Genomics of Brain Tumor Imaging

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KEYWORDS

• Imaging genomics • Radiogenomics • Glioblastoma • Microarray • Glioma • Bioinformatics

KEY POINTS

- Imaging genomics seeks to develop a method that leverages and integrates large datasets to identify predictive and prognostic biomarkers and new therapeutic targets in patients with glioblastoma.
- A substantial methodological framework including new data analysis methods has been developed to meet the challenge of working with big data.
- Malignant imaging phenotypes determined by MRI have genetic correlates; therefore, imaging may provide a means of panoramic and noninvasive surveillance of oncogenic pathway activation as patients are treated for GBM.

INTRODUCTION

Imaging genomics, radiogenomics, and radiomics are different names for essentially the same thing, a field of study focused on understanding the relationship between medical imaging data and molecular features of disease.[1–4] It is the integration of big data, quantitative imaging features taken from large numbers of images (typically MRI and computed tomography [CT]) and "-omic" data, which represent gene, protein or metabolite expression, as well as gene copy number, DNA methylation, and other important molecular markers. In oncology, this approach is being used to combine cancer phenotypes that can be globally assessed by imaging, with relevant molecular data, in order to develop prognostic and predictive biomarkers (**Fig. 1**). Improved diagnostic tests, better clinical decision making, new therapeutic targets, and improved understanding of tumor biology are all potential deliverables. Another promise of this approach is the ability to tailor therapy to enhance treatment effectiveness at the individual patient level. This article focuses on the application of imaging genomics to glioblastoma, one of the first pathologies for which this concept was applied.

BACKGROUND

Microarray Technology

Genomic information is a measure of gene expression based on mRNA isolated from tissue of interest. Microarrays, which contain thousands of complementary oligonucleotide or cDNA sequences (referred to as probes) are affixed in designated positions to a glass slide, so that mRNA-derived nucleic acids can be specifically detected via hybridization. The plates are washed, and the signal from these hybridized probes is detected and recorded. In this way the expression of thousands of genes can be quantified in a single experiment (**Fig. 2**).[5] Microarray technology and analysis have generated great interest among investigators of brain cancer for over a decade.[6]

Microarray Technology—Limitations

Oftentimes tissue for microarray analysis will be derived from surgical resections without precise tissue sample localization. This introduces sampling error in tumors such as glioblastoma (GBM) that are spatially heterogeneous in gene expression and imaging features. Additionally, tissue may not be composed of 100% tumor cells but may be of variable tumor cell concentration. This

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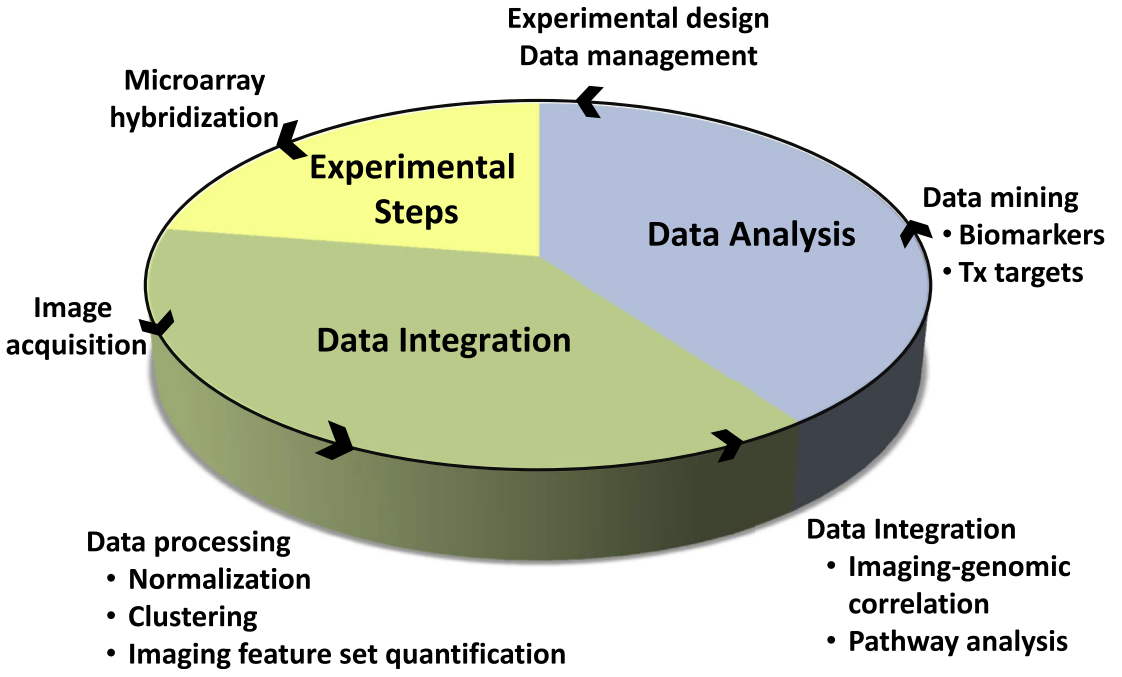

Fig. 1. Cycle of data acquisition, integration, analysis, and hypothesis generation/testing for imaging-genomics. Tx, treatment.

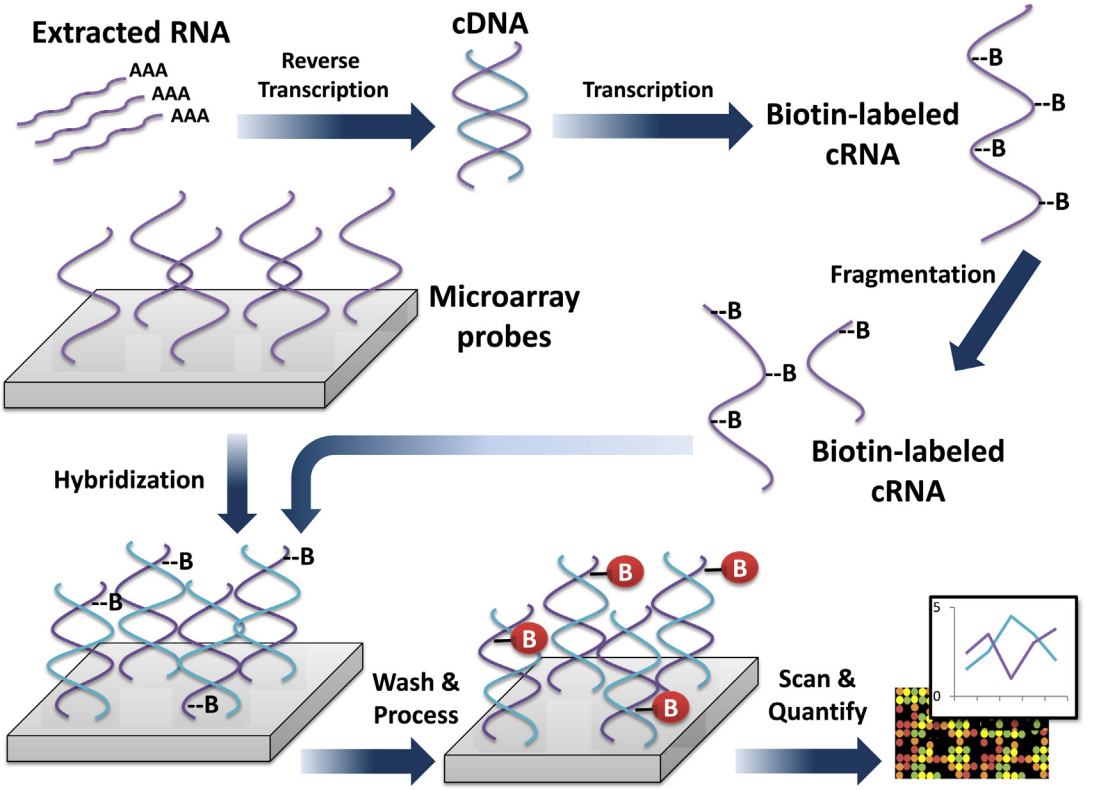

Fig. 2. Schematic for assessing gene expression using microarray analysis. Automated methods allow for the measurement of expression of thousands of genes in a single experiment. B, biotin.