Solving Research Problems: Integrating Radiology Observation Data with Genotypic/Phenotypic Analysis

Imaging Knowledge Center

Radiologists and pathologists need the ability to store, annotate, search, retrieve, and distribute medical images. The Imaging Knowledge Center provides support for six key imaging services and applications, including National Biomedical Imaging Archive (NBIA), a searchable national repository integrating cancer images with clinical and genomic data, and Annotation Imaging Markup (AIM) project that proposes/creates a standard means of adding information/knowledge to an image in a clinical environment. *Note that the Imaging Knowledge Center was officially launched on March 1, 2011, but the caBIG® program has been developing and supporting imaging applications for approximately five years.*

The Problem: Integrating Radiology Observation Data with Genotypic/Phenotypic Analysis in Support of The Cancer Genome Atlas

New databases are rapidly expanding available information about relationships between genomics and disease. One of these databases is The Cancer Genome Atlas (TCGA), a comprehensive and coordinated effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis, including large-scale genome sequencing. Among the biggest challenges facing those creating databases in support of personalized medicine is finding ways to integrate medical imaging information. Performing imaging in a highly structured, quantitative manner can make the resulting anatomic and functional observations available for cross correlation with genomic, proteomic, pathologic, and clinical data. This can allow imaging to noninvasively identify cellular pathways present in specific cancers, more accurately predict disease course, and provide useful information about progression of disease over time.

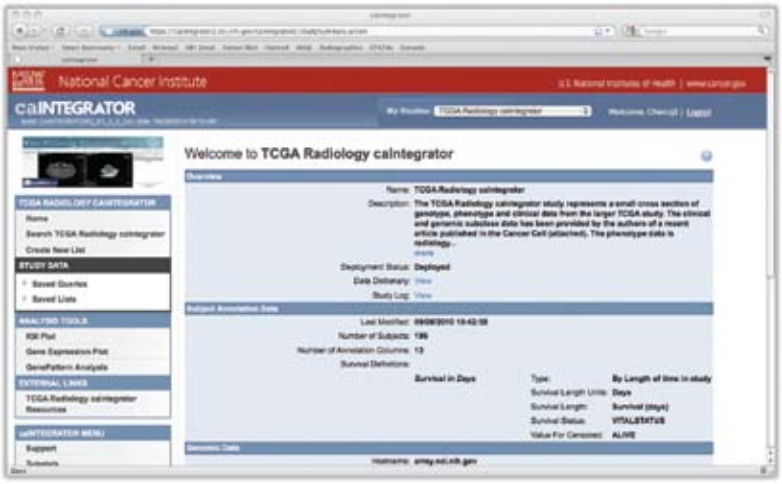
The Solution: Imaging Applications and caIntegrator

The community used an application called caIntegrator to demonstrate that imaging observations can be correlated with TCGA data to obtain new insights into the relationships between imaging and genomics. They used multiple technologies, supported by caBIG®, together to create a practical system for capturing diagnostic imaging "knowledge" in a structured, standardized manner to allow for integration with both genomic and clinical data.

The steps to begin exploring correlations between imaging data and genomics are simple.

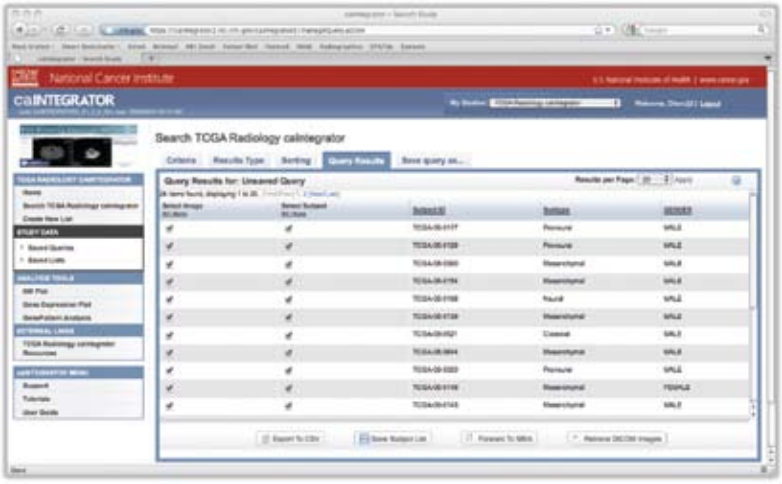
1. Log in to the caIntegrator Web site at: *https://caintegrator2.nci.nih.gov/caintegrator2/workspace.action*. From the dropdown menu labeled Public Studies, select TCGA Radiology caIntegrator. The TCGA Radiology caIntegrator2 aggregates data from TCGA (including genomic/proteomic and demographic data), caBIG® services, the National Biomedical Imaging Archive (NBIA), and Annotated Imaging Markup (AIM).

2. The user can then see the different datasets available, including TCGA demographic information, microarray data from caArray, and imaging/imaging observation data from the NBIA and AIM via caGrid.

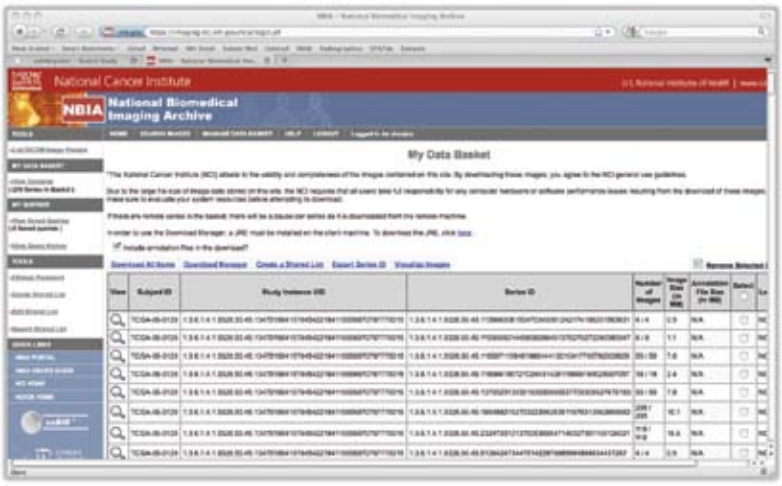


3. The user then selects which characteristics of study subjects are to be searched; for example, all study subjects with specified genomic criteria, clinical characteristics, or imaging observations or measurements. More than 20 categories of imaging observations are available. In our example, for a search for all subjects with hemorrhages associated with glioblastoma multiforme tumors, the user selects "hemorrhage" and "yes."

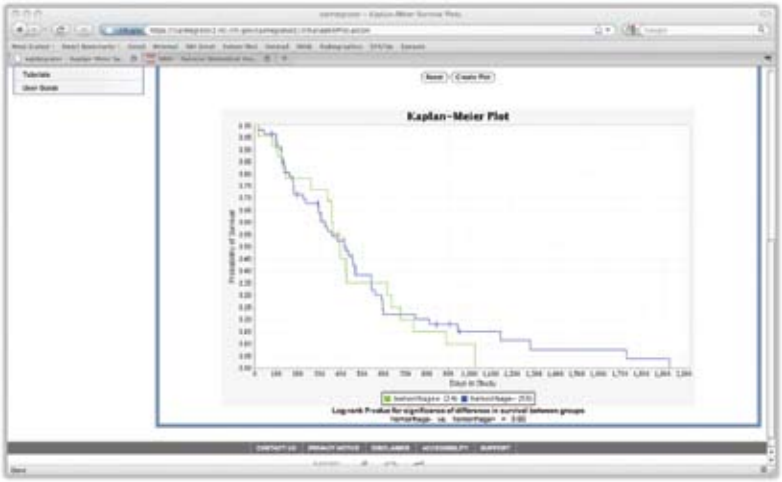
4. The user then asks for additional information on these patients, such as other imaging observations or clinical, histologic, and/or gene expression characteristics. Then "run query" is selected. The result is a list of 24 patients with hemorrhage associated with their tumors.



The user can review the different subtypes and genders of these patients, export and save the data, and go to the NBIA to see the relevant images.

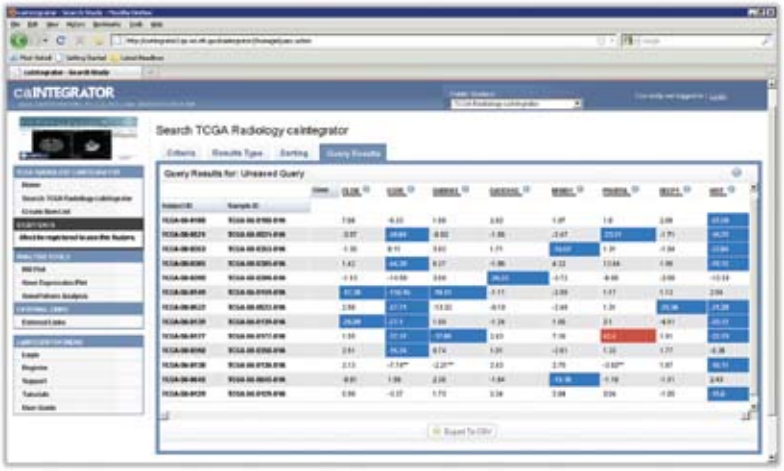


5. Once the database is queried and the results saved, the user can analyze the data in real time. One example is automatic generation of a Kaplan–Meier Survival Plot by clicking on KM plot, in this case to determine how patients with hemorrhagic tumors are likely to fare in comparison to those without hemorrhage.



6. caIntegrator also allows the user to cross correlate imaging characteristics with genomic data. For example, if the user wants to know whether certain genes are over- or underexpressed in hemorrhagic tumors compared with nonhemorrhagic tumors, hemorrhage is selected as the imaging observation to be evaluated and gene expression is selected as a "fold change," followed by selection of a set of genes to study. In this example, all patients without hemorrhagic tumors are selected as the control group. For this example, the user chose ≥15 folds of either up- or downregulation of the selected genes as relevant.

7. The columns represent the genes with their expression levels; the rows are the patients with hemorrhagic tumors. Of these selected set of genes, EGFR and XIST appear to be significantly downregulated by 15 folds or more in most of the patients with hemorrhagic brain tumors but not in patients without hemorrhagic tumors.



The Benefits:

Approaches such as the one outlined here can facilitate rapid testing of various hypotheses about the ability of imaging to predict gene expression data noninvasively and help to determine the added value of imaging in prediction of patient outcomes, such as response to chemotherapy, radiation therapy, or surgery. Such techniques can also be used to determine whether imaging data can identify specific subtypes of disease to enhance personalization of cancer staging and treatment.

Key Contributors:

caBIG® Imaging Community
caBIG® Imaging and Integrative Cancer Research Programs
NCI Cancer Imaging Program

For More Information:

Imaging Knowledge Center: *https://cabig-kc.nci.nih.gov/Imaging/KC/index.php/Main_Page*

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