Biology and Pathology

Cancer Biology

Image Analysis and Informatics

Robert J. Gillies
Department of Cancer Imaging and Metabolism, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida, USA

Learning Objectives:

- Describe the motivation underlying analyses of tumor heterogeneity
- Describe the role of Image 'omics in Oncology
- List the different levels of biomarker qualification

Image "Omics" involves the high throughput extraction of quantitative imaging features with the intent of creating mineable databases from images (1). Such profound analyses and mining of image feature data will reveal quantitative predictive or prognostic associations between images and medical outcomes. In cancer, current quantitative measurements are limited to dimensional measurements of tumor size via one (RECIST) or two (WHO) dimensional long axis measures (2). These measures do not reflect the complexity of tumor morphology or behavior, nor, in many cases, are changes in these measures predictive of therapeutic benefit (3). When additional quantitative measures are performed, they generally average values over an entire region of interest (ROI).

In focused studies, texture features have been shown to provide significantly higher prognostic power than ROI based methods (4-7). This is reflective of the fact that tumors are highly heterogeneous systems, and that such heterogeneity has high prognostic power (8). Profound analyses of such image features can improve prediction of clinical CT (9), MR (10) or PET (11) images. Although paradigm-shifting, these analyses have been performed manually and the studies were underpowered. In order to qualify as a clinically useful biomarker, such studies have to be performed with larger cohorts in prospective, multi-institutional trials. In the current iteration of radiomics, image features have to be extracted automatically and with high throughput, putting a high premium on novel machine learning algorithm developments.

The goal of radiomics is to convert images to mineable data, with high fidelity and high throughput. The radiomics enterprise can be divided into five processes with definable inputs and outputs, each with its own challenges that need to be overcome: (i) image acquisition and reconstruction: (ii) image segmentation and rendering: (iii) feature extraction and feature qualification (iv) databases and data sharing; and (v) ad hoc informatics analyses (12). Each of these steps must be developed de novo and, as such, poses discrete challenges that have to be met. For example, optimum protocols for image acquisition and reconstruction have to be identified and harmonized. Segmentations have to be robust and involve minimal operator input. Features have to be generated that robustly reflect the complexity of the individual volumes, but cannot be overly complex or redundant. Informatics data bases that allow incorporation of image features and image annotations, along with medical and genetic data have to be generated. Finally, the statistical approaches to analyze these data have to be optimized, as radiomics is not a mature field of study.

Variation in results may come from variations in any of these individual processes. Thus, after Optimization, another level of challenge is to harmonize and standardize the entire process, while still allowing for improvement and process evolution.

References:

1. Lambin P. Rios-Velazquez E. Leijenaar R. et al. Radiomics: extracting more information from medical images using advance feature analysis. The European Journal of Cancer 2011.
2. Jaffe CC. Measures of response: RECIST, WHO, and new alternatives Journal of clinical oncology: official journal of the American Society of Clinical Oncology. Jul 10 2006:24(20):3245-3251
3. Burton A. RECIST: right time to renovate? The Lancet Oncology. 2007;8(6):464-465.
4. Jackson A, O'Connor JPB, Parker GJM, Jayson GC. Imaging tumor vascular heterogeneity and angiogenesis using dynamic contrast enhanced magnetic resonance imaging. Clinical Cancer Research. 2007;13(12}:3449-3459.
5. Rose CJ. Mills SJ, O'Connor JPB. et al. Quantifying spatial heterogeneity in dynamic contrast-enhanced MRI parameter maps. Magnetic Resonance in Medicine.2009;62(2):488-499.
6. Gibbs P. Turnbull LW. Textural analysis of contrast-enhanced MR images of the breast. Magnetic Resonance in Medicine. 2003;50(1):92-98.
7. Canute HC, Mclachlan C. Kettunen MI. et al. Characterization of image heterogeneity using 20 Minkowski functionals increases the sensitivity of detection of a targeted MRI contrast agent. Magnetic Resonance in Medicine. 2009;61(5):1218-1224.
8. Gillies RJ, Verduzco 0, Gatenby RA. Evolutionary dynamics of carcinogenesis and why targeted therapy does not work. Nature reviews. 2012;12(7):487-493.
9. Segal E. Sirlin CB, Ooi C, et al. Decoding global gene expression programs in liver cancer by noninvasive imaging. Nature biotechnology. 2007;25(6):675-680.
10. Diehn M, Nardim C. Wang OS, et al. Identification of noninvasive imaging surrogates for brain tumor gene-expression modules. Proceedings of the National Academy of Sciences. 2008;105(13).5213.
11. Nair VS, Gevaert 0, Davidzon G. et al. Prognostic PET 18F-FDG Uptake Imaging Features Are Associated with Major Oncogenomic Alterations in Patients with Resected Non-Small Cell Lung Cancer. Cancer research. Aug 1;72(15) 3725-3734.
12. Kumar V, Gu Y, Basu S, et al. Radiomics: the Process and the Challenges. Magnetic Resonance Imaging. 2012;(in press).