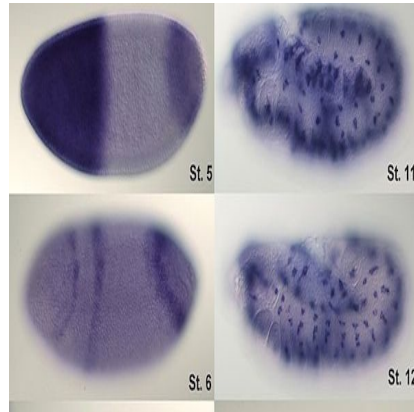




Radiogenomic Imaging Could Replace Biopsy



High-throughput biological techniques have reshaped the perspective of biomedical research allowing for fast and efficient assessment of the entire molecular topography of a cell's physiology, providing new insights into human cancers. However, a main limitation of these techniques is the need to acquire tissue for gene expression profiling through invasive biopsy, thereby limiting the clinical application of this method in an everyday patient care setting.

In addition, in these biopsy samples are frequently obtained from only a part of the lesion and therefore do not entirely represent the lesion's unique anatomic, functional, and physiologic properties, such as size, location, and morphology. Many of these features are obtained in routine clinical imaging exams and are very useful for diagnosis, staging, and treatment planning. Although these image features provide anatomical and morphological information, few studies have generated a "radiogenomics map" integrating the genomic and image data and thereby introducing the field of "radiogenomics" or "radiogenomic imaging".

The use of noninvasive imaging for gene expression profiling is a fast and reliable technique which has the potential to replace high-risk invasive biopsy procedures. This review focuses on the medical imaging part as one of the main drivers for the development of radiogenomic imaging.

Diagnostic Imaging as a Platform for Gene Expression

Radiologic imaging plays an important part in every stage of cancer treatment. Besides screening, detection and staging of disease, imaging is used to predict and evaluate the individual patient's responsiveness to therapies in each stage of cancer treatment. Diagnostic imaging is a safe and accurate tool to noninvasively assess location, morphology and physiology of tissues. However, much of the data generated by radiologic imaging remains largely unspecific at a molecular level. The integration of these noninvasive imaging tools with functional genomic assays has the power for a quick clinical translation of high-throughput technology.

Imaging for Molecular Assessment of Tumour Staging and Diagnosis

A study by Kuo et al. in patients with liver cancer found that a liver-specific gene expression programme was highly correlated with the imaging trait "tumour margin score, arterial phase". The data suggest that this radiophenotype could potentially form the basis to categorise hepatocellular carcinomas (HCCs). Segal et al. also demonstrated that dynamic imaging traits in computed tomography (CT) strongly correlated with the global gene expression of primary HCC. The authors managed to reconstruct 78 percent of the gene expression profiles by combining 28 imaging traits, thereby showing cell proliferation, liver synthetic function, and patient outcome.

In a recent study in patients with glioblastoma multiforme (GBM), Jamshidi et al. showed that magnetic resonance imaging (MRI), messenger RNA expression and DNA copy number variation can identify MR traits which are associated with some known high-grade glioma biomarkers and associated with genomic biomarkers that have been identified for other malignancies but not GBM. Further work is needed to determine the clinical value of these findings.

Imaging for Molecular Assessment of Tumour Prognosis

Radiogenomic imaging is a useful tool for molecular assessment of tumour staging and diagnosis; however, for its success in a clinical setting it is crucial that radiogenomics has the potential to also impact clinical management. Despite much recent activity in developing imaging biomarkers of disease, it is challenging to link these biomarkers to clinical outcomes as it takes years to obtain these outcomes in cohort studies.

The above-mentioned study by Kuo et al. in patients with HCC showed that the tumour margin score highly correlated with a venous invasion gene expression programme as well as histologically-confirmed venous invasion.

A study by Diehn et al. sought to correlate imaging surrogates for gene-expression profiles with prognostic implications in patients with GBM. The radiogenomic maps showed a statistically significant overlap between a survival-associated gene signature and an infiltrative pattern of the oedema on T2-weighted images. In a second part of the study, another 110 GBMs were included; the results revealed a correlation between the infiltrative radiophenotype and a poor prognosis: a median survival of 390 days was found for those without infiltrative pattern compared to 216 for those with infiltrative pattern.

A study by Gevaert et al. explored the clinical prognostic value of radiogenomic imaging by looking at features from non-small cell lung cancer (NSCLC) CT- and positron emission tomography (PET)-cases. Their work demonstrated an imaging approach able to quickly identify prognostically relevant image biomarkers requiring only the paired acquisition of image and gene expression data as well as the existence of a large public gene expression data set where survival outcomes are available. The authors conclude that by mapping image features to gene expression data, it is possible to leverage public gene expression microarray data to determine prognosis and therapeutic response as a function of image features.

Imaging for Molecular Assessment of Optimal Therapy

By using an integrated imaging-genomic approach, Kuo et al. determined whether contrast-enhanced CT was able to assess imaging phenotypes which are associated with a doxorubicin drug response gene expression programme in patients with HCC. The authors included 30 HCCs into the study and scored them individually across six predefined imaging phenotypes. Tumours with higher tumour margin scores were more strongly associated with the doxorubicin resistance transcriptional programme and had a greater prevalence of venous invasion and worse stage. Tumours with lower tumour margin scores, however, showed a converse relationship. The authors conclude that CT has the potential to identify HCC imaging phenotypes correlating with a doxorubicin drug response gene expression programme.

In the previously mentioned study by Diehn et al., the authors identified an imaging phenotype characterised by an infiltrative appearance that was associated with aggressive clinical behaviour and expression of genes involved in central nervous system development and gliogenesis. As this imaging approach is noninvasive and widely available in clinical practice it can be applied to a broad range of human disease processes.

Conclusion

Radiogenomic imaging has the potential to catalyse the health system by creating imaging biomarkers that identify the genomics of a disease. The use of noninvasive imaging as a surrogate for gene expression profiling is a quick and reliable tool which has the potential to replace high-risk invasive biopsy procedures. Additional studies with larger numbers of patients are necessary to confirm links between gene expression patterns and imaging features permitting fast and reliable clinical diagnosis of tumours as well as estimation of prognosis and decision for optimal therapy.

Image Credit: Wikipedia

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