Deep learning for decoding molecular phenotypes with radiogenomics in breast cancer

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Abstract: Objective

It has been believed that traditional handcrafted radiomic features extracted from magnetic resonance imaging (MRI) of tumors are normally shallow and low-ordered. Recent advancement in deep learning technology shows that the high-order deep radiomic features extracted automatically from tumor images can capture tumor heterogeneity in a more efficient way. We hypothesize that MRI-based deep radiomic phenotypes have significant associations with molecular profiles of breast cancer tumors. We aim to identify MRI-based signatures that can explain the potential underlying genetic mechanisms and predict the molecular classification of invasive breast cancers.

Methods

We develop a new deep learning model to retrospectively extract 4,096 MRI-based radiomic phenotypes from breast cancer tumors collected by The Cancer Imaging Archive (TCIA). These phenotypes of tumors are associated with genomic features (commercialized gene signatures, expression of risk genes, and pathways activities) of the corresponding molecular profiles (e.g. gene expression) and other clinical features collected from The Cancer Genome Atlas (TCGA). We develop novel association and classification methods to select the most-predictive radiogenomic features for the clinical phenotypes, including tumor size (T), lymph node metastasis(N) from breast cancer TNM staging system which is wildly used in clinic, and status of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2).

Results

We find that transcriptional activities of various genetic pathways and gene signatures are positively associated with more than 1000 of the 4,096 MRI-based radiomic phenotypes. These radiomic phenotypes are also associated with the mRNA expression of the risk genes identified from other two genome-wide association studies. Higher performances are obtained in the prediction of HER2 status, ER status and tumor size(T) than PR status and lymph node metastasis(N). These identified MRI-based radiomic phenotypes also show significant power to stratify the breast cancer tumors, which may have a significant clinical impact.

Conclusion

Our radiogenomic approach for identifying MRI-based imaging signatures may pave potential pathways for the discovery of genetic mechanisms regulating specific tumor phenotypes and may enable a more rapid innovation of novel imaging modalities, hence accelerating their translation to personalized medicine.