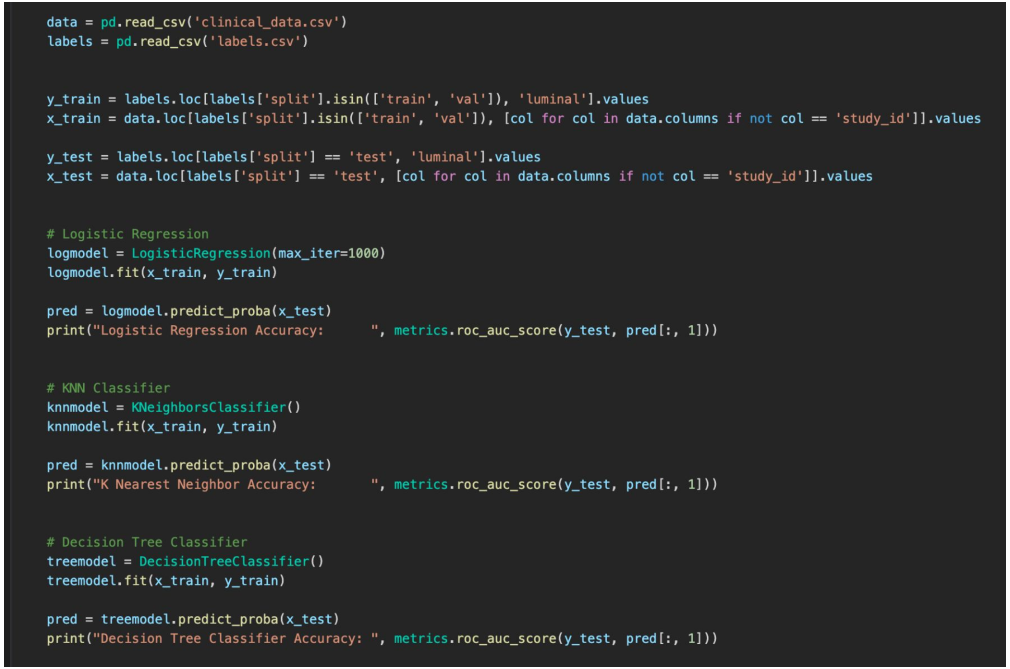
Variable Tracked

- Luminal-Like Molecular Subtype



Code Structure

1. Filter and parse data
2. Logistic regression analysis
3. K-nearest neighbor analysis
4. Decision Tree classifier



```
data = pd.read_csv('clinical_data.csv')
labels = pd.read_csv('labels.csv')


y_train = labels.loc[labels['split'].isin(['train', 'val']), 'luminal'].values
x_train = data.loc[labels['split'].isin(['train', 'val']), [col for col in data.columns if not col == 'study_id']].values

y_test = labels.loc[labels['split'] == 'test', 'luminal'].values
x_test = data.loc[labels['split'] == 'test', [col for col in data.columns if not col == 'study_id']].values


# Logistic Regression
logmodel = LogisticRegression(max_iter=1000)
logmodel.fit(x_train, y_train)

pred = logmodel.predict_proba(x_test)
print("Logistic Regression Accuracy:      ", metrics.roc_auc_score(y_test, pred[:, 1]))


# KNN Classifier
knnmodel = KNeighborsClassifier()
knnmodel.fit(x_train, y_train)

pred = knnmodel.predict_proba(x_test)
print("K Nearest Neighbor Accuracy:       ", metrics.roc_auc_score(y_test, pred[:, 1]))


# Decision Tree Classifier
treemodel = DecisionTreeClassifier()
treemodel.fit(x_train, y_train)

pred = treemodel.predict_proba(x_test)
print("Decision Tree Classifier Accuracy: ", metrics.roc_auc_score(y_test, pred[:, 1]))
```

Results

Logistic Regression	K-Nearest Neighbor	Decision Tree Classifier
AUC: 59.3%	AUC: 57.7%	AUC: 55.9%

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Analysis 2: MR Images

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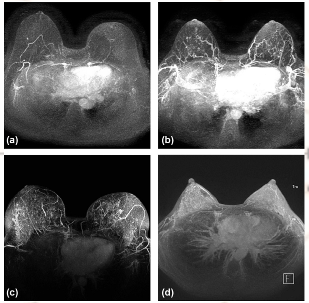
MR Image Analysis- Conv Neural Network

Purpose: Determining a baseline of only image data for training of the overall neural network



Data Input:

- MRI images

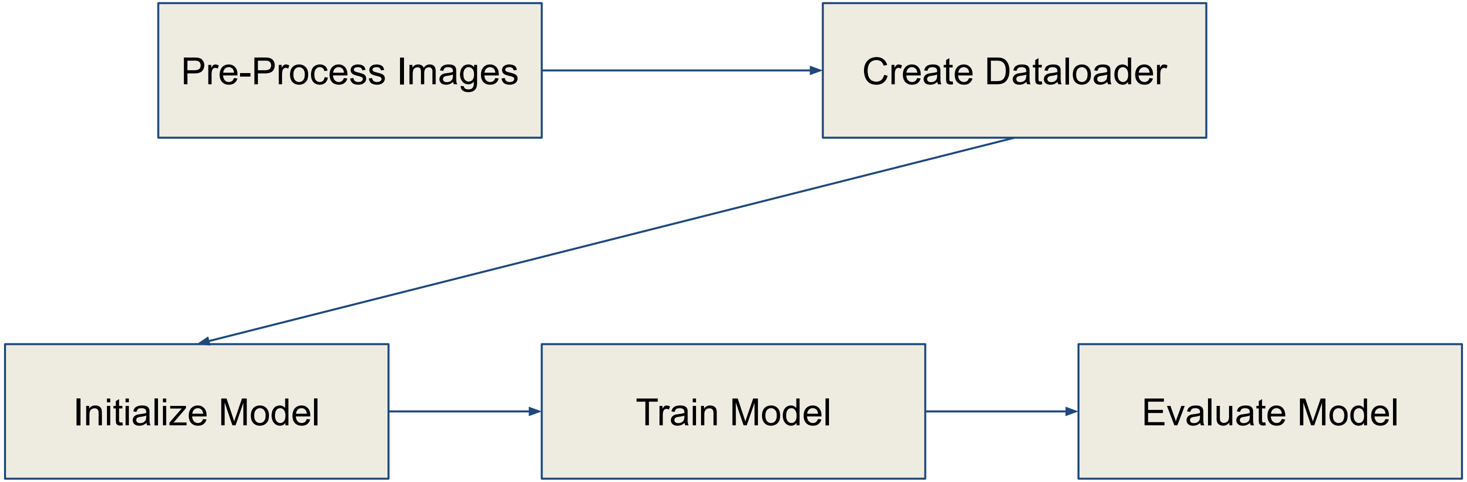
Data Augmentations:

- Random Crop, Random Horizontal Flip, Random Rotation
- **Normalize**

Variable Tracked

- Luminal-Like Molecular Subtype

Code Structure



Pre-Process Images

Create Dataloader

Initialize Model

Train Model

Evaluate Model

Results

Architecture	AUC	Accuracy
Resnet18 Pre-Trained Imagenet Weights	AUC: 55.3%	Accuracy- 60.5%

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Analysis 3: Radiomics Data

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Radiomics Data Analysis- Logistic Regression Model

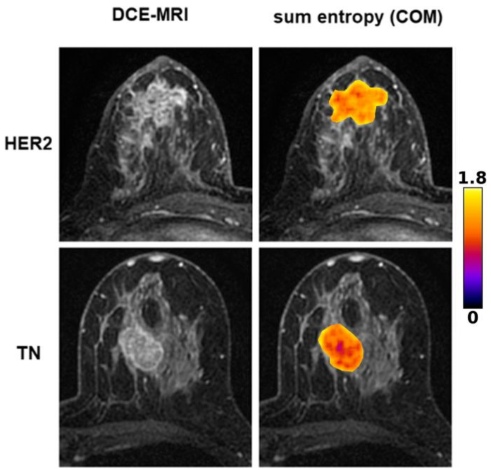
Purpose: Determining baseline accuracy using radiomics data

Data input:

- Radiomics data containing 530 features

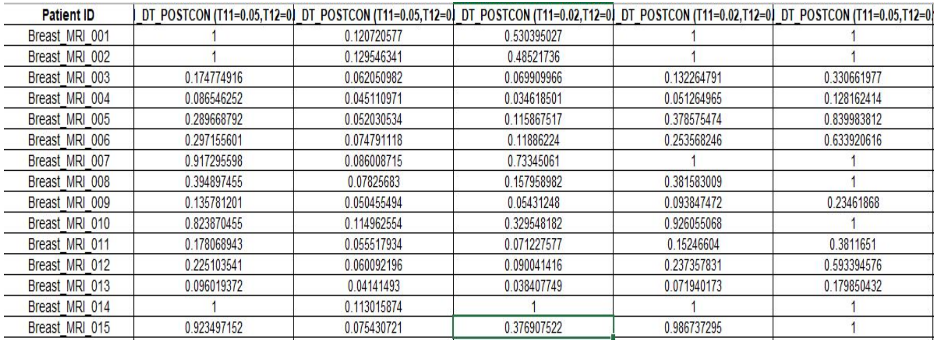
Variable Tracked

- Luminal-Like Molecular Subtype



Data Preprocessing

1. Recursive Feature Elimination
2. Removal of correlated features
3. Removal of features with a p-value higher than 0.05



Patient ID	_DT_POSTCON (T11=0.05,T12=0	_DT_POSTCON (T11=0.05,T12=0	_DT_POSTCON (T11=0.02,T12=0	_DT_POSTCON (T11=0.02,T12=0	_DT_POSTCON (T11=0.05,T12=0
Breast_MRI_001	1	0.120720577	0.530395027	1	1
Breast_MRI_002	1	0.129546341	0.48521736	1	1
Breast_MRI_003	0.174774916	0.062050982	0.069909966	0.132264791	0.330661977
Breast_MRI_004	0.086546252	0.045110971	0.034618501	0.051264965	0.128162414
Breast_MRI_005	0.289668792	0.052030534	0.115867517	0.378575474	0.839983812
Breast_MRI_006	0.297155601	0.074791118	0.11886224	0.253568246	0.633920616
Breast_MRI_007	0.917295598	0.086008715	0.73345061	1	1
Breast_MRI_008	0.394897455	0.07825683	0.157958982	0.381583009	1
Breast_MRI_009	0.135781201	0.050455494	0.05431248	0.093847472	0.23461868
Breast_MRI_010	0.823870455	0.114962554	0.329548182	0.926055068	1
Breast_MRI_011	0.178068943	0.055517934	0.071227577	0.15246604	0.3811651
Breast_MRI_012	0.225103541	0.060092196	0.090041416	0.237357831	0.593394576
Breast_MRI_013	0.096019372	0.04141493	0.038407749	0.071940173	0.179850432
Breast_MRI_014	1	0.113015874	1	1	1
Breast_MRI_015	0.923497152	0.075430721	0.376907522	0.986737295	1

Models Architecture

Sequential Model:

- 3 dense layers
- Dropout technique

Logistic regression:

- Used ‘saga’ solver
- Used cross validation with k-fold and sk-fold

Different Model Results

Sequential Model

Accuracy: 63.95%

Logistic Regression

Accuracy: 64.53%

Cross-Validation

Using k-fold → Accuracy: 68.10%
Using sk-fold → Accuracy: 70.48%

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Analysis 4: Multimodal Neural Network

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Neural Network Architecture

Inputs:

- MR Image
- Clinical Data
- Radiomics Data

Output:

Neural Network predicting presence of luminal-like molecular subtype in breast tumors

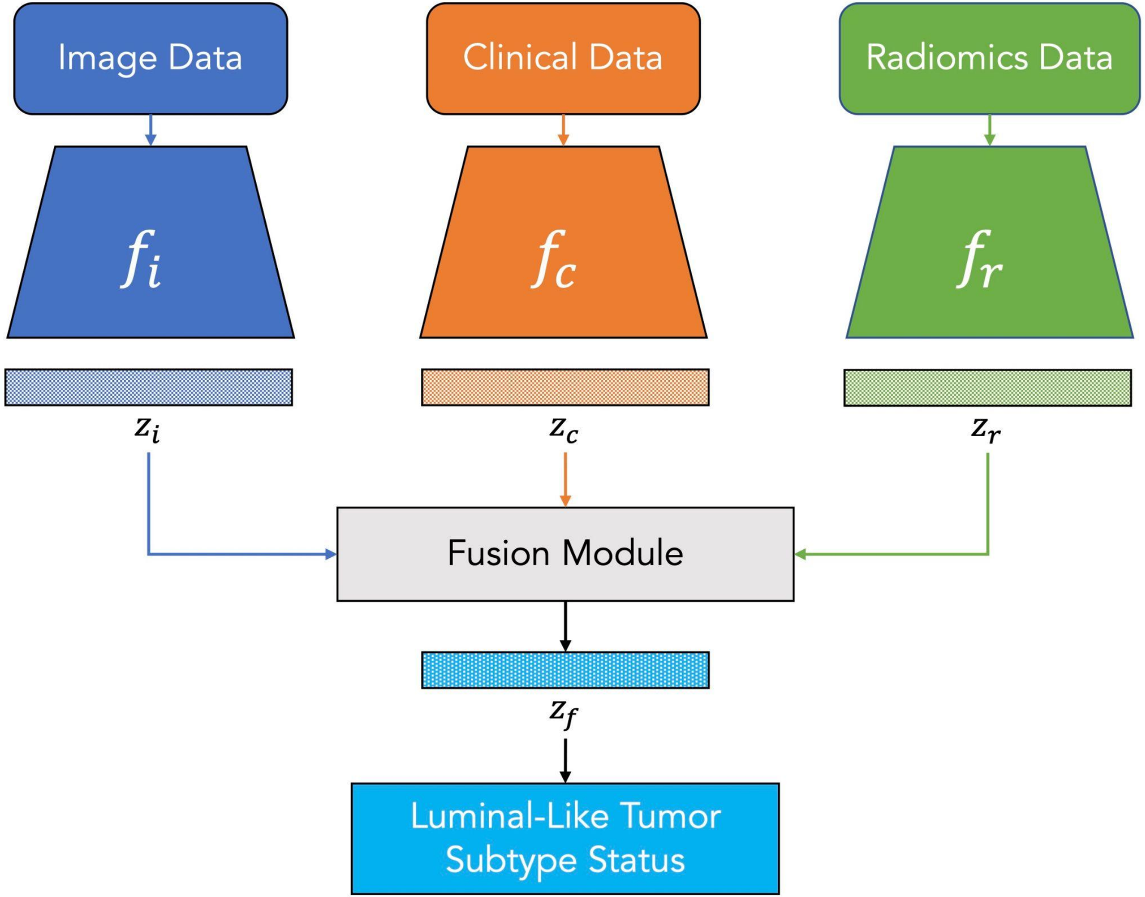

Image Data

Clinical Data

Radiomics Data

f_i

f_c

f_r

z_i

z_c

z_r

Fusion Module

z_f

Luminal-Like Tumor Subtype Status

Results

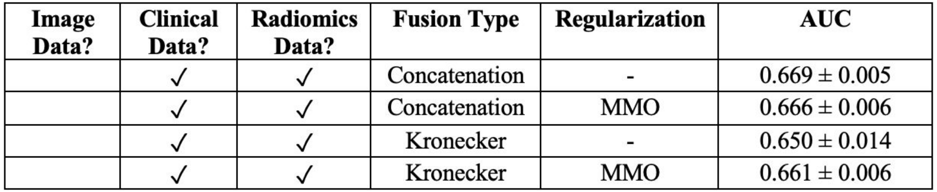

Image Data?	Clinical Data?	Radiomics Data?	Fusion Type	Regularization	AUC
	✓	✓	Concatenation	-	0.669 ± 0.005
	✓	✓	Concatenation	MMO	0.666 ± 0.006
	✓	✓	Kronecker	-	0.650 ± 0.014
	✓	✓	Kronecker	MMO	0.661 ± 0.006

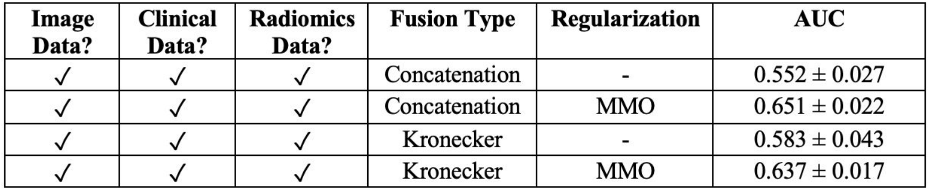

Image Data?	Clinical Data?	Radiomics Data?	Fusion Type	Regularization	AUC
✓	✓	✓	Concatenation	-	0.552 ± 0.027
✓	✓	✓	Concatenation	MMO	0.651 ± 0.022
✓	✓	✓	Kronecker	-	0.583 ± 0.043
✓	✓	✓	Kronecker	MMO	0.637 ± 0.017

Takeaways:

- Multimodal learning improves performance
- Image data hurts performance!
  - Hypothesis: Highly preprocessed images very noisy
  - Solution: incorporate full MRI sequence data
- Concatenation is an adequate fusion method
- MMO regularization only helpful w/ images
  - Hypothesis: image + radiomics info highly correlated
- Difficult task: subtype usually determined by biopsy (not imaging!)