

TCGA imaging as CTSA IWG model

Leveraging 'big science' projects as
strategic opportunities

C. Carl Jaffe, MD
NCI CIP/Boston University

Lessons for CTSA IWG

- IWG 'service' model is difficult to establish without planned 'entitlement' funding
- Imaging has to capture cross-disciplinary scientific imagination by being seen as key to translational progress
- Opportunistic leverage 'big science' projects such as comparative efficacy research, genetics and personalized medicine

**The Cancer Genome Atlas (TCGA):
Opportunities for IMAGING in this key NIH initiative**

The Cancer Genome Atlas (TCGA) is a comprehensive and coordinated effort to accelerate our understanding of the genetics of cancer using innovative genome analysis technologies.

News

NEW* TCGA Identifies Distinct Subtypes of Deadly Brain Cancer That May Lead to New Treatment Strategies
TCGA researchers identified four distinct molecular subtypes of glioblastoma multiforme (GBM), and demonstrated that response to aggressive chemotherapy and radiation differed by subtype. These findings, reported in the January 19 issue of *Cancer Cell*, may result in more personalized

TCGA Expanding to Study 20 or More Cancers
[Learn More](#)

Questions about cancer?
Visit [Cancer.gov](#)
1-800-4-CANCER
[Live! Help online chat](#)

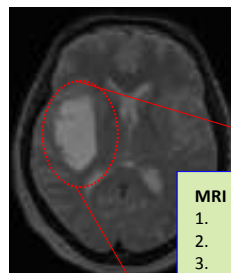
The Cancer Genome Atlas program

- Acquires tumor tissues from surgery
 - NHGRI focus: extensive genomic characterization:
 - m/miRNA expression, CNA, methylation, exome + whole genome sequencing
 - NCI focus: tissue acquisition and limited clinical data
 - Pathology, treatment / response, survival
 - Objective: genetic research on 20 tumor tissue types
 - Is a \$300 M project with personalized medicine spin-offs
 - No plan (originally) to collect diagnostic images

Theme: Image data-sets play a role
Comparative Microarray & MR Feature Analysis

Genome \leftrightarrow Phenome

research enabled by caBIG - NCI



MRI Featureset

1. Infiltration
2. Enhancement
3. Nodularity
4. Necrosis
5. Edema
6. nCET
7. Diffusion
8. Hemorrhage

Cell
PRESS

Cancer Cell
Article

Integrated Genomic Analysis Identifies Clinically Relevant Subtypes of Glioblastoma Characterized by Abnormalities in *PDGFRA*, *IDH1*, *EGFR*, and *NF1*

Roel G.W. Verhaak,^{1,2,17} Katherine A. Hoadley,^{3,4,17} Elizabeth Purdom,⁷ Victoria Wang,⁸ Yuan Qi,^{4,5}

SIGNIFICANCE

This work expands on previous glioblastoma classification studies by associating known subtypes with specific alterations in *NF1* and *PDGFRA/IDH1* and by identifying two additional subtypes, one of which is characterized by *EGFR* abnormalities and wild-type *p53*. In addition, the subtypes have specific differentiation characteristics that, combined with data from recent mouse studies, suggest a link to alternative cells of origin. Together, these data provide a framework for investigation of targeted therapies. Temozolomide and radiation, a common treatment for glioblastoma, has demonstrated a significant increase in survival. Our analysis illustrates that a survival advantage in heavily treated patients varies by subtype, with Classical or Mesenchymal subtypes having significantly delayed mortality that was not observed in the Proneural subtype.

A role for imaging

- Fortuitously, NCI's Center for Bioinformatics and Informatics under the caBIG (cancer Bioinformatics Grid) program, in alliance with the NCI Cancer Imaging Program, was developing an network accessible image archive (NCIA – now titled "NBIA")
- A UPICT-class explanation of cancer imaging protocols is written into the related caHUB RFP biospecimen initiative
- <https://imaging.nci.nih.gov/ncia/login.jsf>

The image archive will network-link to gene tissue data

National Cancer Institute U.S. NCI

NBIA National Biomedical Imaging Archive

TOOLS SEARCH IMAGES HELP

List DICOM Image Viewers

QUICK LINKS

- NBIA PORTAL
- NBIA USER'S GUIDE
- NCI HOME
- NCICB HOME

caBIG™

CANCER IMAGING PROGRAM

Center for Bioinformatics

RSNA

WELCOME TO NATIONAL BIOMEDICAL IMAGING ARCHIVE

Welcome to the National Biomedical Imaging Archive (NBIA). NBIA is a searchable repository of in vivo images that provides the biomedical research community, industry, and academia with access to image archives to be used in the development and validation of analytical software tools that support:

- Lesion detection and classification
- Accelerated diagnostic imaging decision
- Quantitative imaging assessment of drug response

NBIA provides access to imaging resources that will improve the use of imaging in today's biomedical research and practice by:

- Increasing the efficiency and reproducibility of imaging cancer detection and diagnosis
- Leveraging imaging to provide an objective assessment of therapeutic response
- Ultimately enabling the development of imaging resources that will lead to improved clinical decision support.

SEARCH IMAGES
Query the NBIA Image Server

Contrast	<input checked="" type="checkbox"/> Enhanced <input checked="" type="checkbox"/> Unenhanced																			
Anatomical Site	<table border="1"> <thead> <tr> <th>Available</th> <th></th> <th>Selected</th> </tr> </thead> <tbody> <tr> <td>ABDOMEN</td> <td rowspan="6"> <input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/> </td> <td></td> </tr> <tr> <td>BRAIN</td> <td></td> </tr> <tr> <td>BRAIN WITH _WITH</td> <td></td> </tr> <tr> <td>BREAST</td> <td></td> </tr> <tr> <td>CHEST</td> <td></td> </tr> <tr> <td>CHEST - PA AND L</td> <td></td> </tr> <tr> <td>CHEST 1B</td> <td></td> <td></td> </tr> </tbody> </table>	Available		Selected	ABDOMEN	<input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/>		BRAIN		BRAIN WITH _WITH		BREAST		CHEST		CHEST - PA AND L		CHEST 1B		
Available		Selected																		
ABDOMEN	<input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/>																			
BRAIN																				
BRAIN WITH _WITH																				
BREAST																				
CHEST																				
CHEST - PA AND L																				
CHEST 1B																				
Image Slice Thickness	<input type="checkbox"/> I would like to filter by "Image Slice Thickness" <input type="button" value=">"/> <input type="text" value="0 mm"/> <input type="button" value="AND"/> <input type="button" value="<="/> <input type="text" value="5 mm"/> <input type="button" value="<"/>																			
Collection(s) Collection Descriptions	<table border="1"> <thead> <tr> <th>Available</th> <th></th> <th>Selected</th> </tr> </thead> <tbody> <tr> <td>CT Colonography</td> <td rowspan="6"> <input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/> </td> <td></td> </tr> <tr> <td>GBM Avastin</td> <td></td> </tr> <tr> <td>GBM Rembrandt</td> <td></td> </tr> <tr> <td>Head-Neck Cetuximab</td> <td></td> </tr> <tr> <td>IDRI</td> <td></td> </tr> <tr> <td>LIDC</td> <td></td> </tr> </tbody> </table>	Available		Selected	CT Colonography	<input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/>		GBM Avastin		GBM Rembrandt		Head-Neck Cetuximab		IDRI		LIDC				
Available		Selected																		
CT Colonography	<input type="button" value="SELECT >"/> <input type="button" value="SELECT ALL >>"/> <input type="button" value="REMOVE ALL <<"/> <input type="button" value="REMOVE <"/>																			
GBM Avastin																				
GBM Rembrandt																				
Head-Neck Cetuximab																				
IDRI																				
LIDC																				
Series Includes Annotations	<input checked="" type="checkbox"/> Annotated <input checked="" type="checkbox"/> Non-Annotated																			
Available on NCIA (mm/dd/yyyy)	From: <input type="text"/> <input type="button" value="calendar"/> To: <input type="text"/> <input type="button" value="calendar"/>																			

New horizons for imaging research

- With 20+ tumor types on the TCGA horizon, clinical imagers at institutions that contribute tissue specimens, have the opportunity to add images to a network-accessible framework that enables cross-disciplinary discovery of gene-image linkage.
- Especially promising is research on the potential gene-connections of diagnostically acquired advanced imaging such as PET, MRI and CT from patients whose tissues will be analyzed in TCGA

Assembling intra-institutional alliances

- All politics is local
- Active outreach and a specific 'theme' is critical
 - Assume CTSA funding is impenetrable
- Natural allies: surgery, pathology, oncology clinical trials office (CC), sponsored trials

Making extra-institutional connections

- Human networking, professional societies
- Science gap analysis
- Leverage caBIG tools and infrastructure
- Encourage R01/R21 applications that stress the advantages/efficiencies of connectivity
- Take note of imaging in the ISPY-2 precedent

As of 2008, institutions contributing GBM biospecimens for TCGA include:

- Duke University, Durham, North Carolina
- Cedars-Sinai Medical Center, Los Angeles, California
- Emory University School of Medicine, Atlanta, Georgia
- Henry Ford Hospital System, Detroit, Michigan
- Mayo Clinic, Rochester, Minnesota
- MD Anderson Cancer Center, Houston, Texas
- Toronto Western Hospital, Ontario, Canada
- University of California at San Francisco Medical Center, San Francisco, California
- University Hospitals Case Medical Center, Cleveland, Ohio

How do institutions gain from participation ?

- Broader faculty engagement in genomics
 - Intra-institutional collaborative possibilities
 - National participation & preparing for “personalized medicine”
- Disease-space research participation
 - Robust size collections, freedom to explore individually and without barriers
- Cost recovery to institution per contribution
- Leverage conceptual research for R01s etc
- Translational medicine leads

New horizons for imaging research

- With 20+ tumor types on the TCGA horizon, clinical imagers at institutions that contribute tissue specimens, have the unparalleled opportunity to add images to a network-accessible framework that enables cross-disciplinary discovery of gene-image linkage.
- Especially promising is research on the potential gene-connections of diagnostically acquired advanced imaging such as PET, MRI and CT from patients whose tissues will be analyzed in TCGA

Current TCGA image teams

- Thomas Jefferson U. (Lead)
 - Adam Flanders (neurorad); David Andrews (surgery)
- Univ. Virginia
 - Max Wintermark (neurorad)
- Emory
 - Chad Holder (neurorad); Joel Saltz (IT/path)
- NIH/NCI
 - Dima Hammoud (neurorad)