Iowa Initiative for Artificial Intelligence

Final Report

Project title:	Lesion Segmentation and Use of Multiparametric deep learning-based radiomics model for differentiating between glioblastoma, primary CNS lymphoma and brain metastasis on magnetic resonance imaging
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Date:	

Were specific aims fulfilled:	Y	
Readiness for extramural proposal?	Y	
If yes … Planned submission date	8/03/2020	
Funding agency	American Cancer Society	
Grant mechanism	Seed grant	
If no … Why not? What went wrong?		

Brief summary of accomplished results:

We have developed and validated a Random Forest model to accurately classify three tumor types (Glioblastoma: GBM, Lymphoma: LYM, Metastasis: MET) using extracted radiomics features in MR images of human brains. The achieved accuracy was 0.8 using all features.

Research report:

Aims (provided by PI):

1. To create a workflow to evaluate a highly automated LOGISMOS approach for tumor segmentation followed by extraction of quantitative radiomics features characterizing brain tumors.

2. To develop a convolutional neural network model for classification of brain tumors into one of the three most common brain malignancies by utilizing MR image data patches centered on detected lesions together with multiple quantitative radiomic descriptors.

3. To validate and test the developed deep learning model on independent data set (separate from the training set) for verifying the performance of the model.

As the project progressed, the team decided to focus on Random Forest model and the pilot project successfully completed all 3 aims as the aims were modified accordingly.

Data:

Following an internal UIHC data search for relevant patients with accompanying MR datasets, 253 patients were identified with the following distribution of brain pathologies (GBM: 93; LYM: 40; MET: 120). Up to five different axial 3D MR imaging sequences (T1, T2 FLAIR, ADC and T1 post contrast) were available for each case.

AI/ML Approach:

In this study, supervised machine learning algorithm was implemented for classification using Python. As many extracted features may be noisy, or highly correlated with each other, Random Forest (RF) algorithm was selected to classify tumor type. Training RF to distinguish between different classes of objects was based on radiomics features as described below. Training: validation split was 70%/30%.

Experimental methods, validation approach:

Data preparation

Data preparation or pre-processing is an essential step in any machine learning study. In this project, we converted all our MRI datasets in compressed Nifti format (nii.gz). Due to different resolution at different sequences, we resampled our MRI images to (1mm,1mm,5mm) resolution using the 3dresample function of AFNI package (https://afni.nimh.nih.gov/) and registered all other sequences to T1 using antsRegistration function of ANTs (http://stnava.github.io/ANTs/.). After that, we normalized the image intensities to [0,255] using the feature scaling method, implemented by the ImageMatch function of the ANTs registration suite.
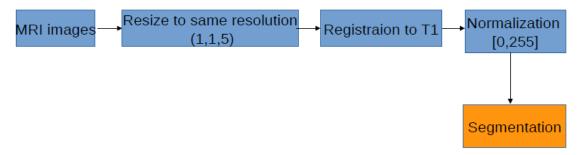

Figure 1. Block diagram showing data preparation

Semi-Automated Lesion Segmentation

Highly accurate 3D segmentation was achieved by a semi-automated approach using LOGISMOS software. [1, 2] After the automated LOGISMOS graph segmentation, the next step allows the expert observer to efficiently fix small localized segmentation inaccuracies by interacting with the LOGISMOS optimization algorithm instead of redrawing surfaces on all affected 2D slices. As such, only a few additional expert-identified points indicating correct surface locations are typically needed to modify the 3D surfaces and thus correct the 3D segmentations in their entirety.

Radiomics Feature extraction

For each segmented lesion, PyRadiomics toolbox was used to extract 107 features from each 3D image including 14 shape features, 18 first-order intensity features and 75 texture features such as gray level co-occurrence and run length matrices. In order to extract radiomic features using the publicly available PyRadiomics package, for each patient, two types of pathology-outlining masks (see Fig. 2)were segmented from CE and Flair sequences: masks depicting necrotic area (only necrotic) and enhancing area (necrotic plus enhancing tumor) obtained from CE MRI sequence ; masks depicting edema area (enhancing plus necrotic plus edema component)obtained from Flair MRI sequence . Based on these two masks, we created 4 separate masks: necrotic mask (only necrotic area), enhancing mask(necrotic plus enhancing tumor), enhancing mask2 (enhancing mask-necrotic mask), edema mask (mask got from Flair - mask got from CE). For each patient, we had 4 masks and 5 images, total mask and image combination number was 20. For each combination, PyRadiomics was used to extract 107 radiomic feature. Total number of features was 2,140 for each 3D MR dataset (consisting of images using several MR sequences).

RF model

RandomForestClassifier from sklearn python package was used for this project. 3 hyperparameters (n_estimators, min_sample_leaf and criterion) were tuned for highest accuracies.

Results:

For the task of tumor classification, the goal of which is to distinguish among three tumor types, the achieved accuracy was 0.8 using all features. The number of missing data in each feature was calculated. After removing features that have the maximum number of missing data, the accuracy increased to 0.81.

When exploring a simpler classification task of classifying tumors in two classes, accuracies further improved: 2-class GBM and LYM classification: achieved accuracy=100%; GBM and MET: achieved accuracy=88%; LYM and MET: achieved accuracy=88%.

In this project, we clearly showed that Random Forest machine learning method can classify different tumor types using extracted radiomics features (3 classes or 2 classes) with reasonable accuracies. Due to the time limit for this pilot project, we only explored the use of an RF algorithm. Other machine learning algorithms could be explored for tumor classification. In addition, the missing data in radiomics features was not fully analyzed in this project. Different missing data imputation methods and its effect on accuracy of classification could be further analyzed.
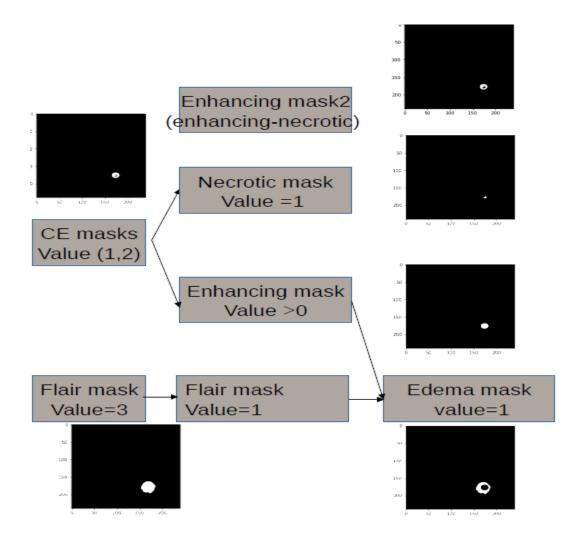
Figure 2. Block diagram showing mask separation

Ideas/aims for future extramural project:

Objective/ Hypothesis: Our objective with the current study is to develop and optimize a machine/ deep learning model to successfully differentiate between the three most common tumor types non-invasively. This is based on our hypothesis that different tumors have different microenvironments. These likely manifest as variations in higher order radiomic/ abstract features which are imperceptible to human eye but can be picked up through advanced computational learning. These features could be used to provide a more robust classification. This is also supported by our preliminary data where we noted that a machine learning based approach has good discriminatory value in differentiating these entities (AUC of 0.79, unpublished work).

Specific aims of current study include development, optimization, internal and external validation of the model in terms of distinguishing between the three entities. The external dataset will include cases from the cancer genome atlas (TCGA) and an independent institute

(University of Pennsylvania). A secondary aim of the study will be to compare the different machine/ deep learning approaches to determine the optimal methodology for lesion characterization and generalizability.

ACS seed grant through HCCC has been funded. We will focus on specific aims (mentioned above) on the follow up study.

Publications resulting from project:

1. Radiomics Based Differentiation Between Glioblastoma and Primary Central Nervous System Lymphoma: A Comparison of Diagnostic Performance Across Different Sequences and Machine Learning Techniques. Submitted
2. Three tumor classification. In preparation
3. Radiomics Based Differentiation Between Glioblastoma and Brain Metastases: A Comparison of Diagnostic Performance Across Different Sequences and Machine Learning Techniques. In preparation

References:

1. Li K, Wu X, Chen DZ, Sonka M. Optimal surface segmentation in volumetric images — a graph-theoretic approach. IEEE Transactions on Pattern Analysis and Machine Intelligence 2006;28(1):119–134-119–134.

2. Zhang H, Lee K, Chen Z, Kashyap S, Sonka M. Handbook of Medical Image Computing and Computer Assisted Intervention 2020, Pages 249-272