A Novel Imaging-Genomic Approach to Predict Outcomes of Radiation Therapy in Head-and-Neck Carcinoma

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Introduction: Head and Neck Squamous Cell Carcinoma (HNSCC) is usually treated with Radiation Therapy (RT). Recurrence of the tumor occurs in some patients post-treatment. The purpose of this study was to determine whether the information present in the heterogeneity of tumor regions in the pre-treatment PET-CT scans of HNSCC patients can be a useful measure of the efficacy of radiation therapy in their treatment. We have now extended our study to include the gene mutation information of a group of patients to see if it can be used as an additional feature in the determination of treatment efficacy.

Materials and Methods: The project started with acquisition of the HNSCC database from The Cancer Imaging Archive (TCIA). It has pre- and post-treatment diagnostic scans in DICOM format of 215 patients treated at the M.D. Anderson Hospital, USA. The follow-up duration varies between two and ten years. Clinical data accompanying the database are used to divide the patients into two categories: local recurrent and non-local recurrent, on the basis of whether they have had a recurrence of the tumor post-treatment. Radiation structures included in the database, when overlain on the PET-CT scans are used to delineate the tumor in the scans. Texture analysis of the tumor was carried out in two ways, treating each slice as a 2D image and treating the collection of slices from a patient as a 3D volume. This radiomics workflow was then tested on the patients of our second database- Head-Neck-PET-CT, which has scans for 298 patients treated at Quebec, Canada. A group of 20 patients from the first database and 53 patients from the second database was chosen for the study. A new aspect of the study deals with the inclusion of gene expression information for a group of 11 patients in the third database: TCGA-HNSC. The TCGA identified mutations in PIK3CA expression in patients who were Human Papillomavirus positive (HPV+), while mutations in CDKN2A and TP53 were observed in patients who were HPV-. We combined the gene expression features with tumor texture features for these patients and re-evaluated accuracies of classification of the patients into the local vs non-local recurrent categories.

Results and Discussion: The texture features extracted from the tumor slices are used in the Classification Learner Application in MATLAB, which makes use of a variety of classification methods including Weighted K Nearest Neighbors (KNN), Linear Support Vector Machine (SVM), Bagged Trees and several others. Slice-wise and patient-wise classification results are computed for both the 2D and 3D cases using 50-fold cross-validation for the HNSCC and Head-Neck databases separately and by combining them. For the computation of patient-wise classification results, we assign the class label possessed by at least 55% of the slices. We achieved overall classification accuracies of 78% in the 2D case and 82% in the 3D case by combining patients of both the databases. The classification accuracy for the patients of the TCGA-HNSC database increased from 80% using only texture information to 100% by combining gene information in the 2D case for local recurrent patients and from 60% to 100% for the non-local recurrent patients.

Translational Impact: Prediction of the response of a patient to radiation therapy can be used to reduce the number of patients who are unnecessarily exposed to radiation. The combination of various tumor texture measures that have been extracted from pre-treatment PET scans can provide a measure of tumor heterogeneity that in turn can be used to predict the recurrence status of the tumor post-treatment. Our experiments further show that identification of gene expression patterns in head and neck carcinoma patients can provide information which, when combined with tumor texture measures can improve the therapy response prediction scores. Our current study involves validation of our approach using patients from the TCGA-LUAD (Lung adenocarcinoma) and TCGA-LUSC (Lung squamous carcinoma) databases to develop a more comprehensive method of therapy personalization in cancer patients.

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