Athinoula A. Martinos Center For Biomedical Imaging

Enabling technologies for research using clinically acquired medical image data: Clinical Image Bank and MI2B2

Randy L. Gollub, MD, PhD

Departments of Psychiatry and Radiology, MGH

Professor, Harvard Medical School

Affiliate Faculty, Health Sciences and Technology, MIT

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

Boston Children's Hospital Until every child is well™

THE HARVARD MEDICAL SCHOOL

Acknowledgements

- RPDR
  - Shawn N Murphy
  - Christopher Herrick
  - Mariah Mitchell
  - Stacey Duey
  - Laurie Bogosian
  - Eugene Braunwald
  - Anne Klibanski
  - Henry Chueh
- CIB
  - Shawn N Murphy
  - Randy L Gollub
  - Vivian Gainer
  - Andrew Cagan
  - Nich Wattanasin
  - Christopher Herrick
  - Bill Wang
  - Reeta Metta
  - Rudolph Pienaar
  - Yangming Ou

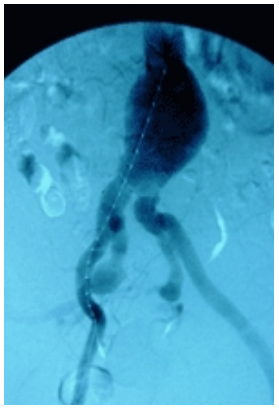
- Mi2b2
  - Randy L Gollub
  - Shawn N Murphy
  - Christopher Herrick
  - Bill Wang
  - David Wang
  - Kathy Andriole
  - Darren Sack
  - P Ellen Grant
  - Nathaniel Reynolds
  - Kallirroi Retzepi
  - Rudolph Pienaar
  - Victor Castro
  - Steve Pieper
  - Lilla Zollei
  - Yangming Ou

Partners Healthcare, NIH/NCBC; /NIMH; /NCBI; /NCATS; /NIBIB
NIH RO1 EB014947
NIH R01 AT006364
NIH R01 AT005280
NIH P01 AT006663

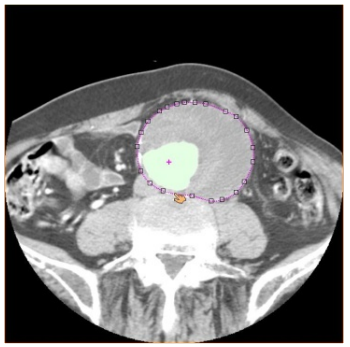
Medical Imaging in EHR

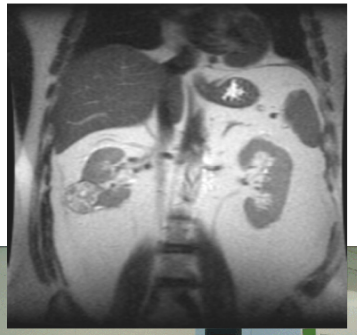
Radiology Report (NLP-able)

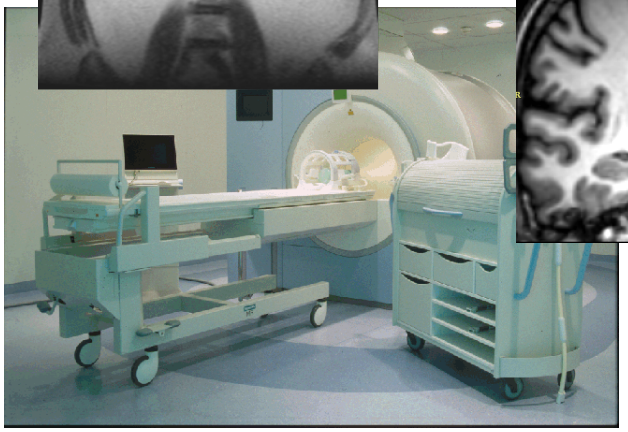
Order for imaging

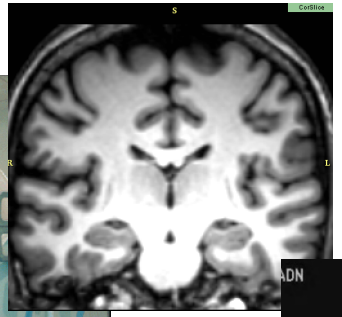


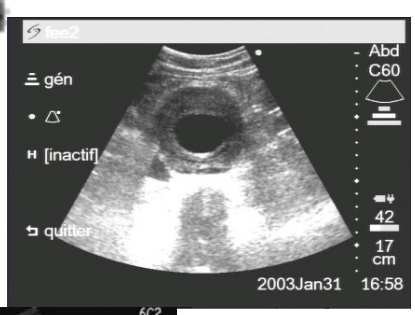
Order for imaging

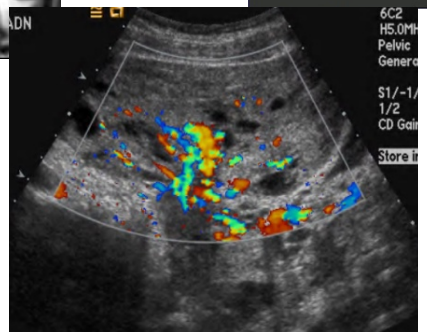












Billing for image acquisition

Billing for image interpretation

Billing for image processing

Research != Clinical

Research	Clinical
Common acquisition protocol	Customized per-patient
Controlled context and data curation	Wide variability
Highest reasonable image resolution	Best clinically justified images
Coverage of target structures	Only what is needed to answer the question at hand
Acquisition often custom for research software	Acquisition paired with commercial workstation features
Often normal subjects	Almost never normal (pathology and other variability)
Quantitative	Qualitative

Advancing High-Value Imaging to Support Patient Care and Research

DECEMBER 22, 2016 AT 10:30 AM ET BY RODERIC PETTIGREW, RICHARD CAVANAGH, JERRY SHEEHAN, AND MICHAEL CHEETHAM

	Referral	Scan	Interpretation	Next Steps
Current Practice	Driven by professional habit, time pressure, defensive medicine, networks	Lengthy techniques or imaging series	Qualitative: much information is discarded	Further imaging or consultation
Future Possibility	Driven by evidence-based Appropriate Use Criteria (AUC)	Faster, high-value techniques with shorter targeted protocols	Quantitative assessments: analytical tools mine image data for more useful information	Reduced need for further imaging: more timely and precise diagnostics and treatment

And yet…..

H_0: Clinically acquired images have tremendous potential to advance biomedical research as well as clinical care

Radiomics

"…high-throughput extraction of quantitative features that result in the conversion of images into mineable data and the subsequent analysis of these data for decision support…"

"…it is conceivable that conversion of [standard of care] digital images to mineable data will eventually become routine practice…"

- Gillies et al, Radiology 2016

RISC RESEARCH INFORMATION SCIENCE & COMPUTING

Login Events News Careers Contact Us Search

IT Services | Research Apps & Services | Support & Training | Knowledge Base | About

Home > Research Apps & Services > Identify Subjects / Request Data

Identify Subjects / Request Data

GET HELP

Enterprise-wide data services are available to help Partners investigators and research groups expedite the process of obtaining data for analysis or to gauge study feasibility. Repositories of clinical samples and data, as well as public data sets, are accessible to researchers through the tools and processes outlined below.

A new initiative, the Partners wide Big Data Commons, enables Big Data to be integrated with the RPDR and tighter integration of the RPDR with Epic. The specific areas of focus of the Big Data Commons are to create a Research Patient Portal for direct patient engagement in Epic, creating a distributed query system to allow more types of Partners Big Data to be integrated and become discoverable by researchers, and specific integration platforms such as the Biobank Portal which serve to researchers new forms of Big Data in easily consumable forms.

Research Patient Data Registry

Research Patient Data Registry (RPDR)

RPDR Daily Query Tool

The RPDR has a new Daily Query Tool where users can qu

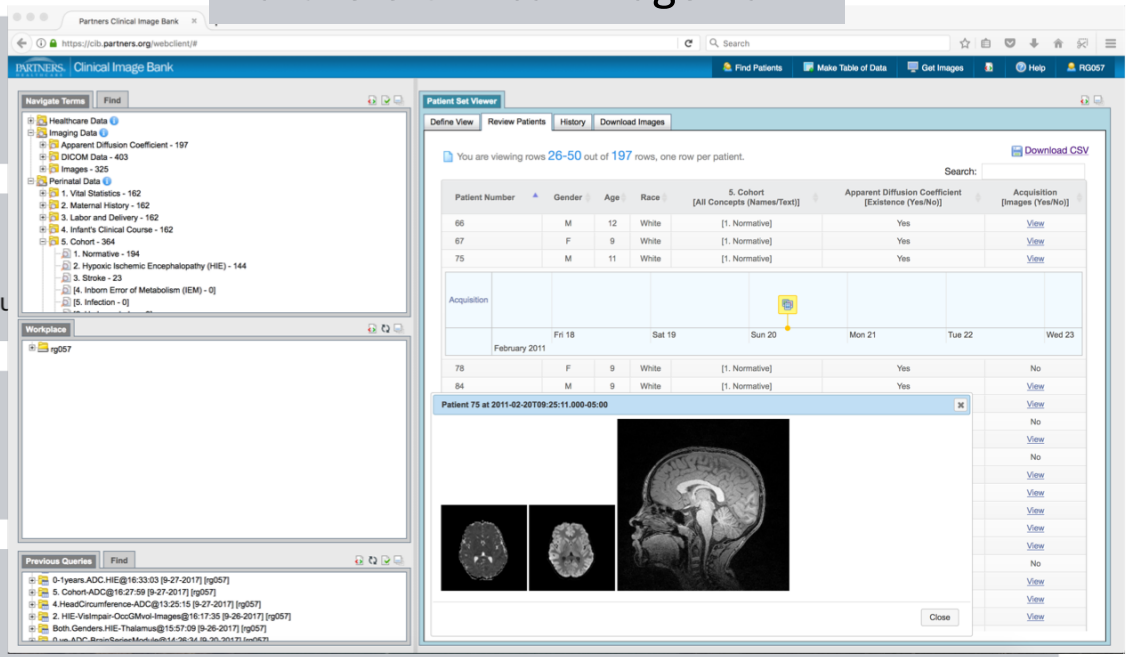
Partners Biobank Portal

Biobank Portal

mi2B2 Medical Image Access Tool

mi2B2 Medical Image Access Tool

Partners Clinical Image Bank



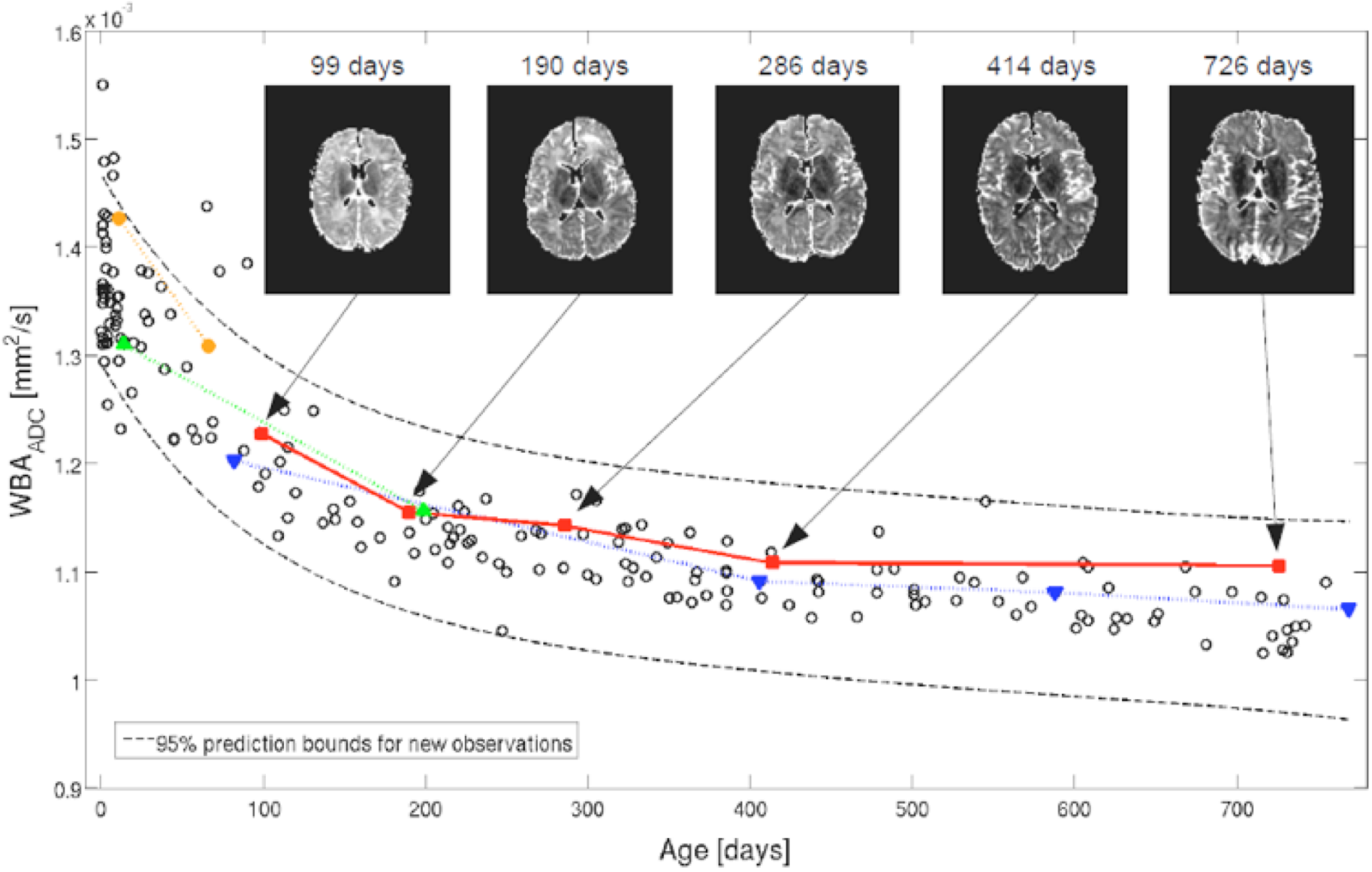
Amassing Pediatric Brain MRI's to Understand "Normal" using Mi2b2

P. Ellen Grant, Yangming Ou, Lilla Zollei, Rudolph Pienaar, Steve Pieper, Sara Bates, Shawn N. Murphy, Randy L. Gollub

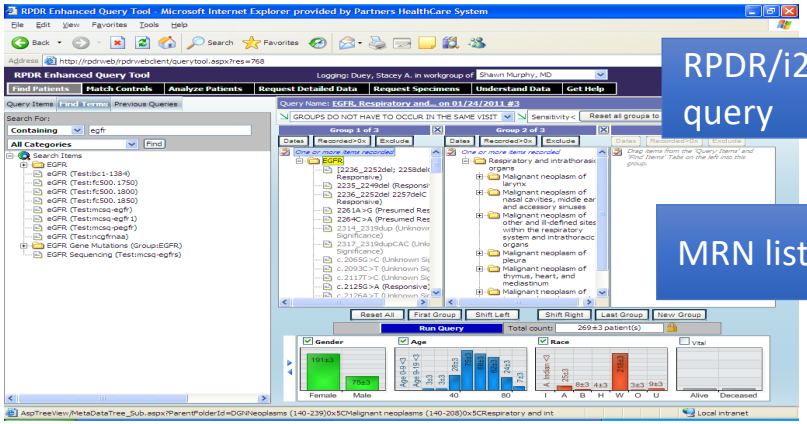
Partners Healthcare System, Children's Hospital Boston, and Massachusetts General Hospital, Boston, MA

Images Of Baby Brains: Priceless

- Whole-brain ADC from 100s of infants allow benchmarking



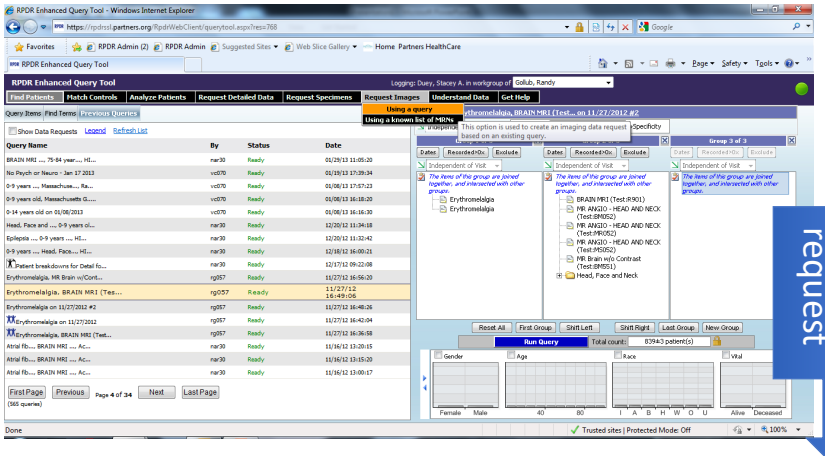
Using the Medical Imaging Informatics Bench to Bedside (mi2b2) Workbench



RPDR/i2b2 query

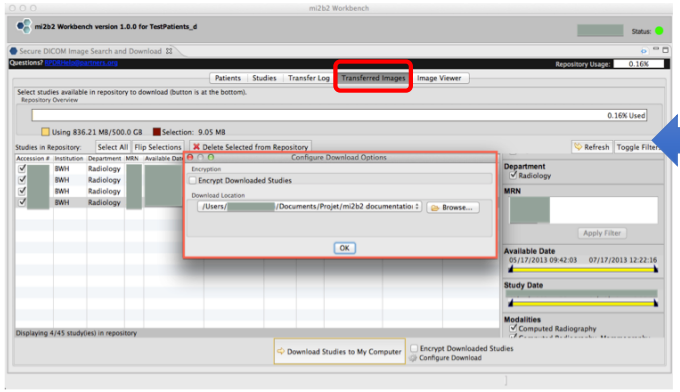
or

MRN list

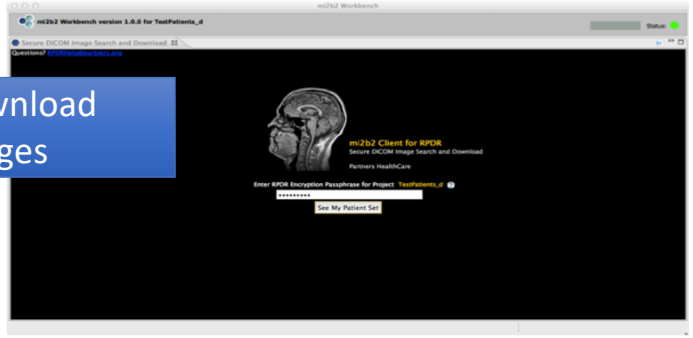


Mi2b2 request

HIPAA compliant mi2b2 Workbench restricts access of investigator to the patient cohort identified in associated IRB, data pulls are audit logged



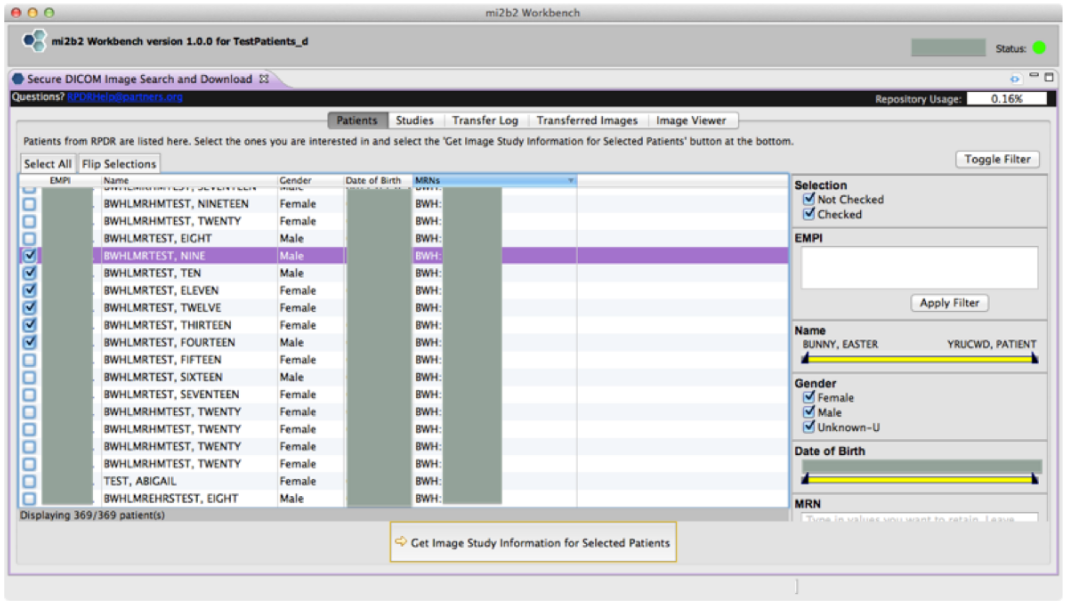
Download images



Murphy SN, Wang Y, Wang TD, Sack D, Reynolds N, Plesniak W, Andriole K, Wei J, Pieper S, Herrick C, Gollub RL. High throughput tools to access images from clinical archives for research, J Digit Imaging. 2015 Apr;28(2):194-204. doi: 10.1007/s10278-014-9733-9

Data Collection- RPDR + mi2b2

To get



Mi2b2 engine: https://www.nmr.mgh.harvard.edu/lab/mi2b2
Lead: Shawn Murphy, Randy Gollub (MGH) [Murphy et al, 2015]

To vet

N=~100,000
- Brain MRI in MGH

N = 2,871
- Scanned 2006-2013 with ADC maps in Siemens 3T scanner
- 0-6 years old at the time of scan
- Radiological reports suggesting free of abnormality

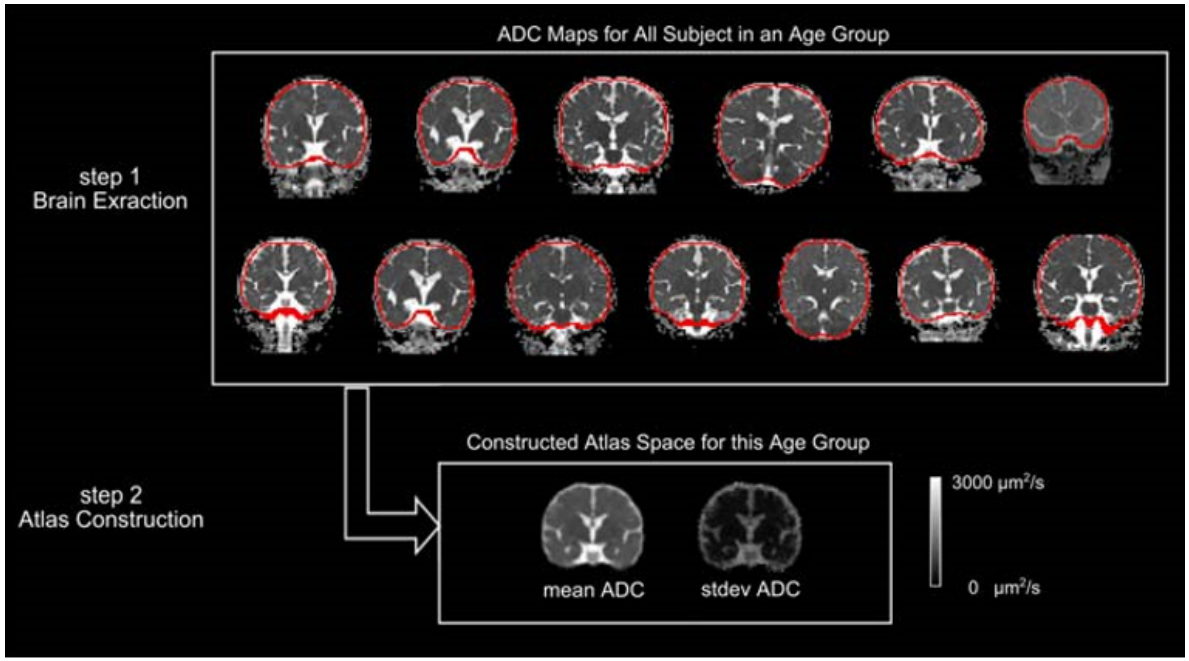
N = 1,648
- ADC maps found and not corrupted

N = 705
- ADC maps re-examined & confirmed to be normal by a neuro-radiologist (Dr. Grant) and a neonatologist (Dr. Bates)

N = 201
- Duplicates and CNS morbidity removed
- Still normal 3 years after the initial visit

Data Analysis Approach – Atlas Construction

Age	Y1					Y2	Y3	Y4	Y5	Y6	**Total**
	W1-2	Rest of Q1	Q2	Q3	Q4						
# Subjects	13	13	8	8	13	34	33	25	21	33	**201**
# Females	4	5	4	5	5	17	14	14	10	15	**93**

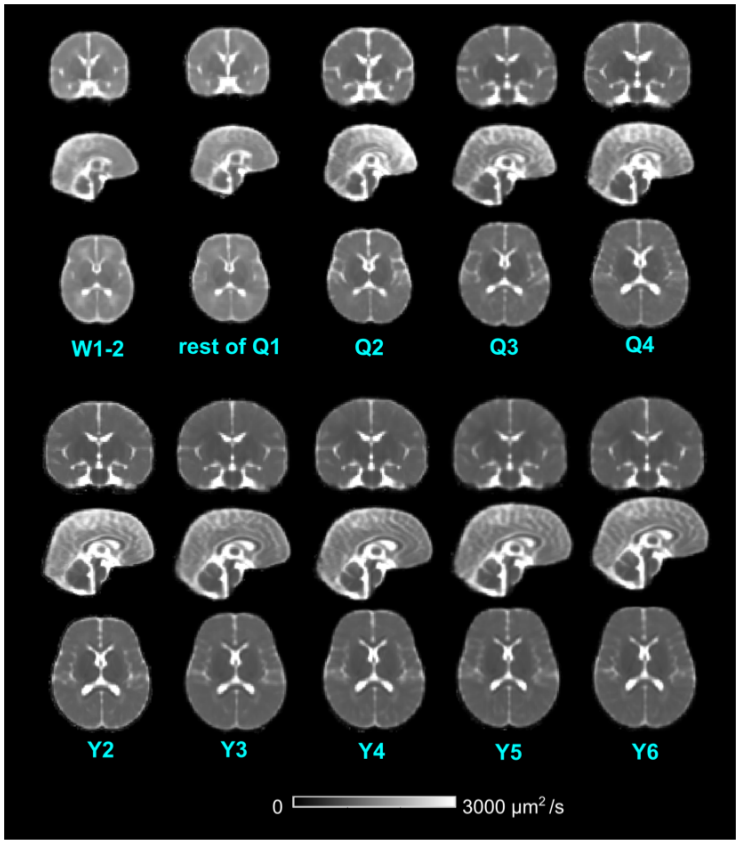


[Software for Atlas Construction]
* Ou et al, https://www.nitrc.org/projects/popdramms

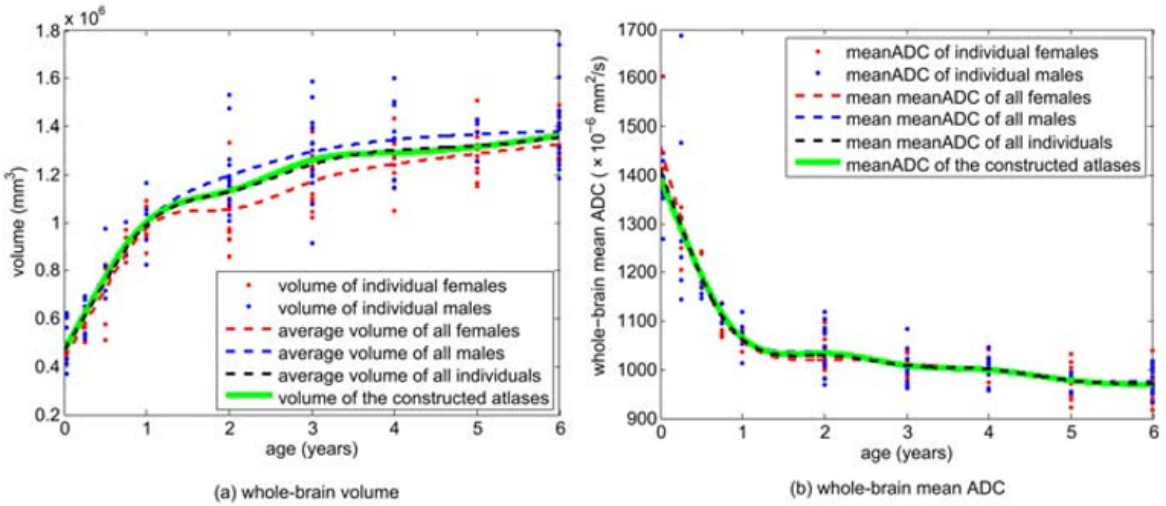
[Atlases released]
* Ou et al,
https://www.nitrc.org/projects/mgh_adcatlases

Ou Y, Zollei L, Retzepi K, Castro V, Bates SV, Pieper S, Andriole KP, Murphy SN, Gollub RL, Grant PE, Human Brain Mapping, 2017

Validation – are the atlases right?



a) Whole-brain volume and ADC values, and changes



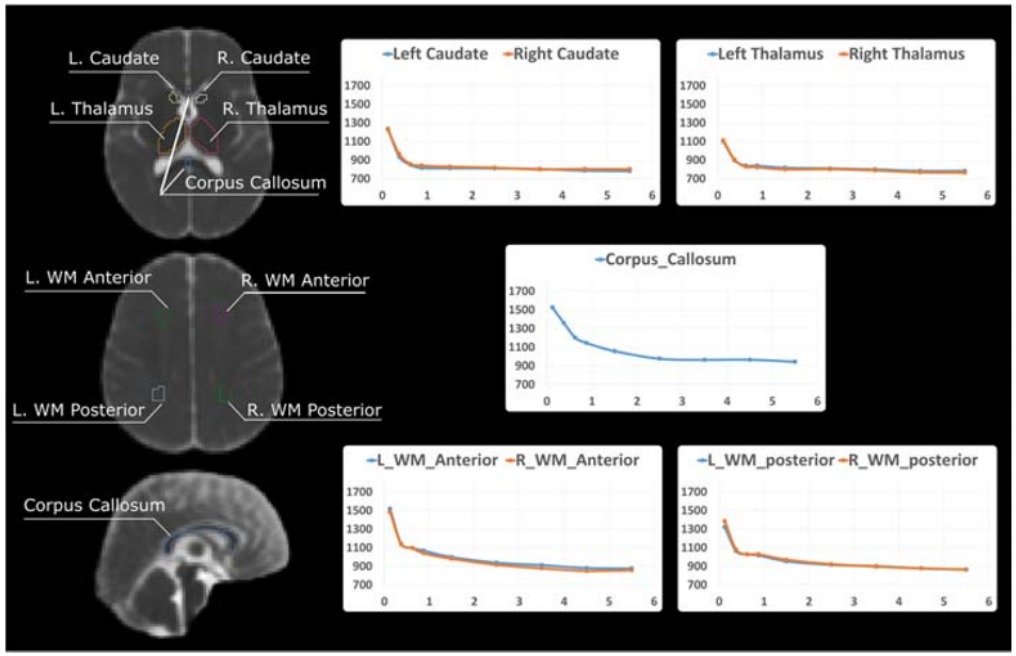
Statistically, at each age,

measurements from 1 atlas == measurements from multiple individuals

Ou Y, et al, Human Brain Mapping, 2017

Validation – are the atlases right?

b) Regional and voxel-wise ADC values, and changes



	birth	Q1	Q2	Q3	Q4	Y2	Y3	Y4	Y5	Y6	20-40yo	Imaging protocol
Caudate												
Our atlases (L)		1235	936	848	814	812	810	804	786	781		Siemens 3T, 2x2x2 mm, b=1000
Our atlases (R)		1226	965	857	840	829	817	800	803	802		
Neil et al [6]	1240											Siemens 1.5T, 2x2x5mm, b=987/800
Sener et al [3]							820					Siemens 1.5T, b=1000
Thalamus												
Our atlases (L)		1101	899	840	840	818	809	799	783	782		Siemens 3T, 2x2x2 mm, b=1000
Our atlases (R)		1111	904	829	823	800	796	789	768	765		
Neil et al [6]	1080											Siemens 1.5T, 2x2x5mm, b=987/800
Sener et al [3]			980					830				Siemens 1.5T, b=1000
Helenius et al [24]											730	Siemens 1.5T, 2x2x5mm, b=1000
Naganawa et al [25]											830-910	Siemens 1.5T, 2x2x6mm, b=1000
Kwan et al [16]	1075	1020										Phillips 3T, 1.8x1.8x1.8mm, b=750
Corpus Callosum												
Our atlases		1524	1359	1204	1145	1057	976	963	960	942		Siemens 3T, 2x2x2 mm, b=1000
Morriss et al [20] (L genu)	1540			1310	1130	940	1080		869			Siemens 1.5T, 2x2x5mm, b=1000
Morriss et al [20] (R genu)	1470			1330	1320	950	1060		933			
Morriss et al [20] (L splenium)	1380			1410	1350	1180	1180		950			
Morriss et al [20] (R splenium)	1380			1240	1350	1030	1120		960			
Zhai et al [21] (genu)	~1200										~780	Siemens 3T, 1.72²x5mm, b=1000
Zhai et al [21] (splenium)	~1150										~850	
Engelbrecht et al [8] (genu)	1280						760					Siemens 1.5T, 2x2x5mm, b=1000
Engelbrecht et al [8] (splenium)	1410						770					
Provenzale et al [74] (genu)			1180									GE 1.5T, 3x3x5mm, b=1000
Provenzale et al [74] (splenium)			1110									
Sadeghi et al [23]	~1350				~1050	~950						Siemens 3T, 2x2x2mm, b=1000
White Matter (Anterior)												
Our atlases (L)		1517	1142	1096	1037	998	938	911	880	875		Siemens 3T, 2x2x2 mm, b=1000
Our atlases (R)		1483	1137	1094	1039	980	915	877	850	856		
Neil et al [6]	1450											Siemens 1.5T, 2x2x5mm, b=987/800
Zhai et al [21]	~1500										~750	Siemens 3T, 1.72²x5mm,b=1000
Engelbrecht et al [8]	1500						920					Siemens 1.5T, 2x2x5mm, b=1000
Helenius et al [24]											710	Siemens 1.5T, 2x2x5mm, b=1000
Naganawa et al [25]											780-860	Siemens 1.5T, 2x2x6mm, b=1000
Provenzale et al [74]			1330									GE 1.5T, 3x3x5mm, b=1000
Kwan et al [16]	1760	1508										Phillips 3T, 1.8x1.8x1.8mm, b=750
Whiter Matter (Posterior)												
Our atlases (L)		1322	1064	1029	1017	952	915	900	876	865		Siemens 3T, 2x2x2 mm, b=1000
Our atlases (R)		1385	1081	1027	1028	970	921	896	877	863		
Neil et al [6]	1500											Siemens 1.5T, 2x2x5mm, b=987/800
Zhai et al [21]	~1550										~880	Siemens 3T, 1.72²x5mm,b=1000
Engelbrecht et al [8]	1640						900					Siemens 1.5T, 2x2x5mm, b=1000
Helenius et al [24]											710	Siemens 1.5T, 2x2x5mm, b=1000
Kwan et al [16]	1494	1379										Phillips 3T, 1.8x1.8x1.8mm, b=750

measures from 1 atlas ~ measures from multiple individuals

Ou Y, et al, Human Brain Mapping, 2017

Most common cause of Neonatal Brain Injury is Hypoxic Ischemic Encephalopathy (HIE)

- HIE occurs in 2-6/1000 infants, most common in term infants
- Therapeutic hypothermia is now the standard treatment
- Survivors often suffer from long-term neuro-cognitive deficits

Figure from cerebralpalsy.org

Standard of care includes brain MRI in first days of life. At MGH, state of the art, research quality acquisition protocol including DWI and quantitative ADC maps was established in 2008 and has been stable since.

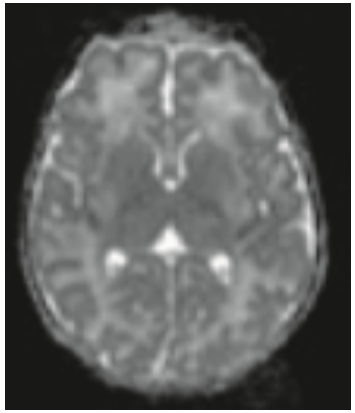
Early MRI in term infants with perinatal hypoxic–ischaemic brain injury: Interobserver agreement and MRI predictors of outcome at 2 years

Goergen, et al, Clinical Radiology, 2014

Yet, 20-50% intra-/inter-rater variability or uncertainty even for experienced pediatric neuroradiologists!

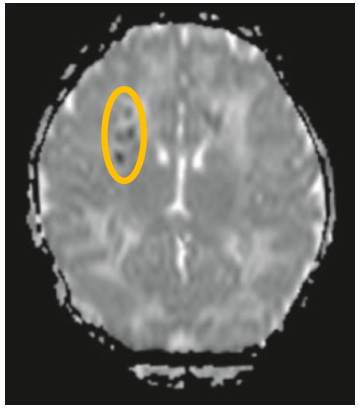
Detecting HIE Injury is difficult

- Gold Standard: Apparent Diffusion Coefficient (ADC) maps
- Abnormally low ADC values => restricted diffusion => lack of oxygen/blood
- Q: How low is too low? What is within normal variation?



Gano et al, Ped. Res., 2012

An easy case



De Veris et al, BMJ, 2010

More challenging cases

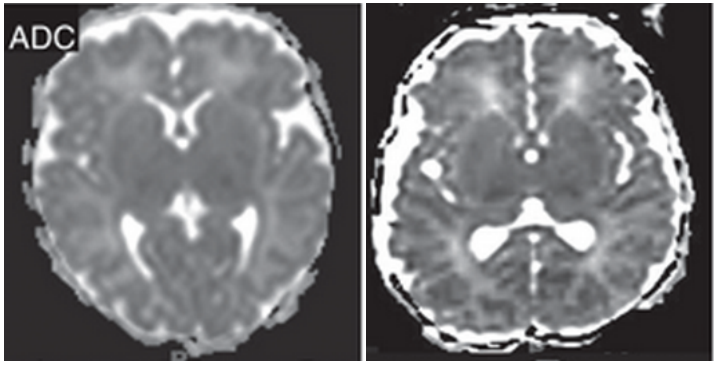
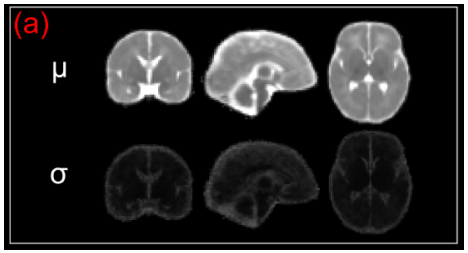


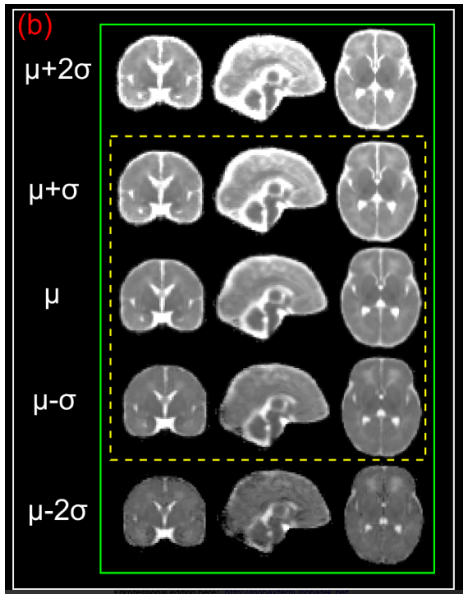
Figure from Howlett et al, Ped Res, 2013

Atlas-based Abnormality Detection --- A naïve but intuitive approach

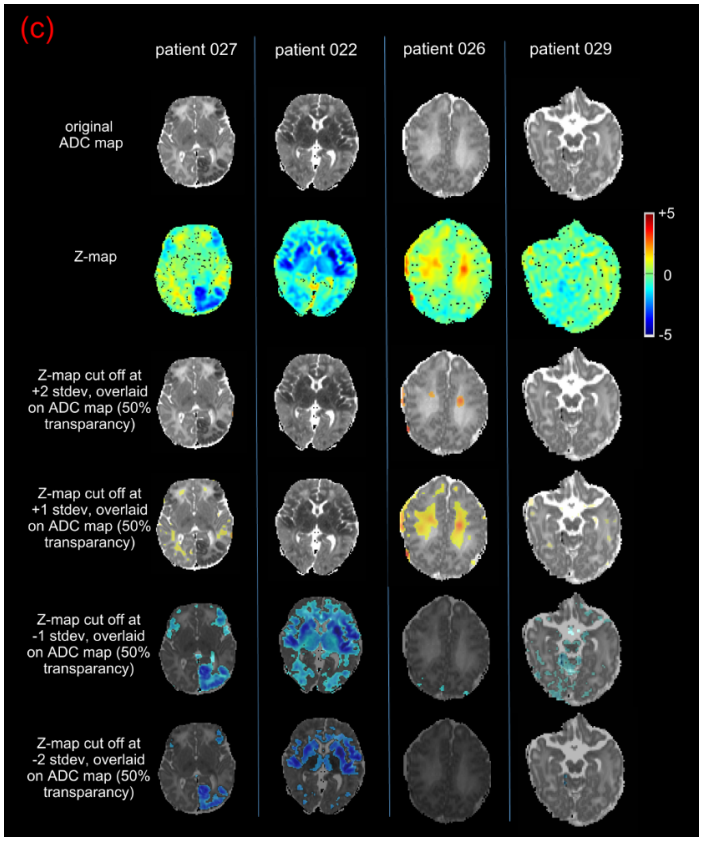
Atlases



Quantification of **Voxel-wise** "Normal ADC Variations"



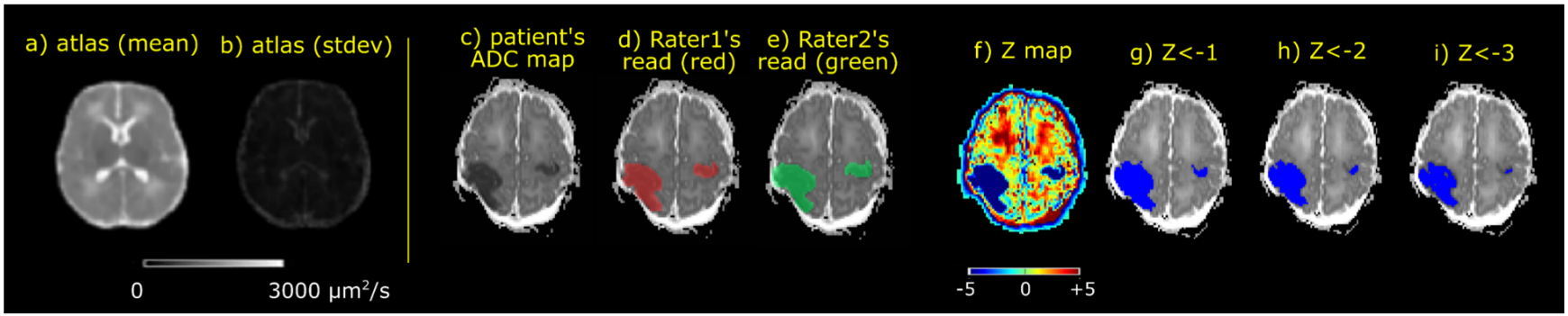
Atlas-based HIE detection



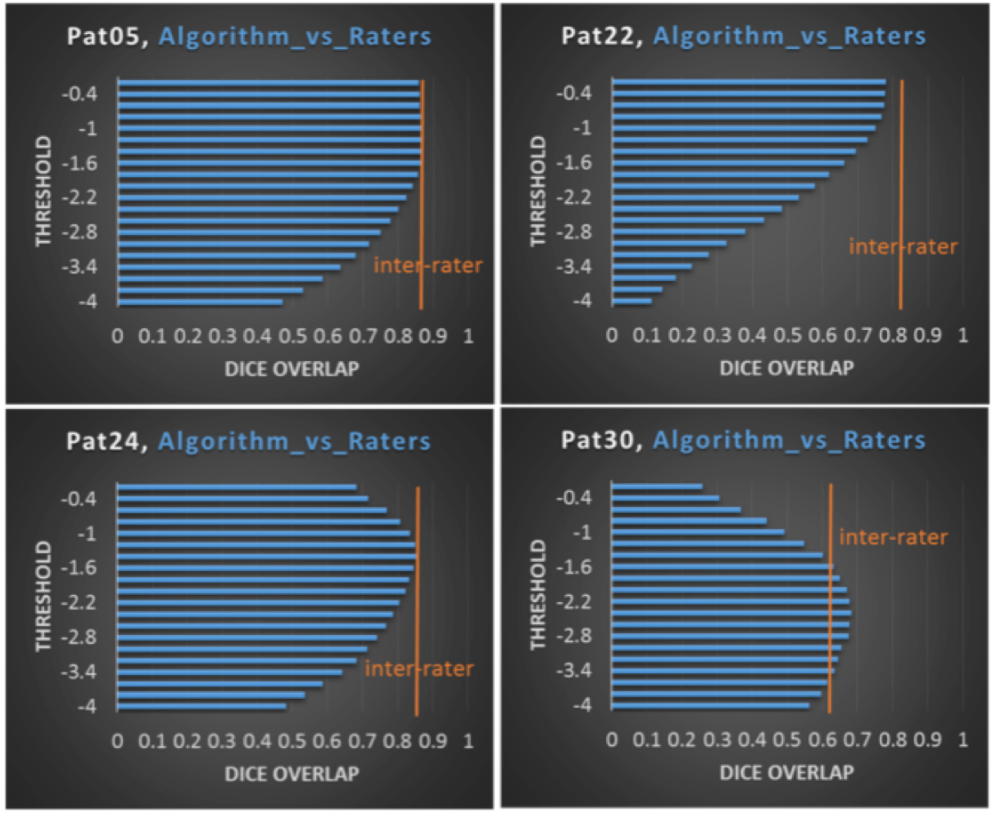
* Ou et al, OHBM, 2015, 2017

Accuracy of Z-map Approach

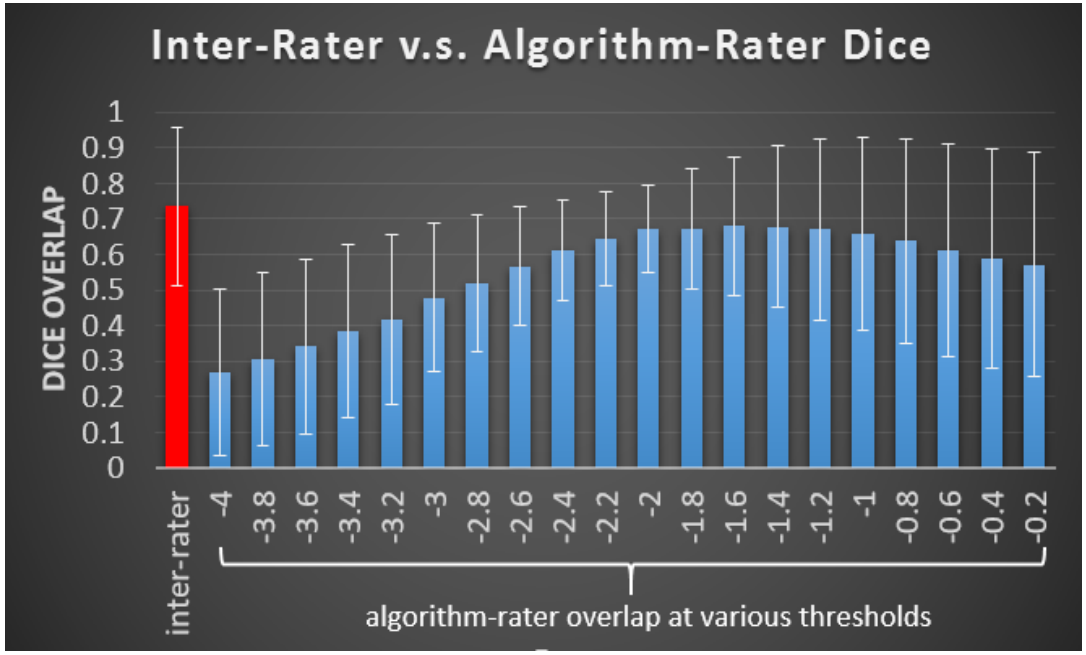
- Compare with expert annotations
- Machine-vs-Human =?= Human-vs-Human



Inter-rater Dice overlap compared to algorithm-rater Dice overlap

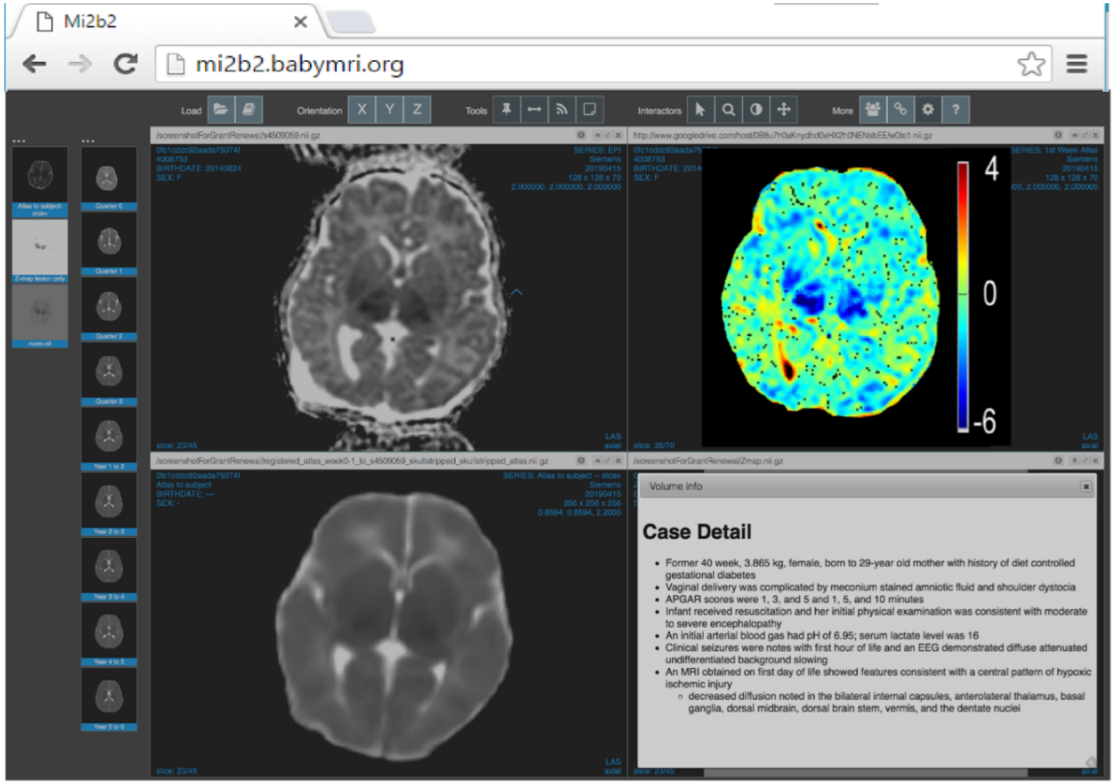


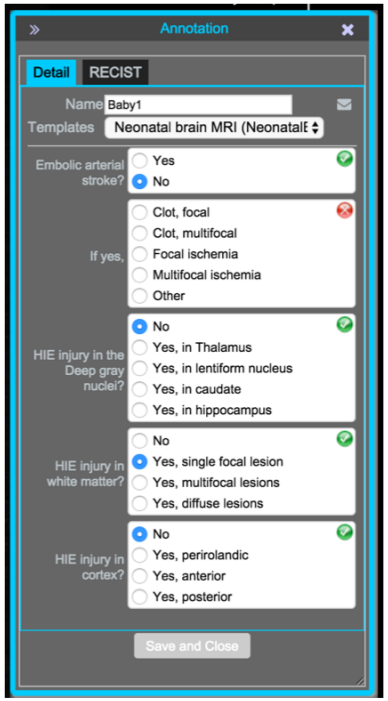
Accuracy of Z-map Approach (n = 6 cases, n =2 raters



An atlas-based **naïve** Z-map approach can provide a **good initiation** for lesion detection, approaching the accuracy of human experts

Ongoing Work –
Bring to Radiology Classroom and Reading Room

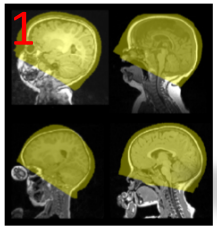


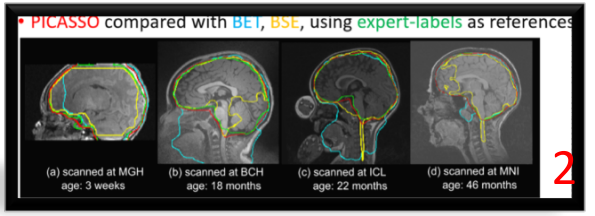


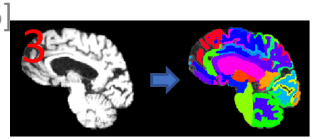
Structured Report template

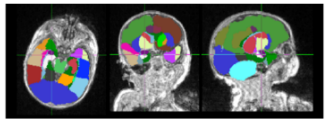
Image analysis approach

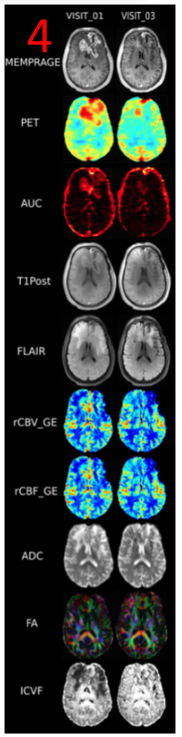
- 1. Field of View Normalization [Ou'16 (pending)]
https://www.nitrc.org/projects/normalizefov
- 2. Skull Stripping [Ou'14; Doshi'14; Ou'16]
https://www.nitrc.org/projects/picasso
- 3. Automatic Structural Segmentation [Ou'14; Doshi'16]
https://www.cbica.upenn.edu/sbia/software/MUSE
- 4. Multi-modal/channel Fusion [Ou'11, '14]
https://www.nitrc.org/projects/dramms
- 5. Tissue Density and Morphometry [Davatzikos'97; Ou'11, '14]
https://www.cbica.upenn.edu/sbia/software/dramms/tools/ravens.html
- 6. Atlas Construction [Ou'14, '15, '16 (u.r.)]
https://www.nitrc.org/projects/popdramms
- 7. Lesion Detection [Ou'07, '09, '16a, '16b (u.r)]
- 8. Longitudinal Change Quantification [Ou'15]
https://www.cbica.upenn.edu/sbia/software/dramms
- 9. Machine learning to predict clinical variables [Ou'09; '16 (u.r.)]

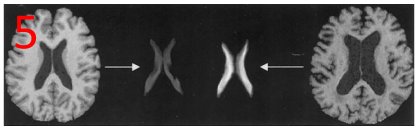


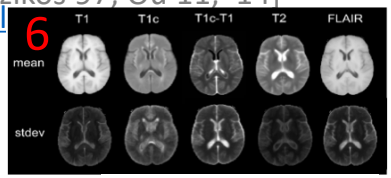


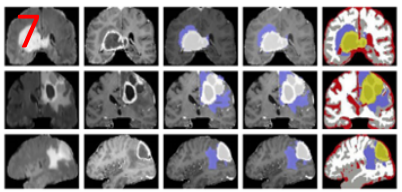


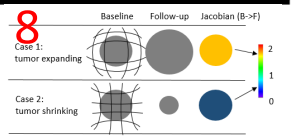


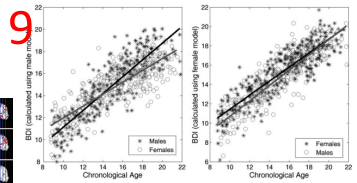


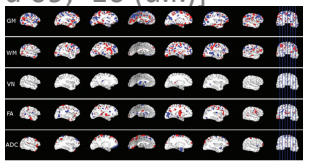












Based on DRAMMS Registration (2, 3, 4, 5D) [Ou'11, '12, '14a,b, '15]

Based on BEFI Machine Learning [Ou'09, '17 (u.r.)]

Acknowledgements

Neonatology
Sara Bates
Joseph Chou
Emily Herzberg
Yieh-Cheh Chen
Rebecca Weiss

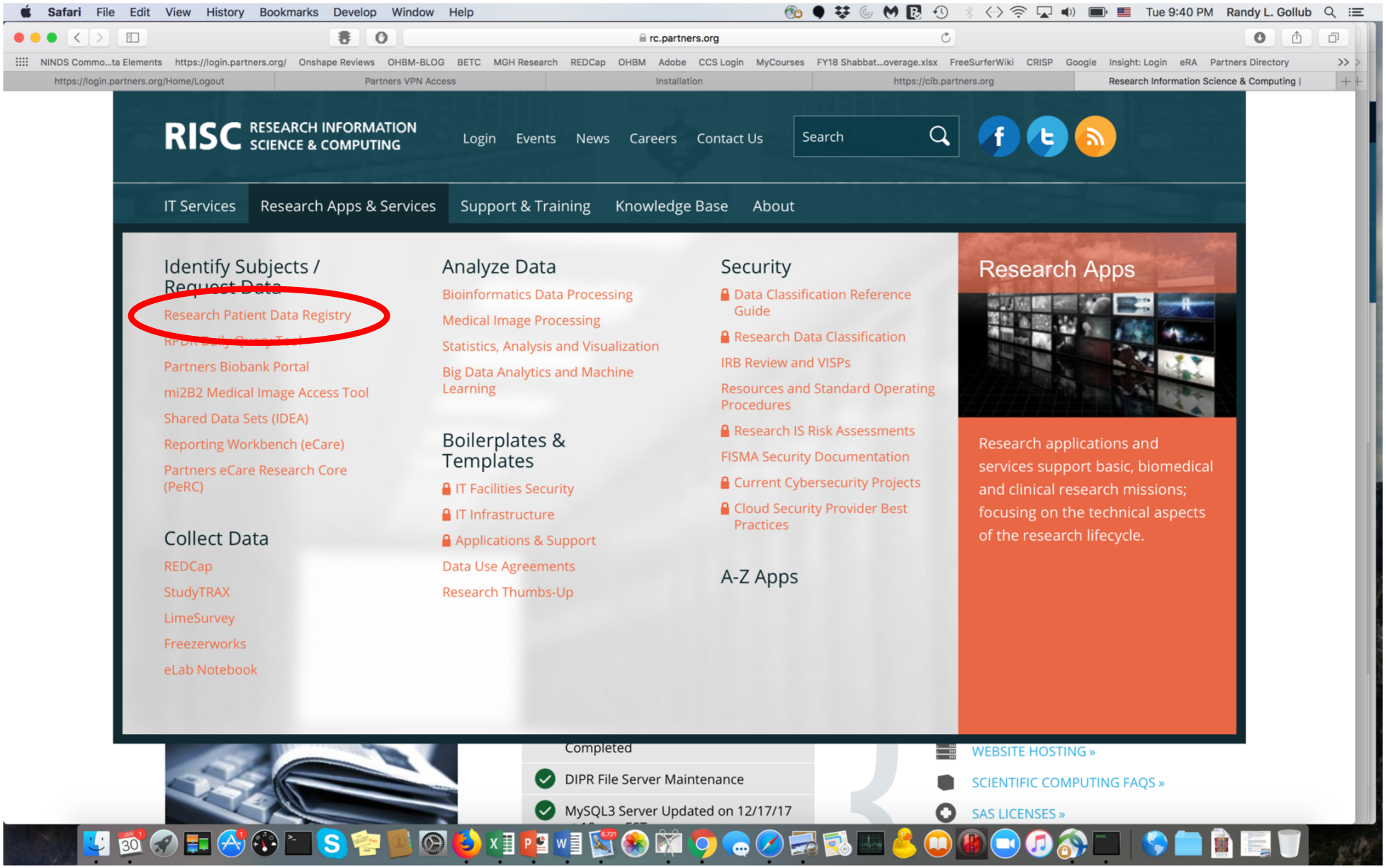
Imaging Informatics
Lilla Zollei
Steve Pieper
Kathy Andriole

Clinical Informatics
Shawn N Murphy
Yanbing Wang
Chris Herrick
David Wang

Boston Childrens Hospital
P. Ellen Grant
Yangming Ou
Rudolph Pienaar

FUNDING:
Partners Healthcare, NIH/NCBC; /NIMH; /NCBI; /NCATS; /NIBIB
NIH RO1 EB014947

rc.partners.org



Research Patient Data Registry

HIDE

Overview of the RPDR

The Research Patient Data Registry (RPDR) is a centralized clinical data registry, or data warehouse that gathers clinical information from various Partners hospital systems. An online Query Tool allows researchers to explore clinical data through a self-service system in order to:

- Assess clinical study feasibility
- Identify patients for clinical trials
- Investigate hospital operations and patient care
- Provide identified patient data with approved IRB protocol
- Find control patients for previously defined populations
- Search clinical notes for specific text terms and phrases in order to identify patient cohorts who have notes/reports that contain the searched text.
- Query for patients with blood samples in the Partners Biobank
- Supply a workbench that allows viewing and download access for MGH and BWH Radiology images

The RPDR ensures the security of patient information by controlling and auditing the distribution of patient data within the guidelines of the IRB and with the use of several built-in, automated security measures. The online search in real time results in a faster data turnaround with extensive specificity of patient criteria.

Functions of the RPDR

The RPDR has two related but separate functions:

- The online query tool provides users with aggregate numbers of patients that meet user-defined characteristics and criteria such as diagnoses, procedures, medications and/or laboratory results.
- The Data Request Wizards allow the user to ask for more detailed medical record information on the identified patient population. **This process requires an approved IRB protocol.**

Obtaining access to the RPDR

In order to use the RPDR, a person must first become registered in the RPDR system. Registration is handled differently for faculty vs. non-faculty members.

RPDR Access

In order to use the RPDR, a person must first become registered in the RPDR.

- Obtaining Access to the RPDR »
- RPDR Tools »
- Training »

CONTACT RPDR SUPPORT »

RPDR Contacts

For help with the RPDR, please contact:

Laurie Bogosian- User Liaison »
857 282-3746

Stacey Duey - Project Specialist »
617 759-8248

Mariah P. Mitchell - Corporate Manager- RPDR Group »
857 282-3767

Chris Herrick - Director of the RPDR Group »
857 282-3758

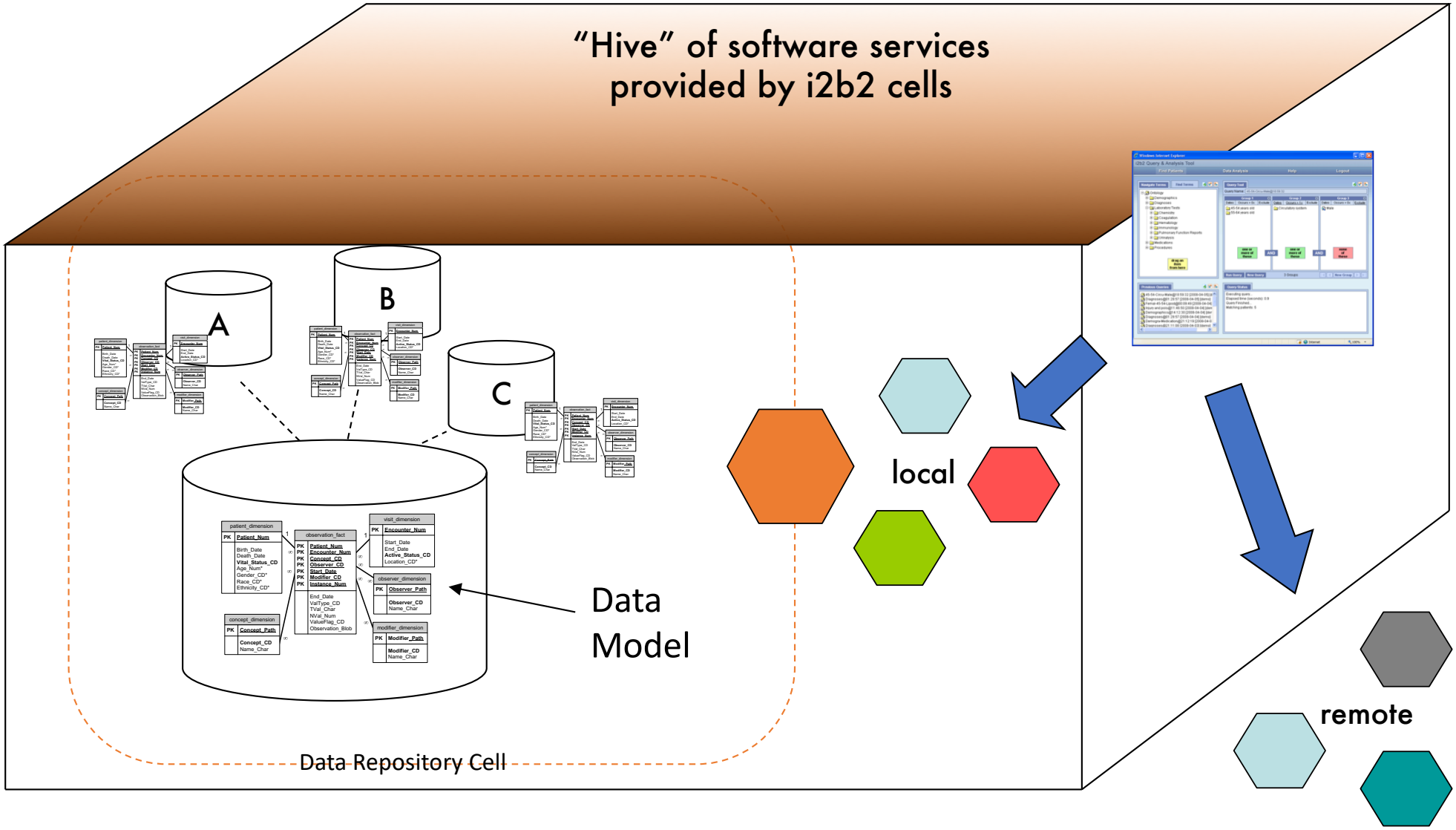
Shawn N. Murphy, MD, PhD Designer of the RPDR & Director for RISC »
857 282-3769

RPDR MAILBOX »

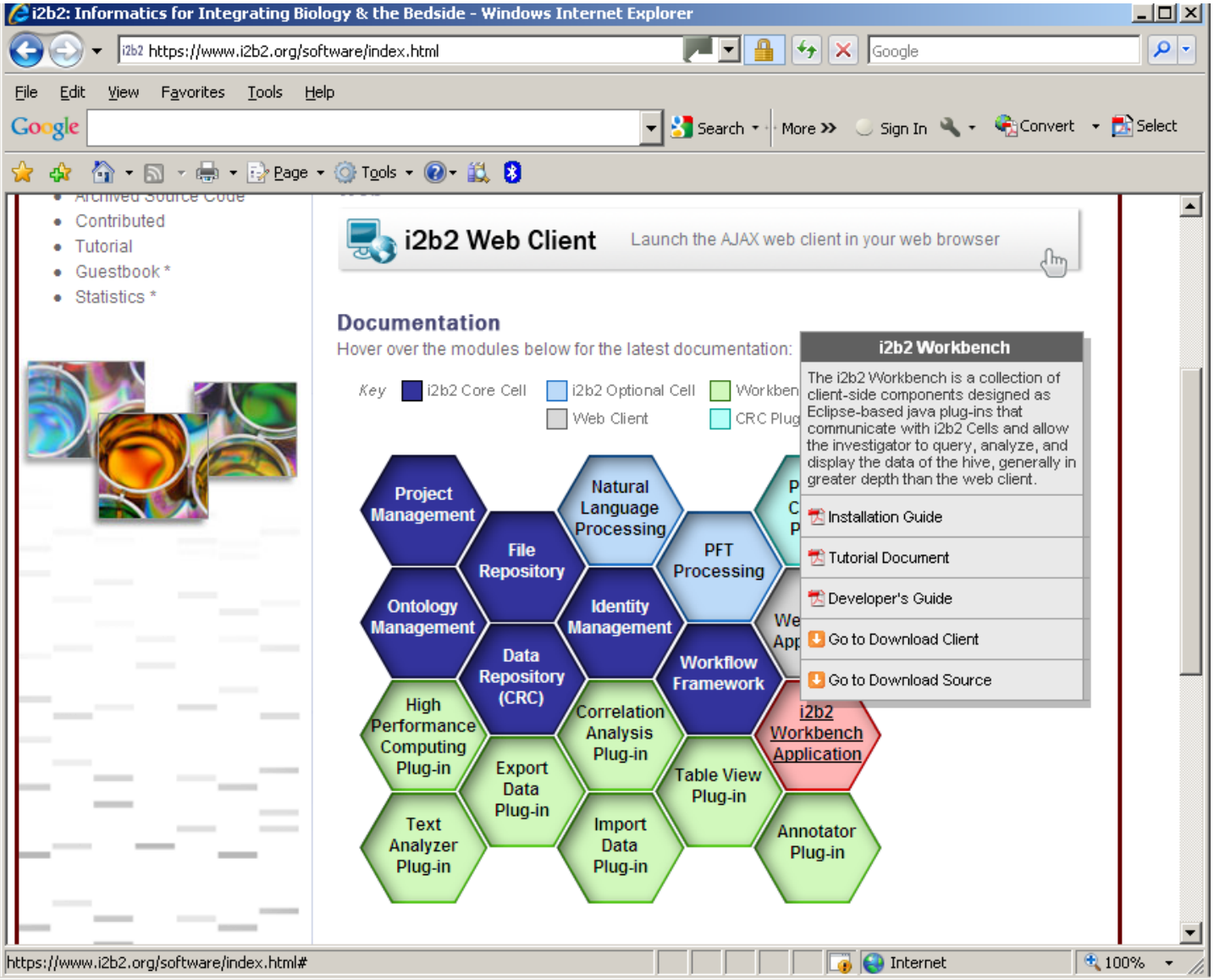
RPDR Evolved into international “Informatics for Integrating Biology and the Bedside (i2b2)” sponsored by the National Institutes of Health, what is it?

- Software for explicitly organizing and transforming person-oriented clinical data to a way that is optimized for clinical genomics research
  - Allows integration of clinical data, trials data, and genotypic data
- A portable and extensible application framework
  - Software is built in a modular pattern that allows additions without disturbing core parts
  - Available as open source at https://www.i2b2.org

An i2b2 Environment (the Hive) is built from i2b2 Cells



I2b2 Software components are distributed as open source



Implementations (a sampling)

CTSA's

- Boston University
- Case Western Reserve University (*including Cleveland Clinic*)
- Children's National Medical Center (GWU), Washington D.C.
- Duke University
- Emory University (*including Morehouse School of Medicine and Georgia Tech*)
- Harvard University (*including Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Children's Hospital Boston, Dana Farber Cancer Center, Joslin Diabetes Center, Massachusetts General Hospital*)
- Medical University of South Carolina
- Medical College of Wisconsin
- Oregon Health & Science University
- Penn State MIlton S. Hershey Medical Center
- Tufts University
- University of Alabama at Birmingham
- University of Arkansas for Medical Sciences
- University of California Davis
- University of California, Irvine
- University of California, Los Angeles*
- University of California, San Diego*
- University of California San Francisco
- University of Chicago
- University of Cincinnati (including *Cinncinati Children's Hospital Medical Center*)
- University of Colorado Denver (including *Children's Hospital Colorado*)
- University of Florida
- University of Kansas Medical Center
- University of Kentucky Research Foundation
- University of Massachusetts Medical School, Worcester
- University of Michigan
- University of Pennsylvania (including *Children's Hospital of Philadelphia*)
- University of Pittsburgh (including their *Cancer Institute*)
- University of Rochester School of Medicine and Dentistry
- University of Texas Health Sciences Center at Houston
- University of Texas Health Sciences Center at San Antonio
- University of Texas Medical Branch (Galveston)
- University of Texas Southwestern Medical Center at Dallas
- University of Utah
- University of Washington
- University of Wisconsin - Madison (*including Marshfield Clinic*)
- Virginia Commonwealth University
- Weill Cornell Medical College

Academic Health Centers (does not include AHCs that are part of a CTSA):

- Arizona State University
- City of Hope, Los Angeles
- Georgia Health Sciences University, Augusta
- Hartford Hospital, CN
- HealthShare Montana
- Massachusetts Veterans Epidemiology Research and Information Center (MAVERICK), Boston
- Nemours
- Phoenix Children's Hospital
- Regenstrief Institute
- Thomas Jefferson University
- University of Connecticut Health Center
- University of Missouri School of Medicine
- University of Tennessee Health Sciences Center
- Wake Forest University Baptist Medical Center

HMOs:

- Group Health Cooperative
- Kaiser Permanente

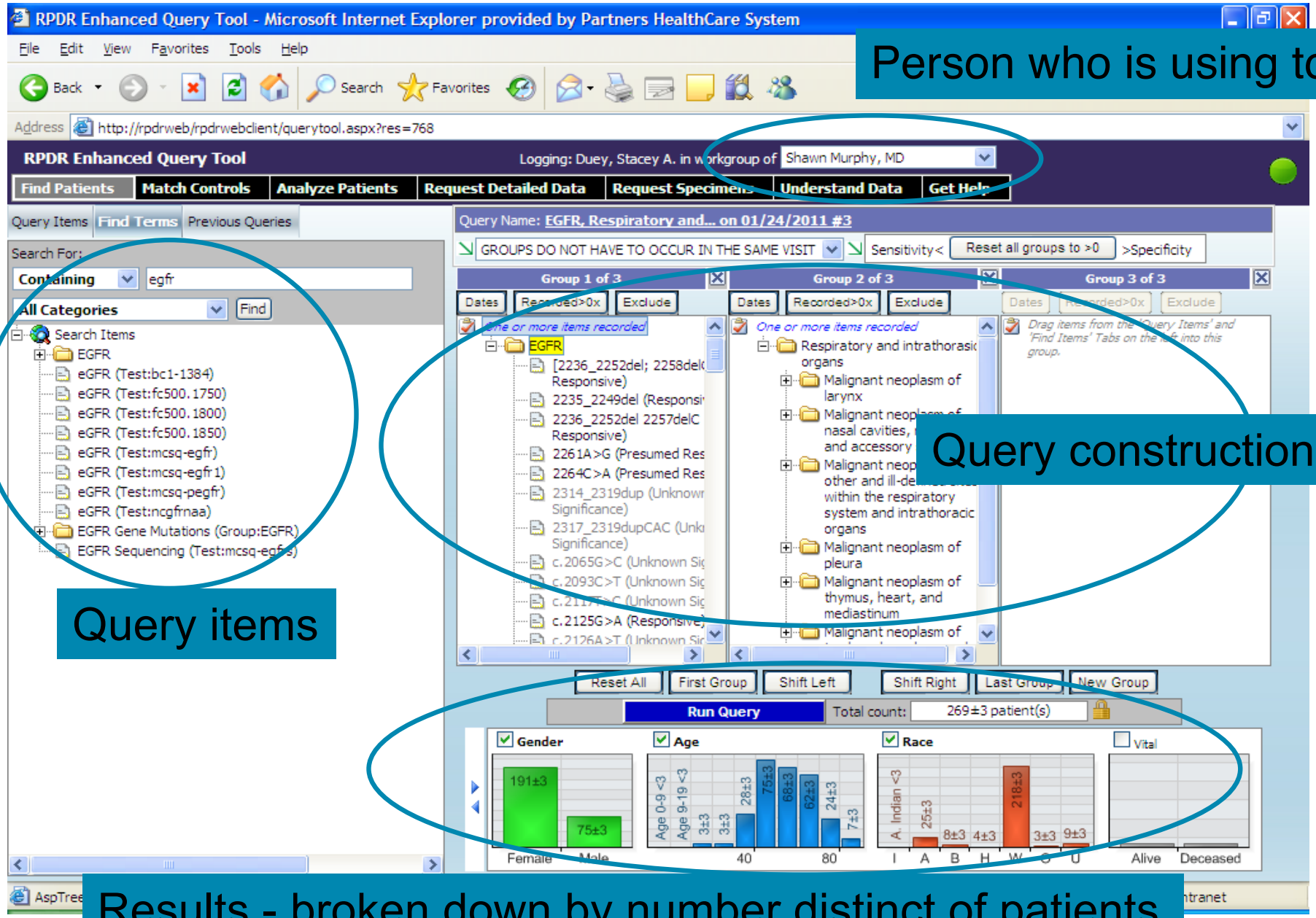
International:

- Georges Pompidou Hospital, Paris, France
- Hospital of the Free University of Brussels, Belgium
- Inserm U936, Rennes, France
- Institute for Data Technology and Informatics (IDI), NTNU, Norway
- Institute for Molecular Medicine Finland (FIMM)
- Karolinska Institute, Sweden
- Landspitali University Hospital, Reykjavik, Iceland
- Tokyo Medical and Dental University, Japan
- University of Bordeau Segalen, France
- University of Erlangen-Nuremberg, Germany
- University of Goettingen, Goettingen, Germany
- University of Leicester and Hospitals, England (Biomed. Res. Informatics Ctr. for Clin. Sci)
- University of Pavia, Pavia, Italy
- University of Seoul, Seoul, Korea

Companies:

- Johnson and Johnson (TransMART)
- GE Healthcare Clinical Data Services

Use RPDR to access detailed clinical data



Research Patient Data Registry

SHOW

Research Patient Data Registry (RPDR)

RPDR Daily Query Tool

SHOW

The RPDR has a new Daily Query Tool where users can query source systems which are updated in the RPDR on a daily basis.

Partners Biobank Portal

SHOW

Biobank Portal

mi2B2 Medical Image Access Tool

HIDE

mi2b2 - Medical Image Access Tool

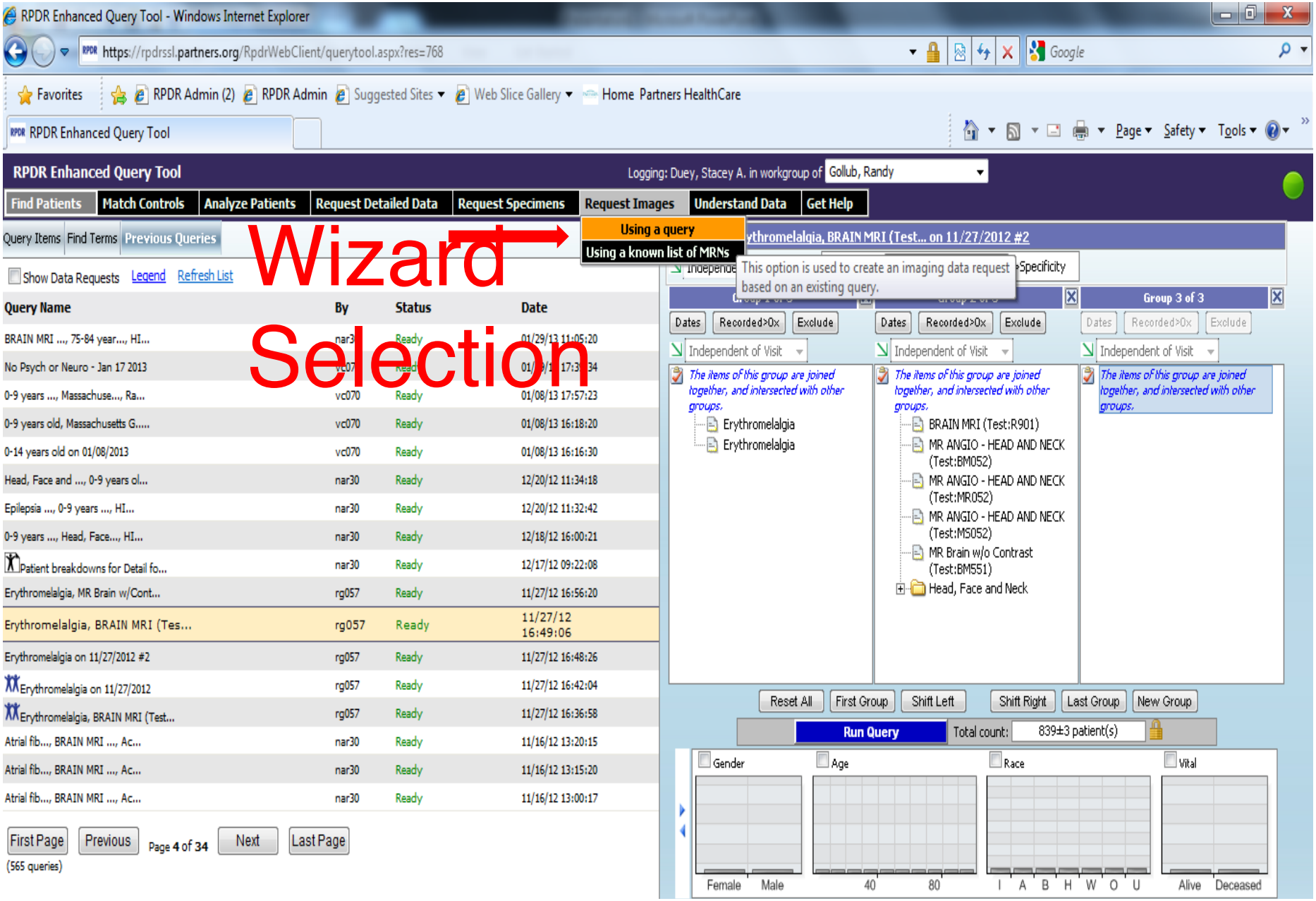
The Medical Imaging Informatics Bench to Bedside (mi2b2) workbench serves as a secure bridge between a researcher and the Partners PACS systems, which aims to:

- Facilitate searching for, previewing, and accessing clinically acquired images that are stored in several PACS (Picture Archive and Communication System) systems that serve the Partners institutions
- Enable researchers to extend the use of the Research Patient Data Registry (RPDR) to access clinical images on patients of interest for enhanced research studies, with proper IRB approval
- Enable efficient retrieval of medical images (DICOM format) for lists of patients generated from research, teaching and clinical activities in keeping with all regulatory guidelines
- Provide access to only patient images authorized by approved IRBs and provide audit trails for HIPAA compliance.

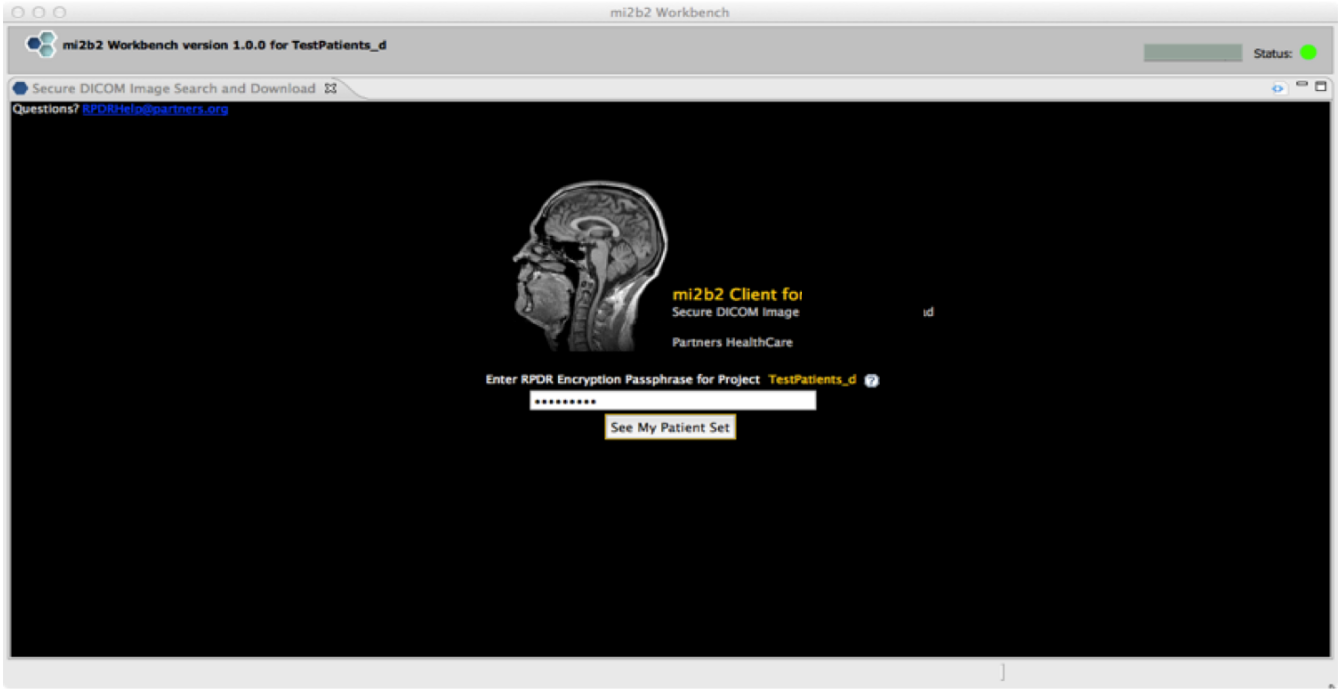
If using the RPDR Query tool and the RPDR Data Acquisition Engine (Image Request Wizard), a user can obtain aggregate numbers of patients with user-defined characteristics based on a query or upload a pre-defined list of Medical Record Numbers and then receive more detailed medical information about the queried patient cohort. Either way, the user is provided with a personalized mi2b2 workbench, directly configured to include the queried cohort information. It is delivered in an folder along with the encrypted RPDR data results. For instructions on how to use the RPDR to request mi2b2 workbench, please visit: (http://RPDR) ->Help -> Request Images Help.

Detailed tutorial support for new users of the mi2b2 software is found at http://mi2b2help.partners.org.

Use mi2b2 to access large medical image sets



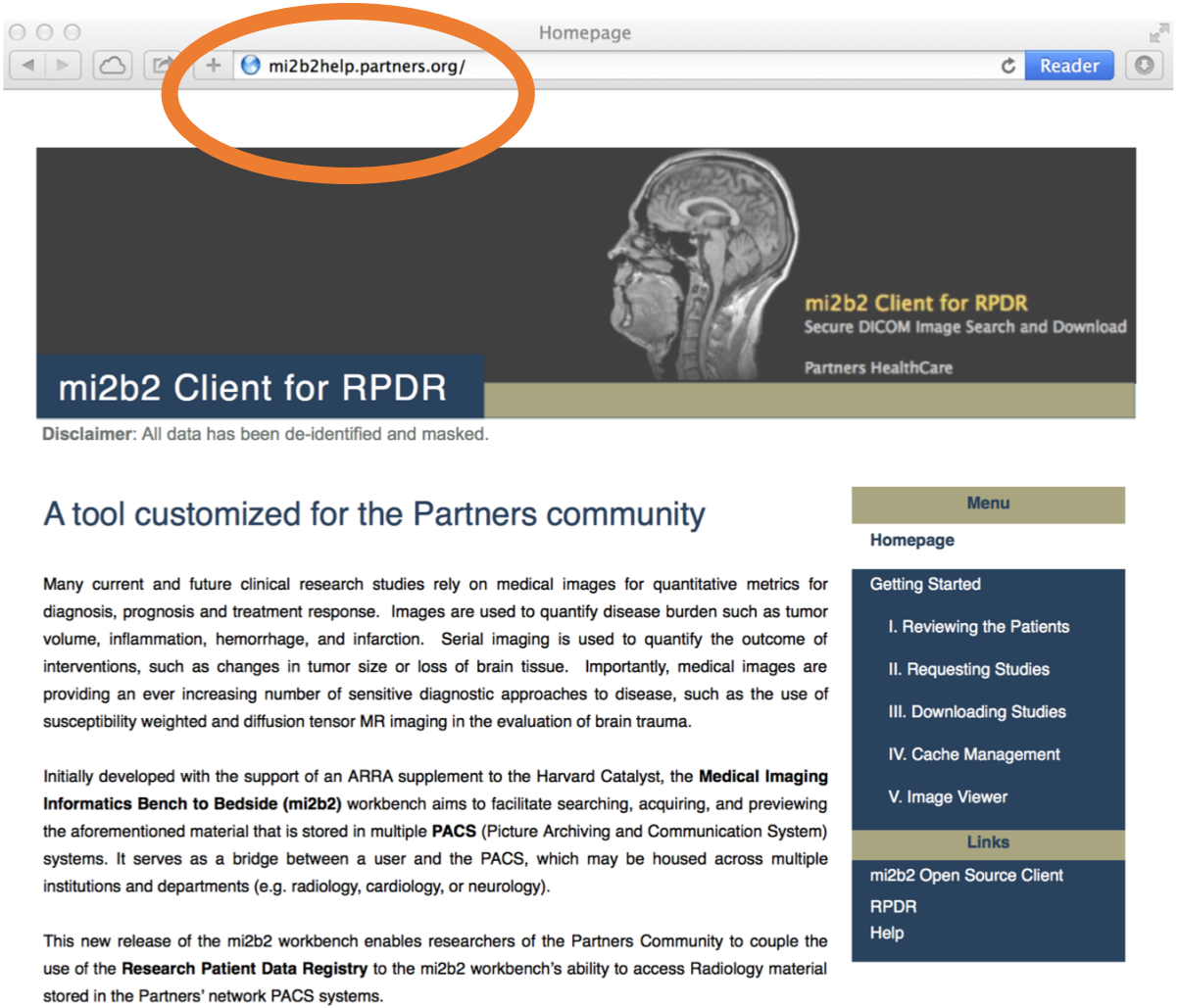
MI2B2 Workbench



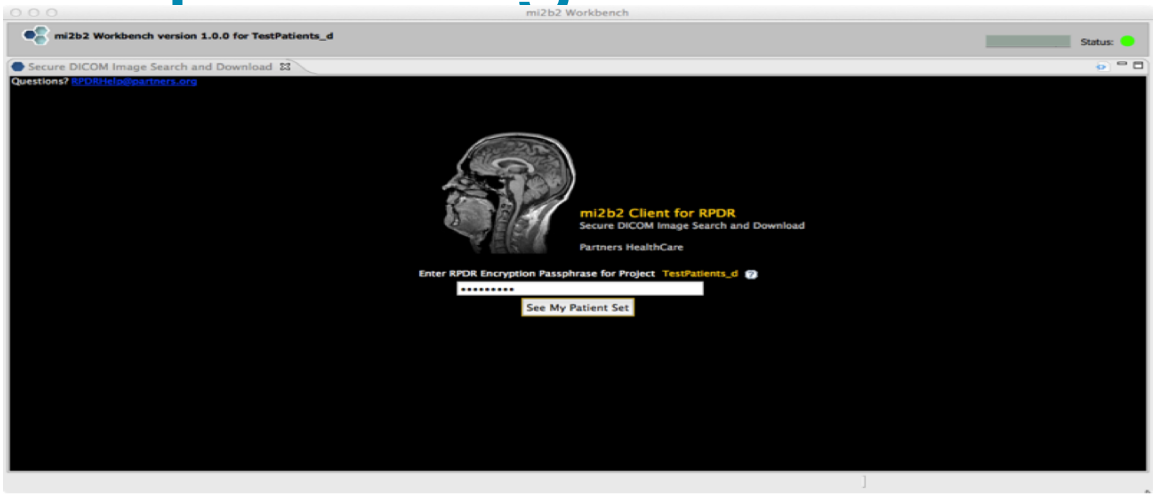
mi2b2 Partners Tutorial
(http://mi2b2help.partners.org)

Mi2b2 at Partners Healthcare

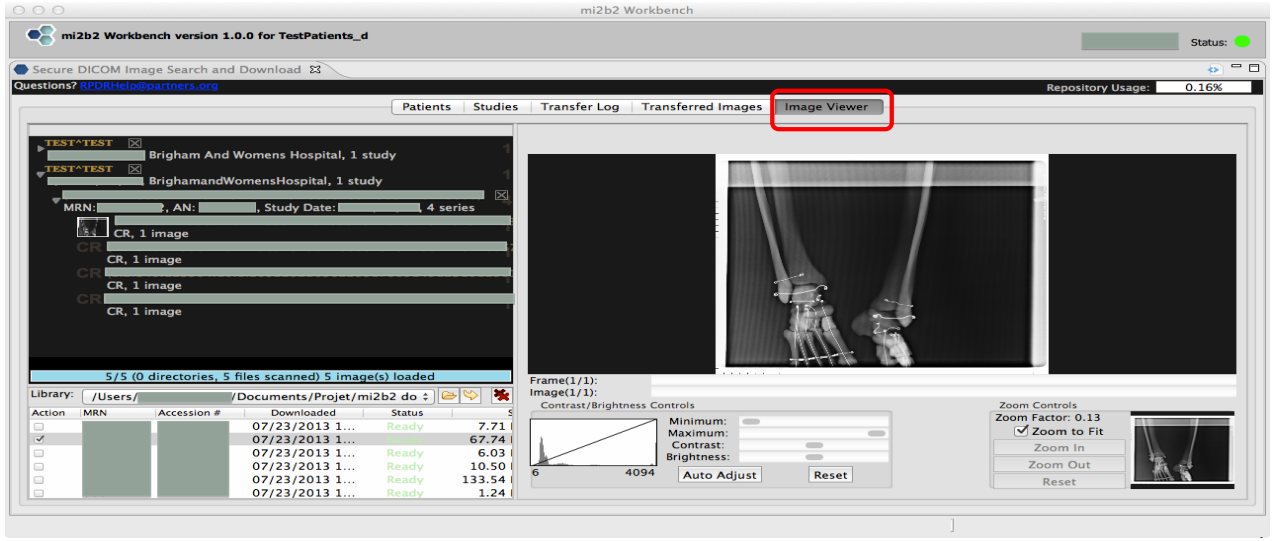
- http://mi2b2help.partners.org



Operating the mi2b2 Workbench



The user inputs the passphrase associated with the IRB protocol of the particular project in order to access the next windows.

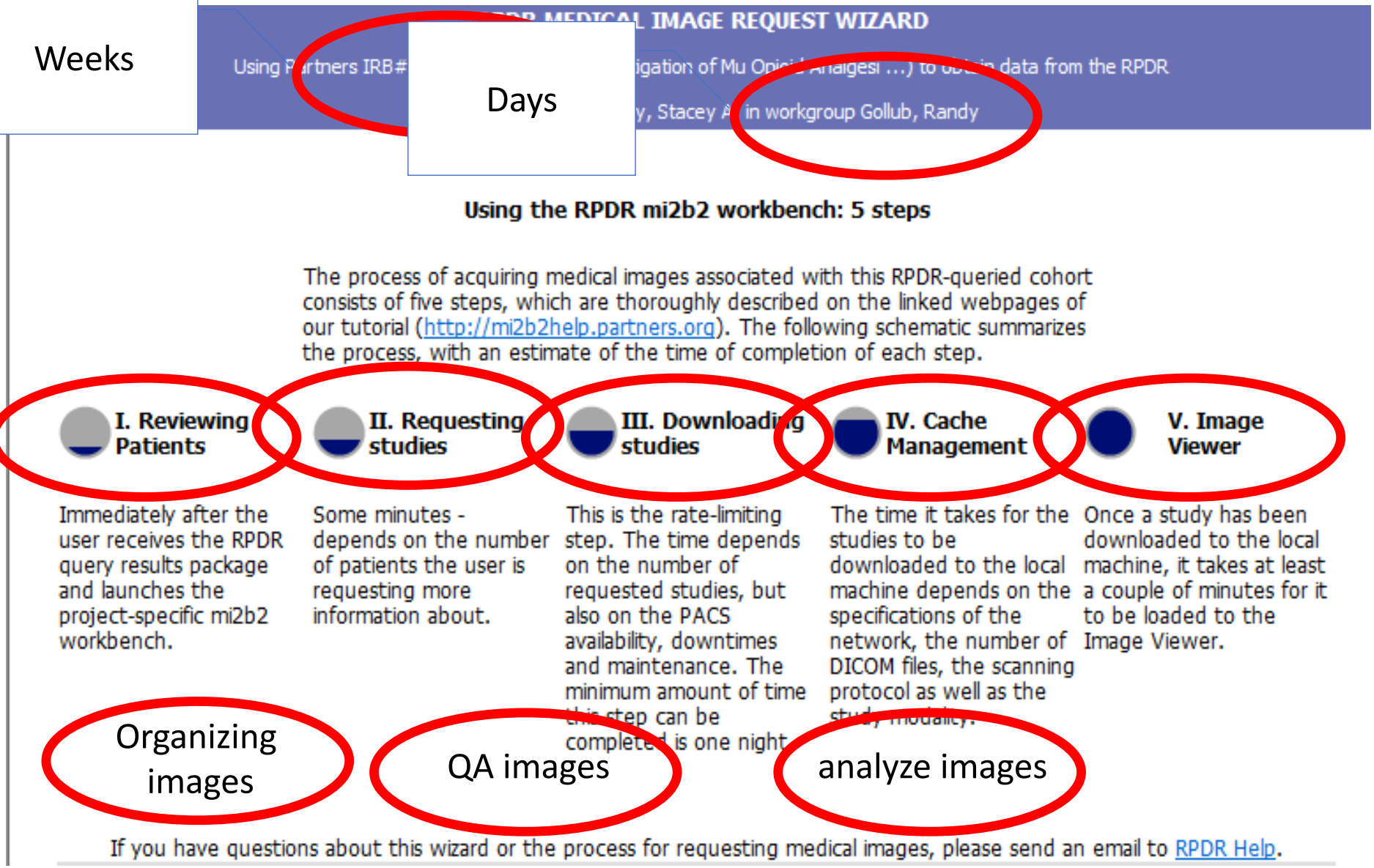


Images are viewed in the Image Viewer and can be manipulated using the tools provided.

Managing Expectations

Weeks

Days



New registry of early childhood Brain MRIs available through Partners Big Data Commons

October 23, 2017 9:35 am

The recently launched **Partners Clinical Image Bank** portal enables researchers to access registries of expertly curated, phenotypically characterized medical images and associated clinical data extracted from the Partners electronic medical records.

The first registry to be made available is a repository of pediatric brain MR images comprised of a cohort of neonates with clinically confirmed hypoxic ischemic encephalopathy (HIE), along with a cohort of "normative" children imaged between the ages of 0-6 years of age with no known CNS pathology. In addition to secure access to the DICOM image data, the portal allows interaction with and download of extracted quantitative metrics from the Apparent Diffusion Coefficient (ADC) maps calculated from the Diffusion Weighted Images for many of the cases.

Each HIE case also has detailed perinatal clinical course information including maternal risk factors, outcomes and much more.

Access to the Clinical Image Bank is available to all registered RPDR users who accept the terms of the Data Use Agreement.

Users with IRB approval who wish to download the fully identifiable clinical data and DICOM medical images may do so easily.

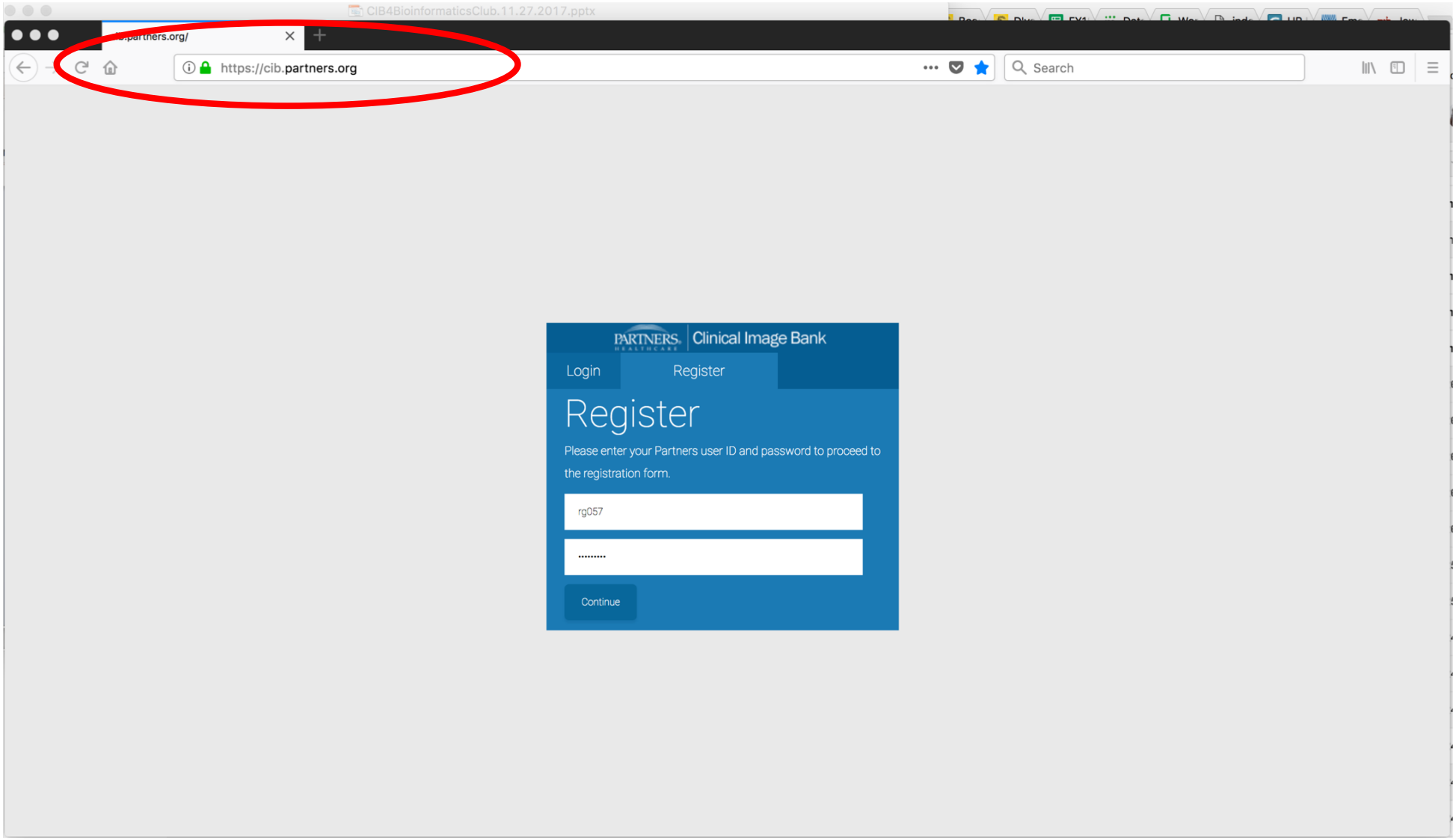
The Clinical Image Bank is available at https://cib.partners.org/ or can be launched from the RPDR homepage at http://rpdr.partners.org

For questions, suggestions for future expansion and feedback about the Clinical Image Bank, contact RPDRHelp@partners.org

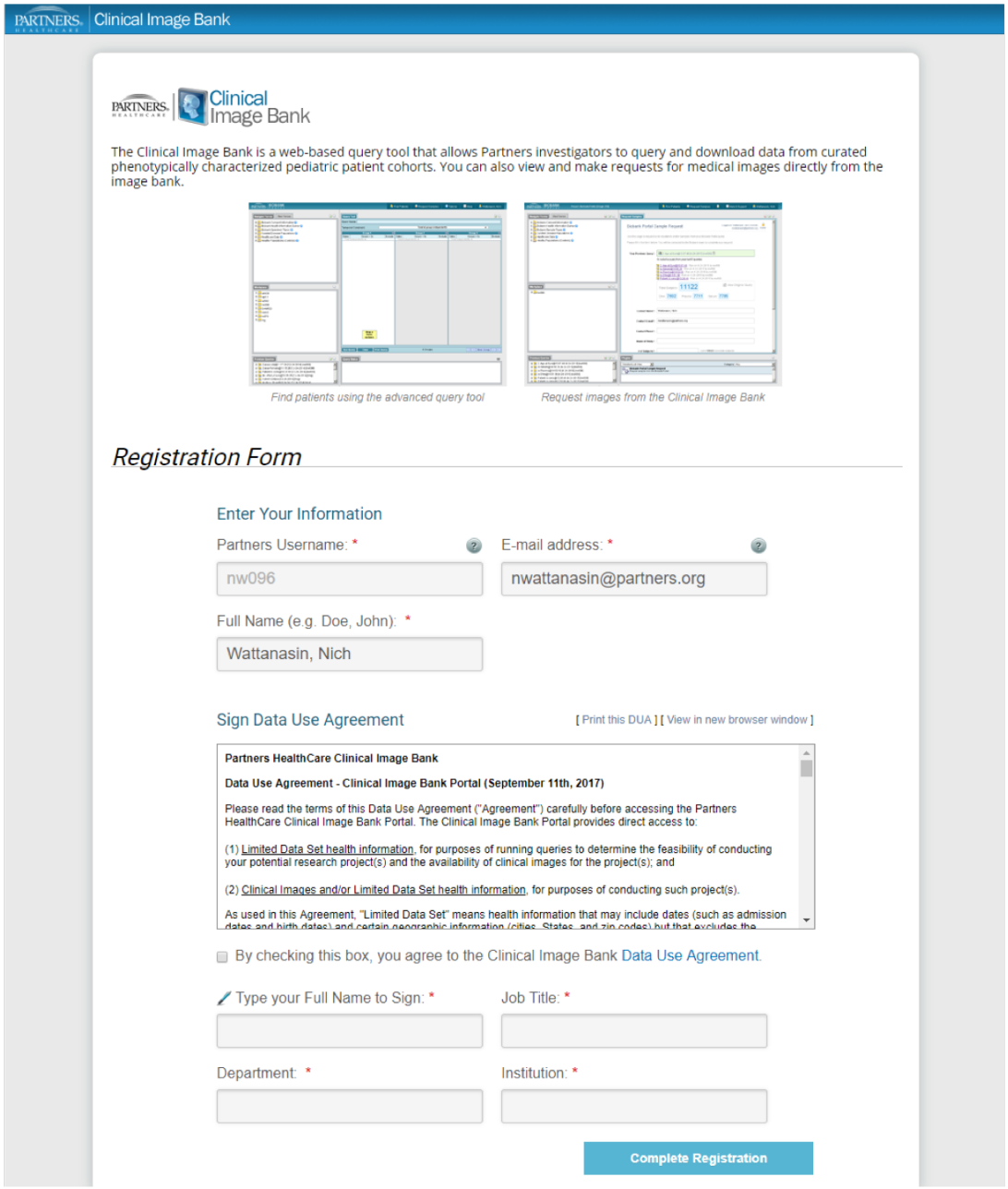
CIB: Motivation and Goals

- The Clinical Image Bank seeks to make valuable collections of patient cohorts available to Partners investigators and their collaborators
  - Well curated phenotypes
  - Clinical images with secondary research utility
  - Clinical information not available in RPDR
- Easily accessible to support robust data mining
  - Web accessible with credentials
  - DUA simplifies management while maintaining patient privacy and all legal protections
- Enables cohort curation across phenotypes over time

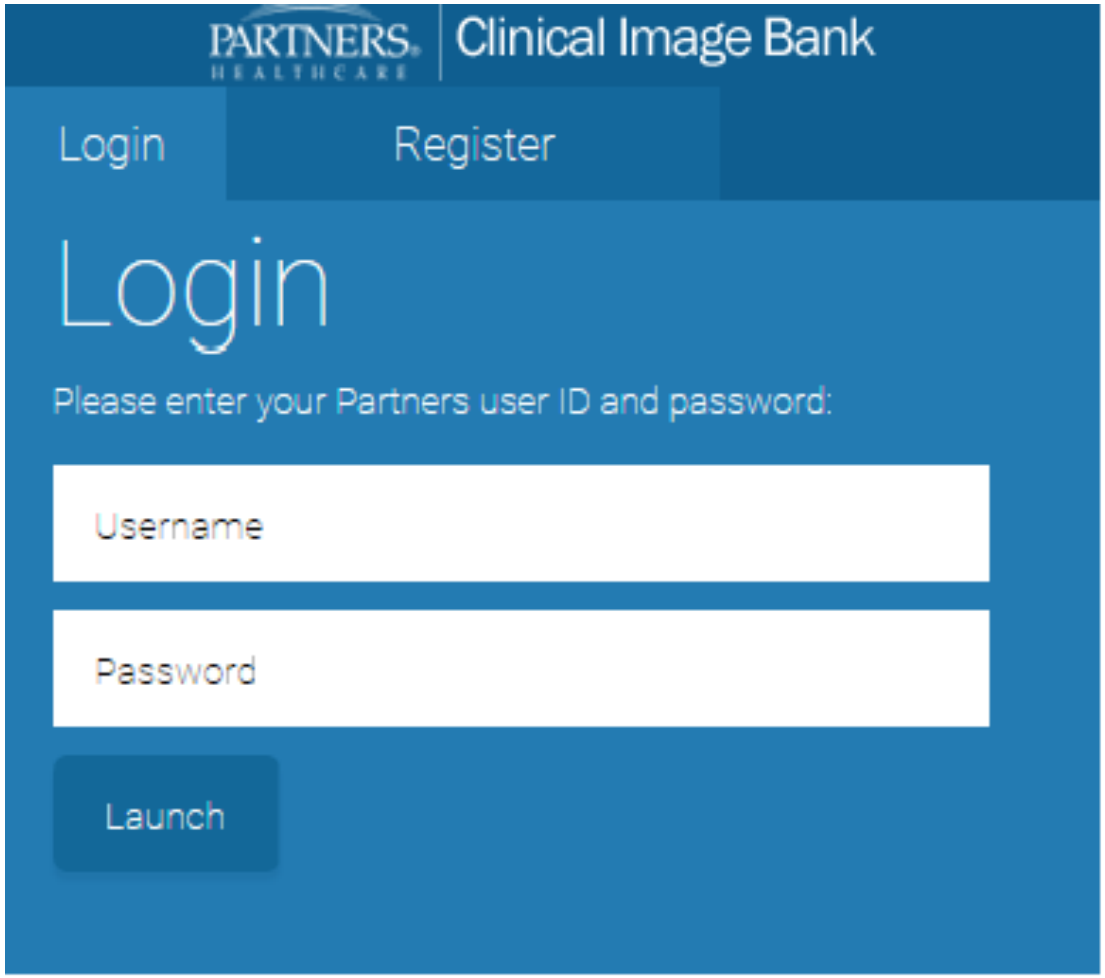
CIB: Register from within firewall (use VPN)



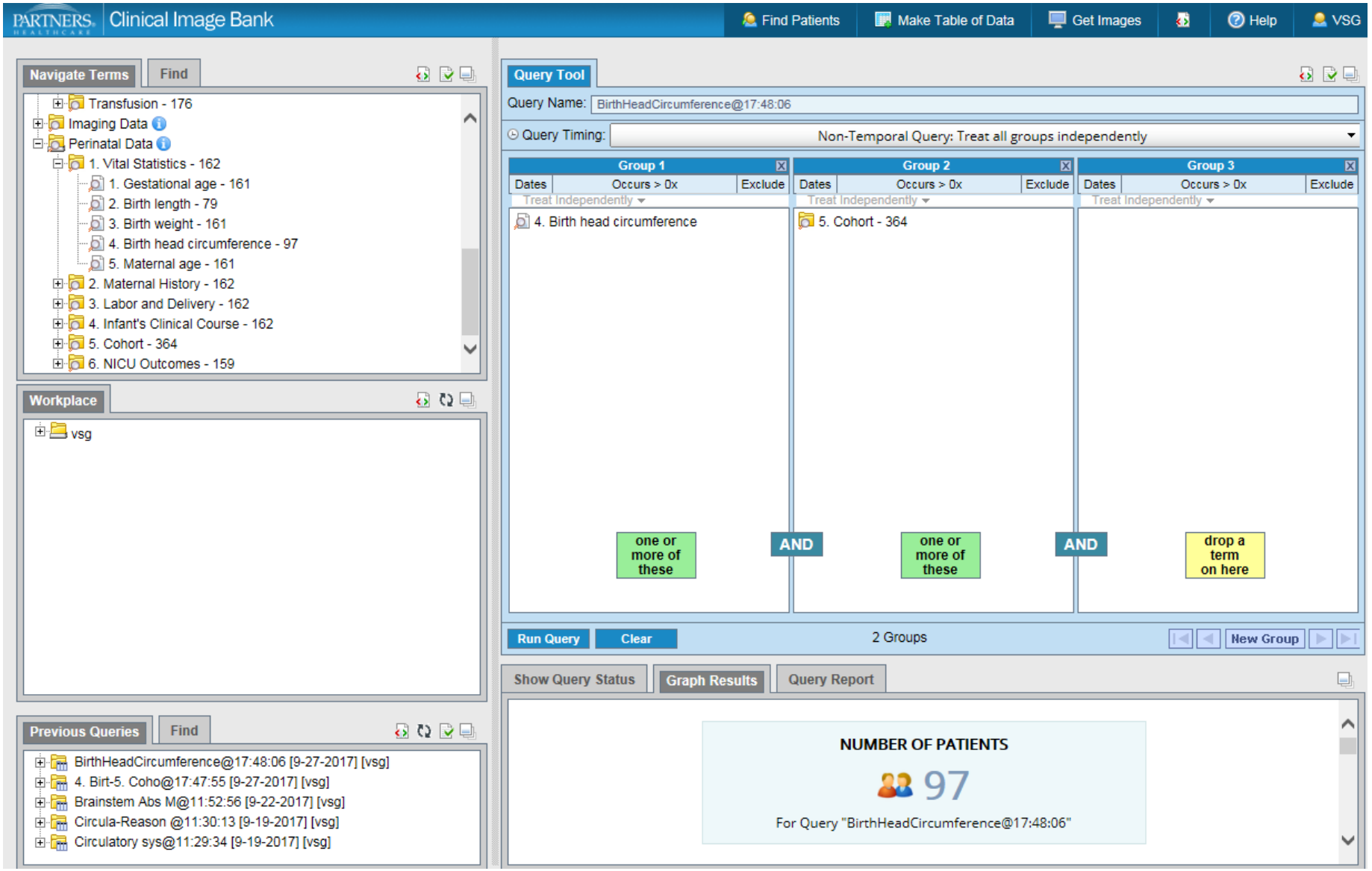
CIB: Sign the DUA



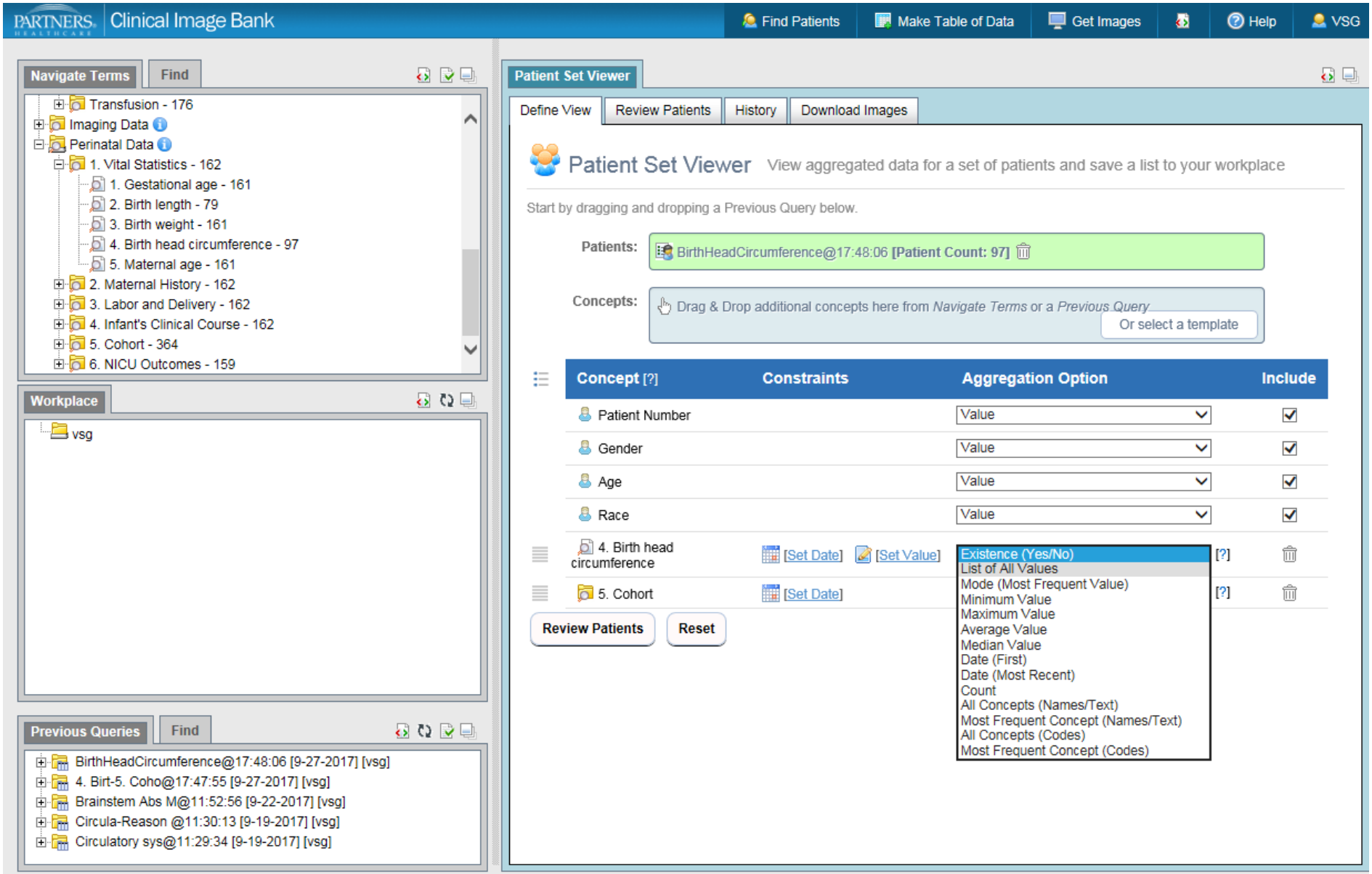
CIB: Login


PARTNERS HEALTHCARE
Clinical Image Bank
Login
Register
Login
Please enter your Partners user ID and password:
Username
Password
Launch

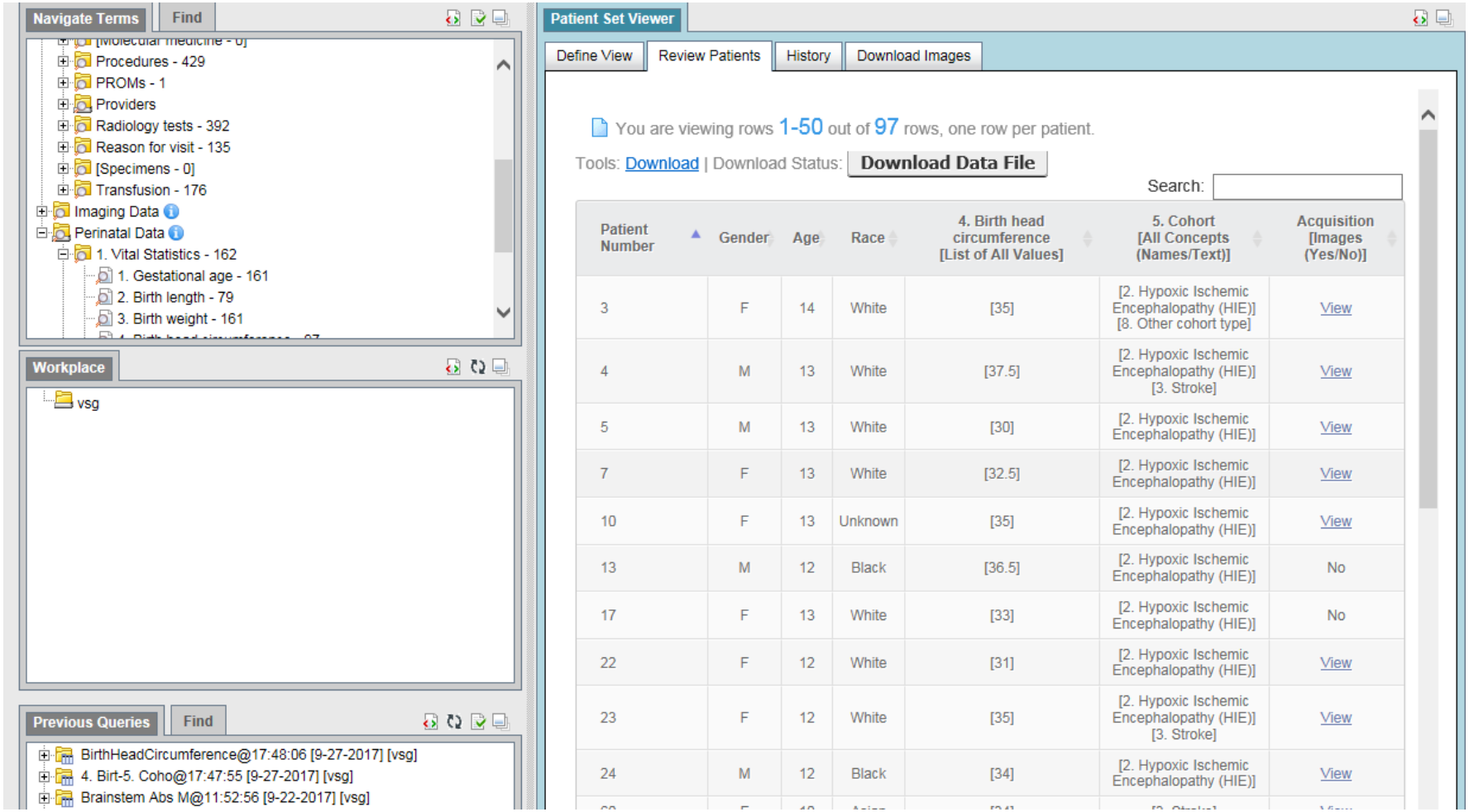
CIB: Run a Query



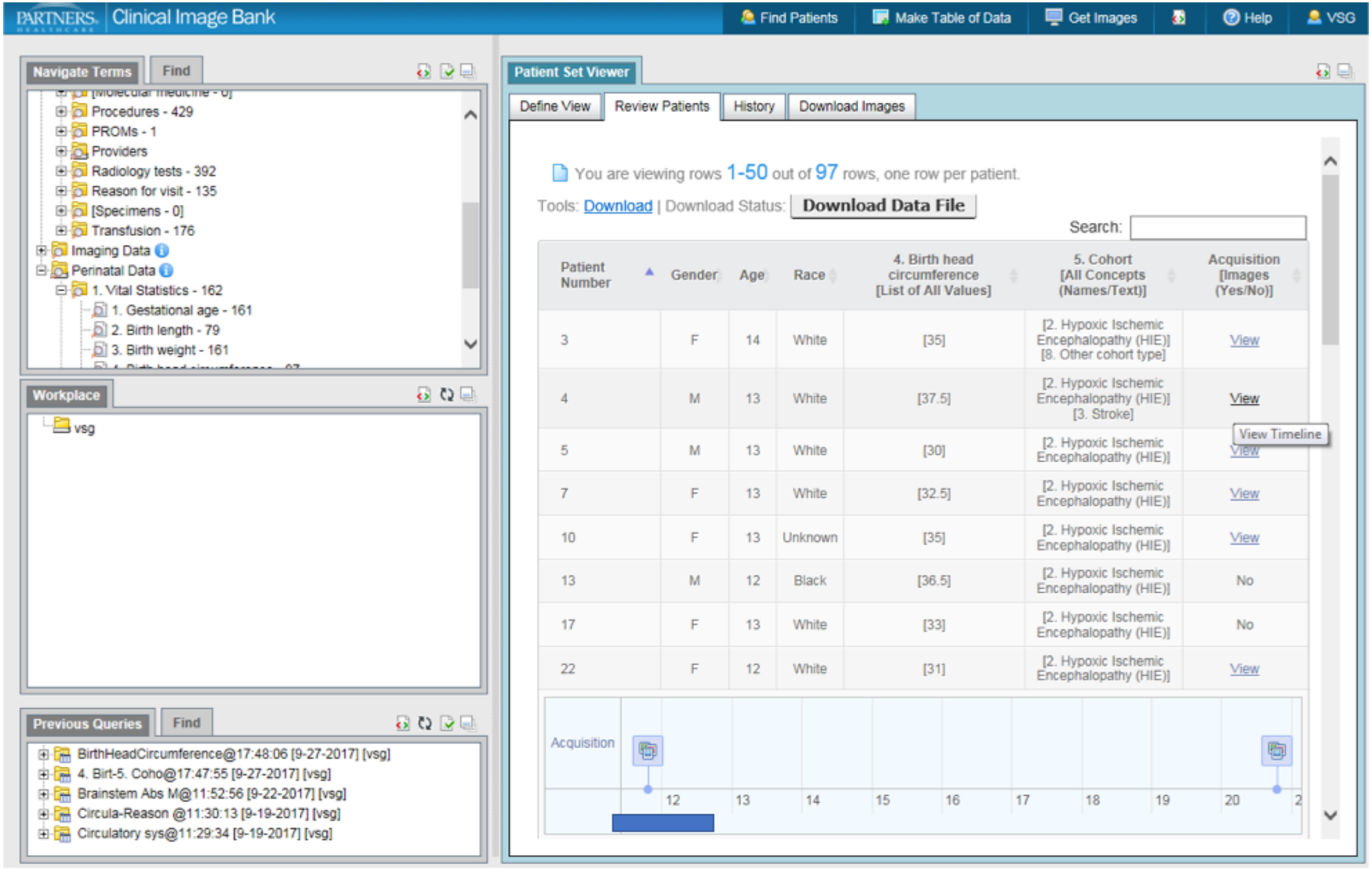
CIB: Create a Table of Data



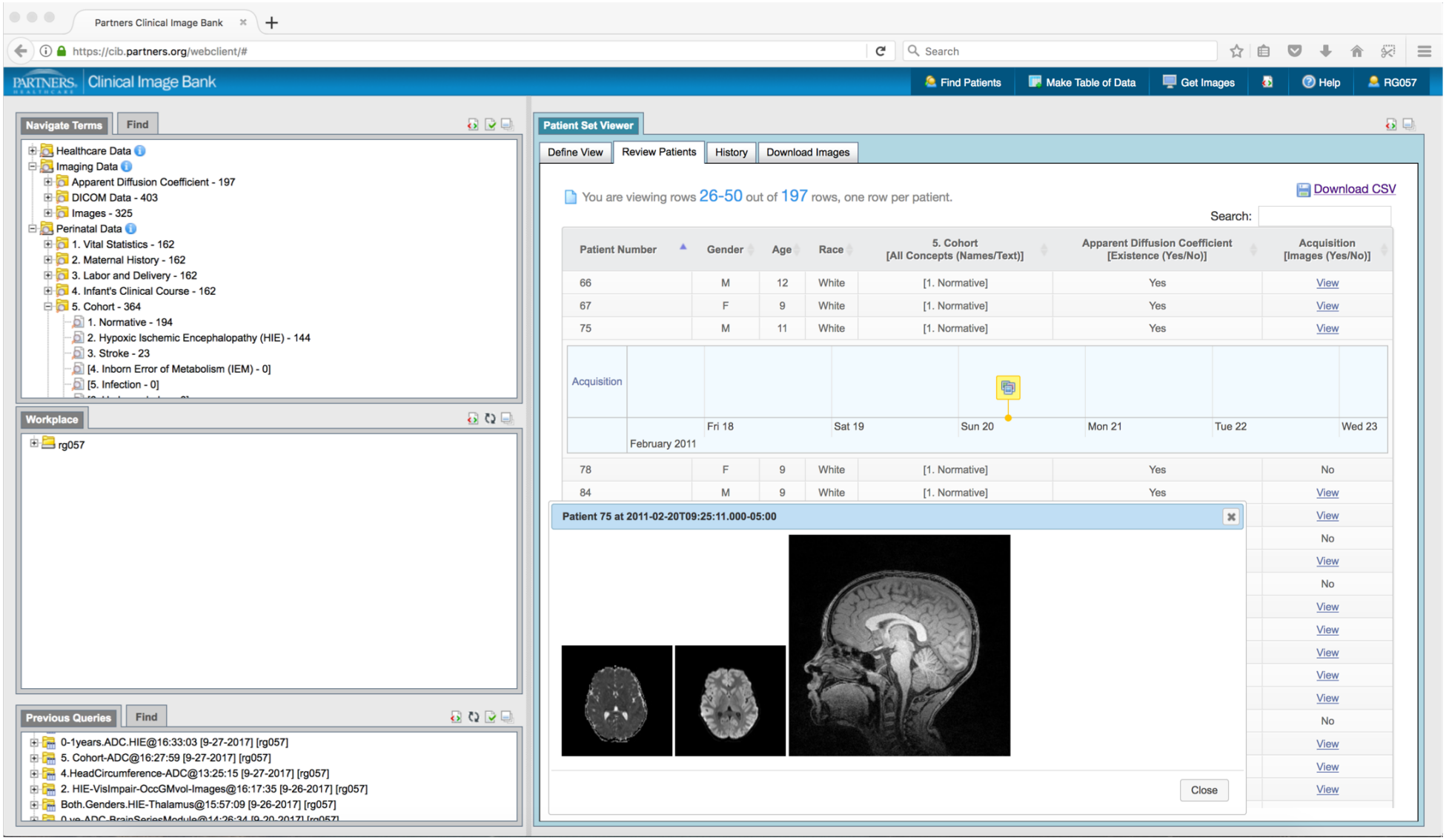
CIB: Review Patients



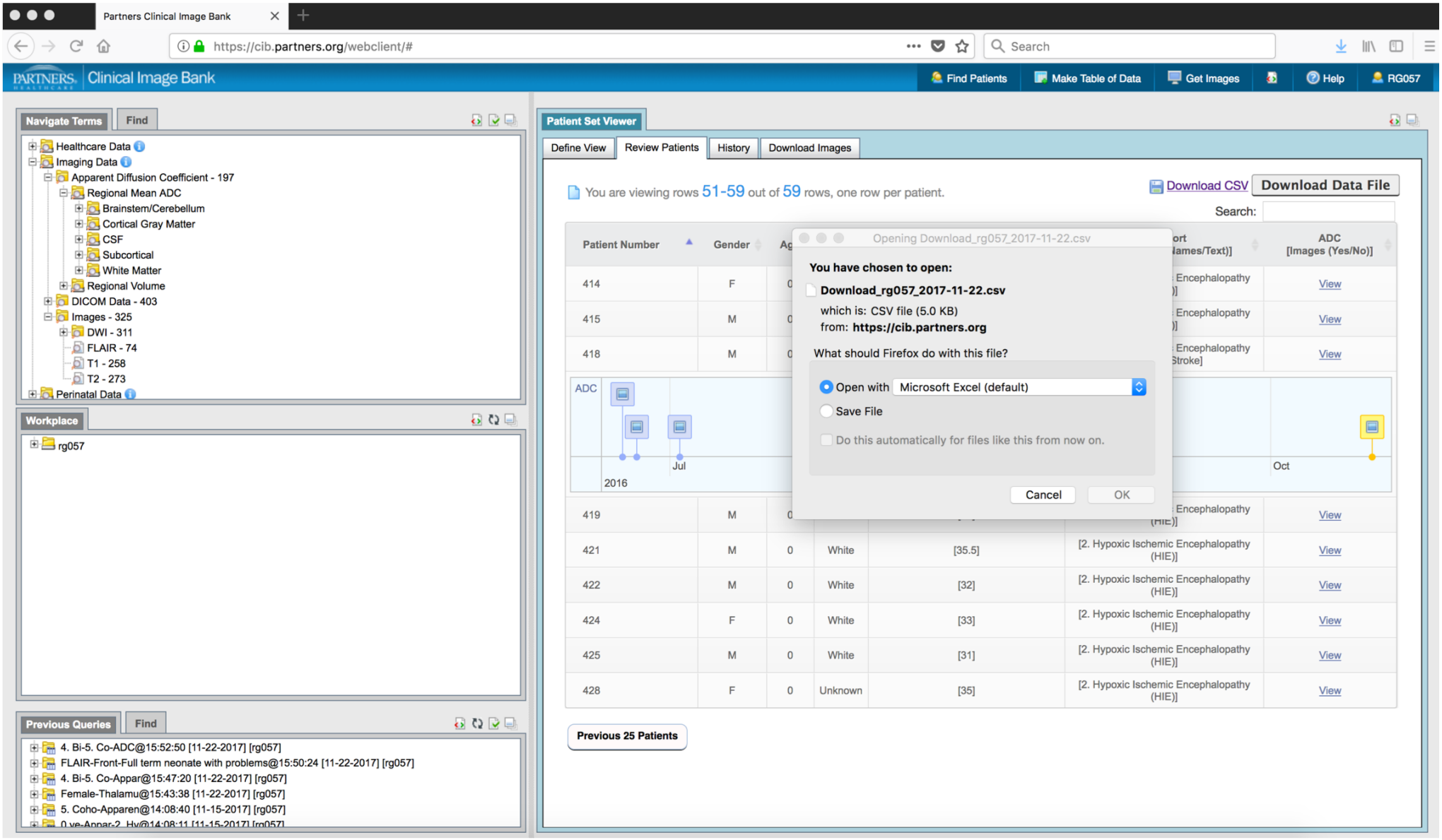
CIB: View Timeline of available images



CIB: View thumbnails of images

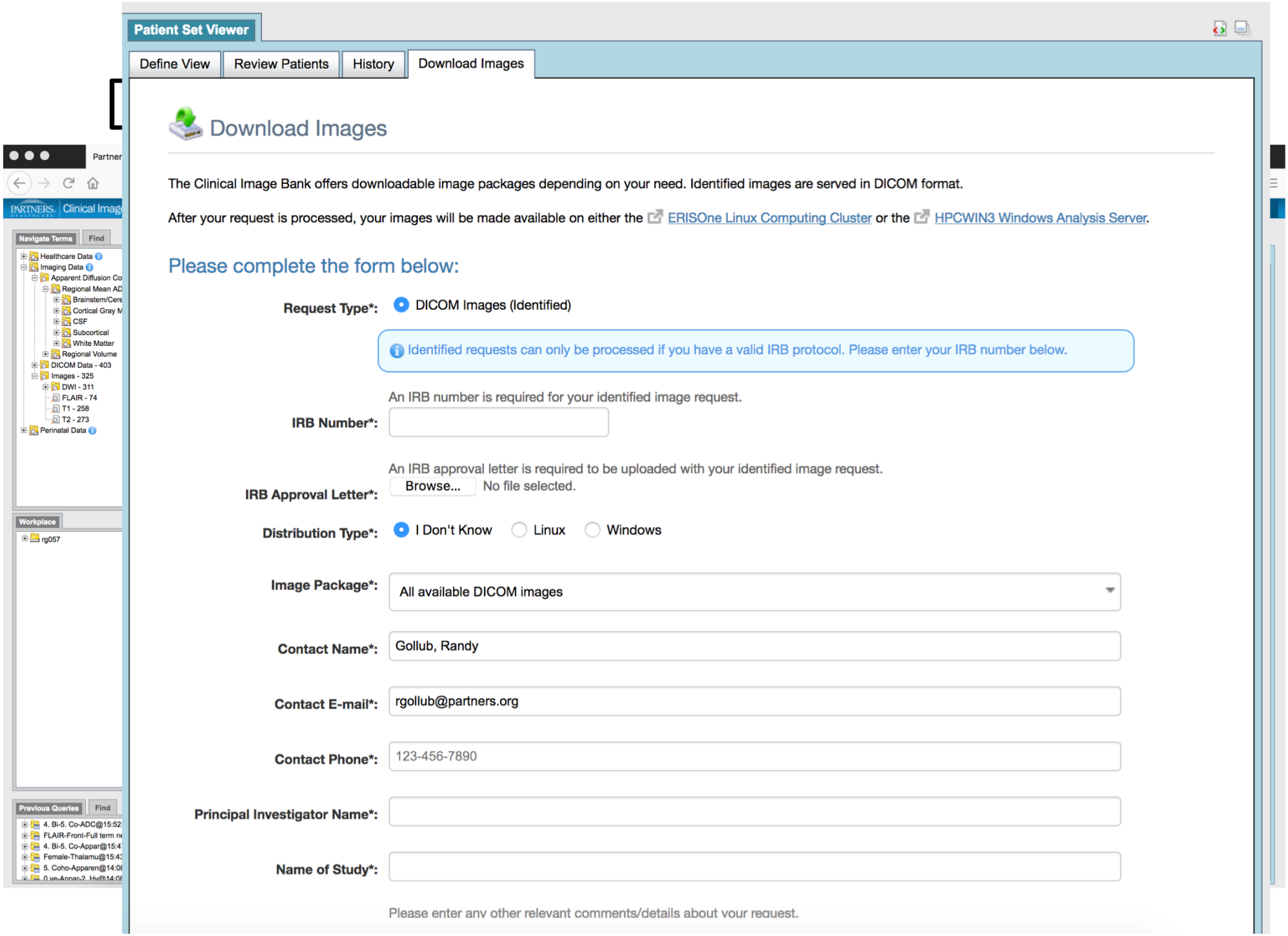


CIB: Download data

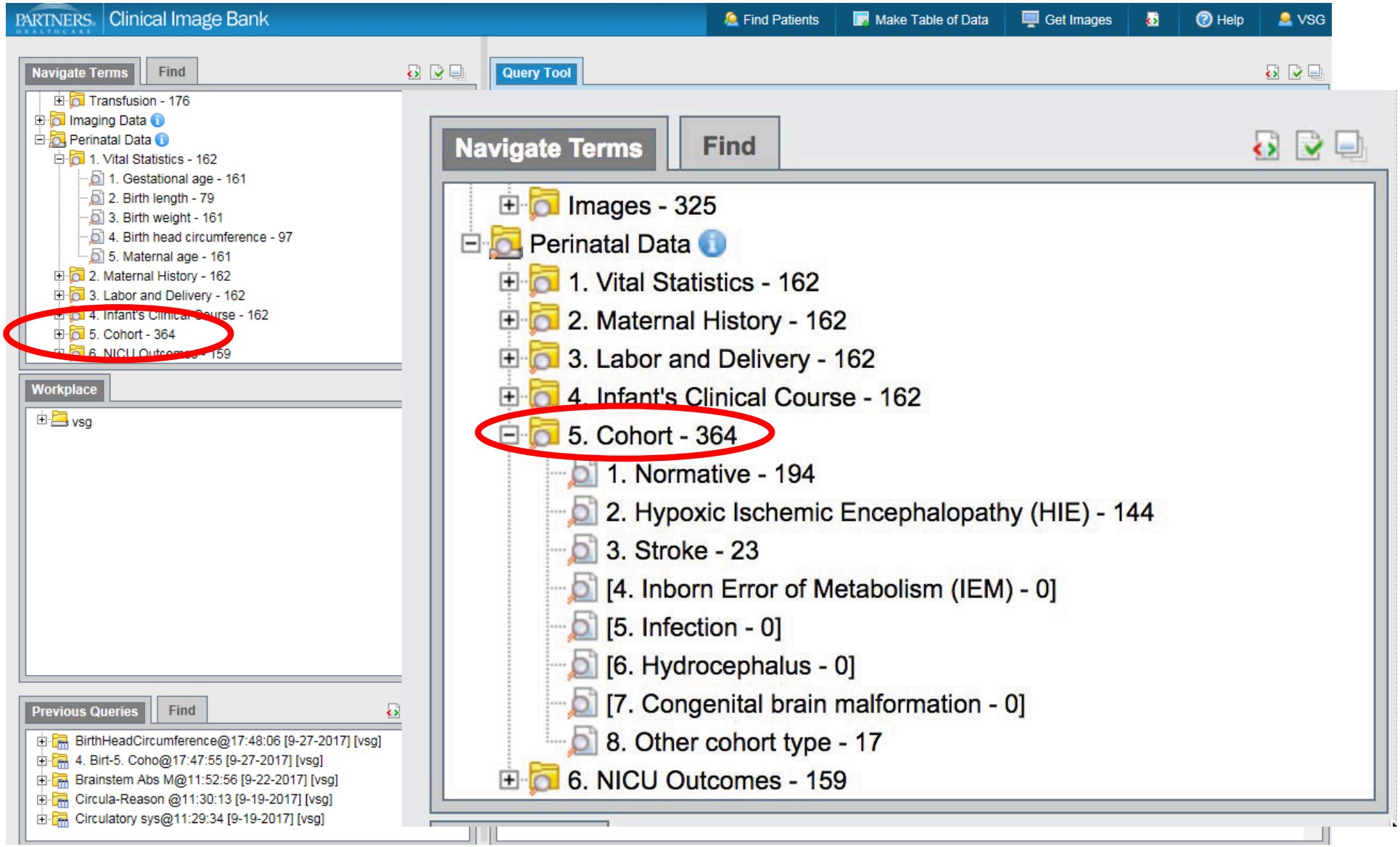


CIB: Download data

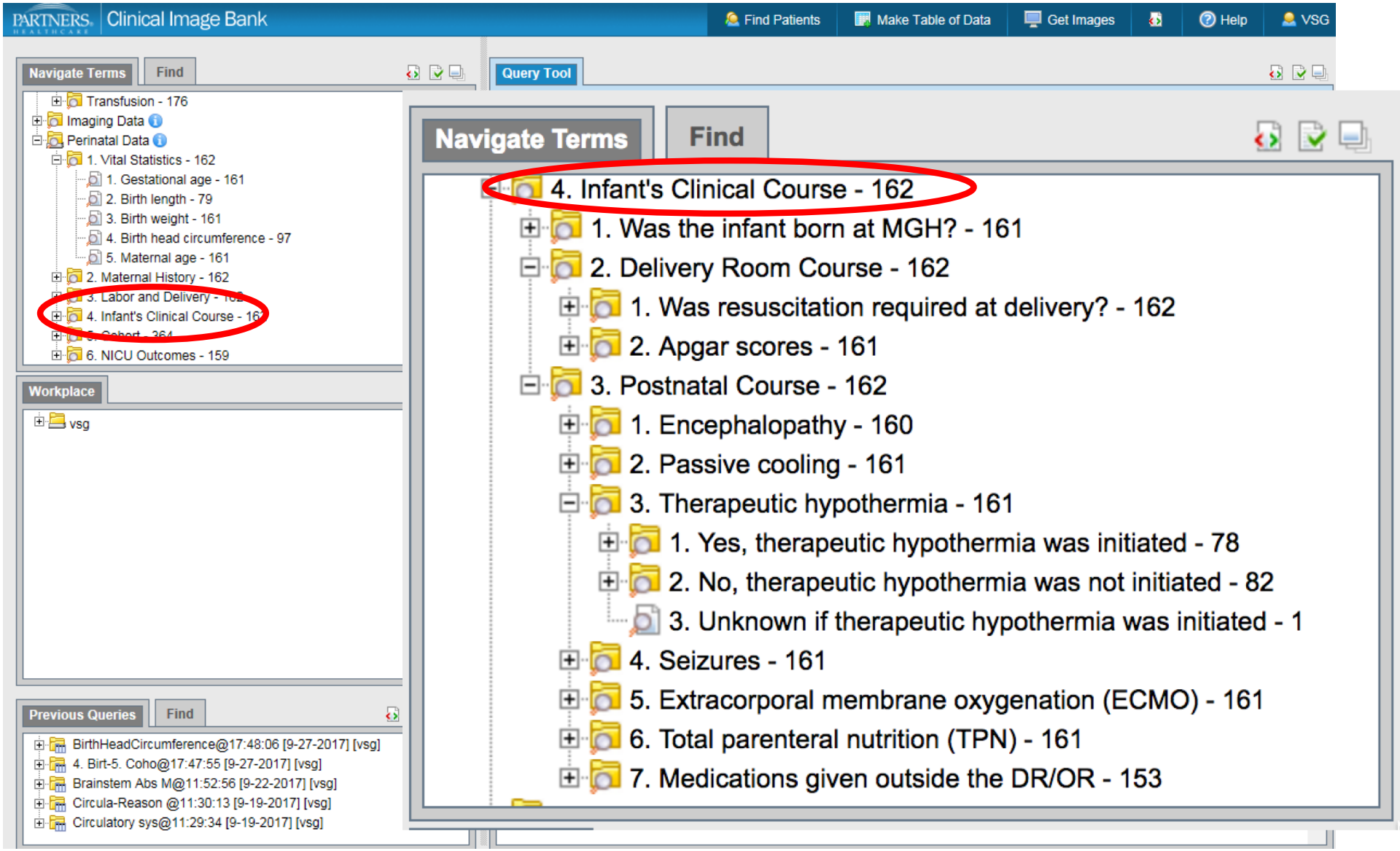
1	Gender	Age	Race	4. Birth head circumference	5. Cohort [All Concepts (Names/Text)]
2	F	14	White	[35]	[2. Hypoxic Ischemic Encephalopathy (HIE)] [8. Other cohort type]
3	M	13	White	[37.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)] [3. Stroke]
4	M	13	White	[30]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
5	F	13	White	[32.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
6	F	13	Unknown	[35]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
7	M	12	Black	[36.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
8	F	13	White	[33]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
9	F	12	White	[31]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
10	F	12	White	[35]	[2. Hypoxic Ischemic Encephalopathy (HIE)] [3. Stroke]
11	M	12	Black	[34]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
12	F	10	Asian	[34]	[3. Stroke]
13	M	9	White	[36]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
14	F	8	Unknown	[32.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)] [3. Stroke]
15	F	0	White	[31]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
16	F	7	White	[34.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
17	F	0	Unknown	[35]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
18	M	7	Black	[35.35]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
19	F	7	White	[34]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
20	M	10	Unknown	[37]	[8. Other cohort type]
21	M	6	Unknown	[34]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
22	F	6	Other	[35]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
23	F	6	White	[34.5]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
24	F	6	Unknown	[32]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
25	F	5	Black	[36]	[2. Hypoxic Ischemic Encephalopathy (HIE)]
26	M	5	Black	[36]	[8. Other cohort type]


Patient Set Viewer
Define View
Review Patients
History
Download Images
Download Images
The Clinical Image Bank offers downloadable image packages depending on your need. Identified images are served in DICOM format.
After your request is processed, your images will be made available on either the ERISOne Linux Computing Cluster or the HPCWIN3 Windows Analysis Server.
Please complete the form below:
Request Type*:
DICOM Images (Identified)
Identified requests can only be processed if you have a valid IRB protocol. Please enter your IRB number below.
An IRB number is required for your identified image request.
IRB Number*:
An IRB approval letter is required to be uploaded with your identified image request.
IRB Approval Letter*:
Browse...
No file selected.
Distribution Type*:
I Don't Know
Linux
Windows
Image Package*:
All available DICOM images
Contact Name*:
Gollub, Randy
Contact E-mail*:
rgollub@partners.org
Contact Phone*:
123-456-7890
Principal Investigator Name*:
Name of Study*:
Please enter any other relevant comments/details about your request.

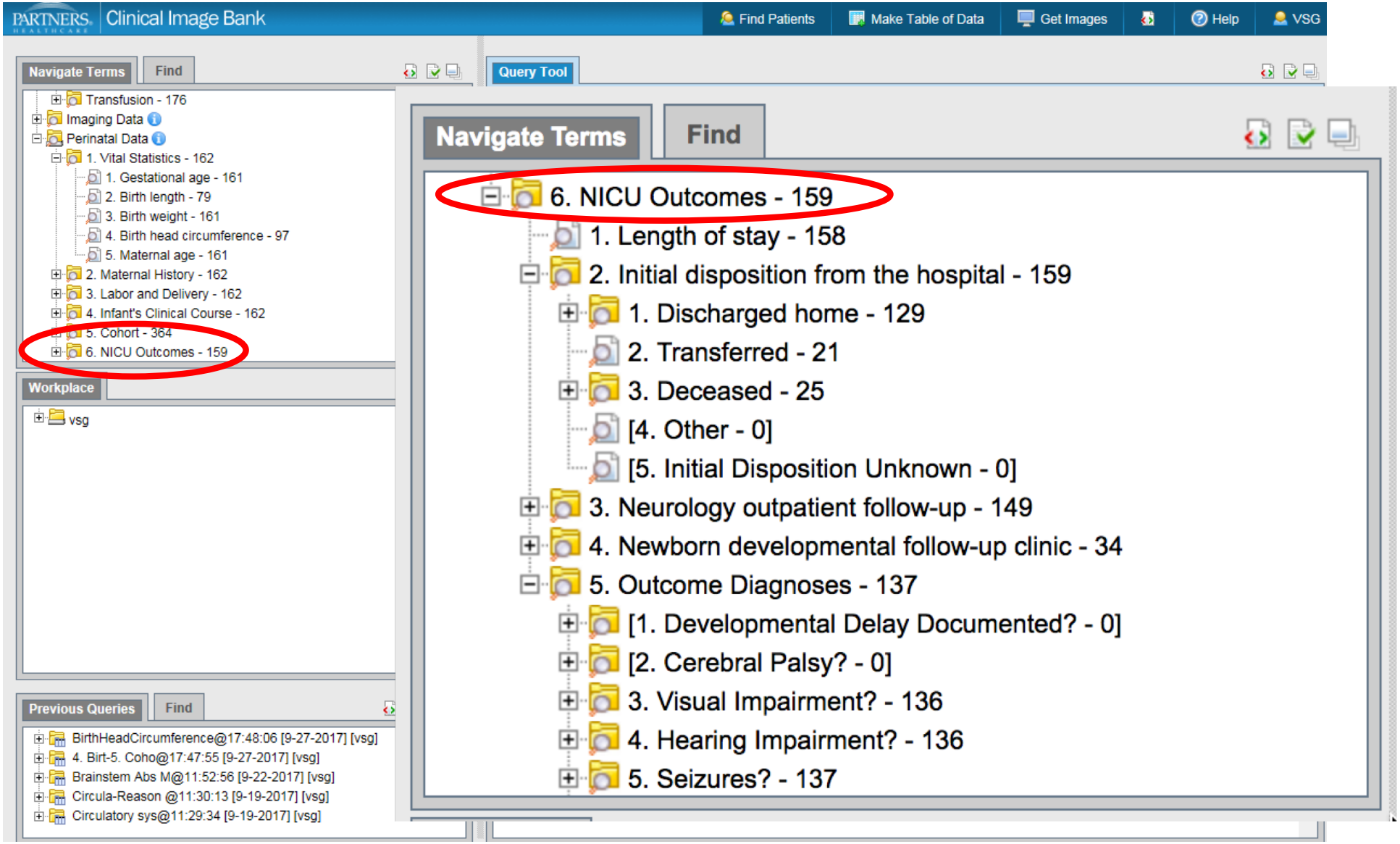
CIB: Currently available data



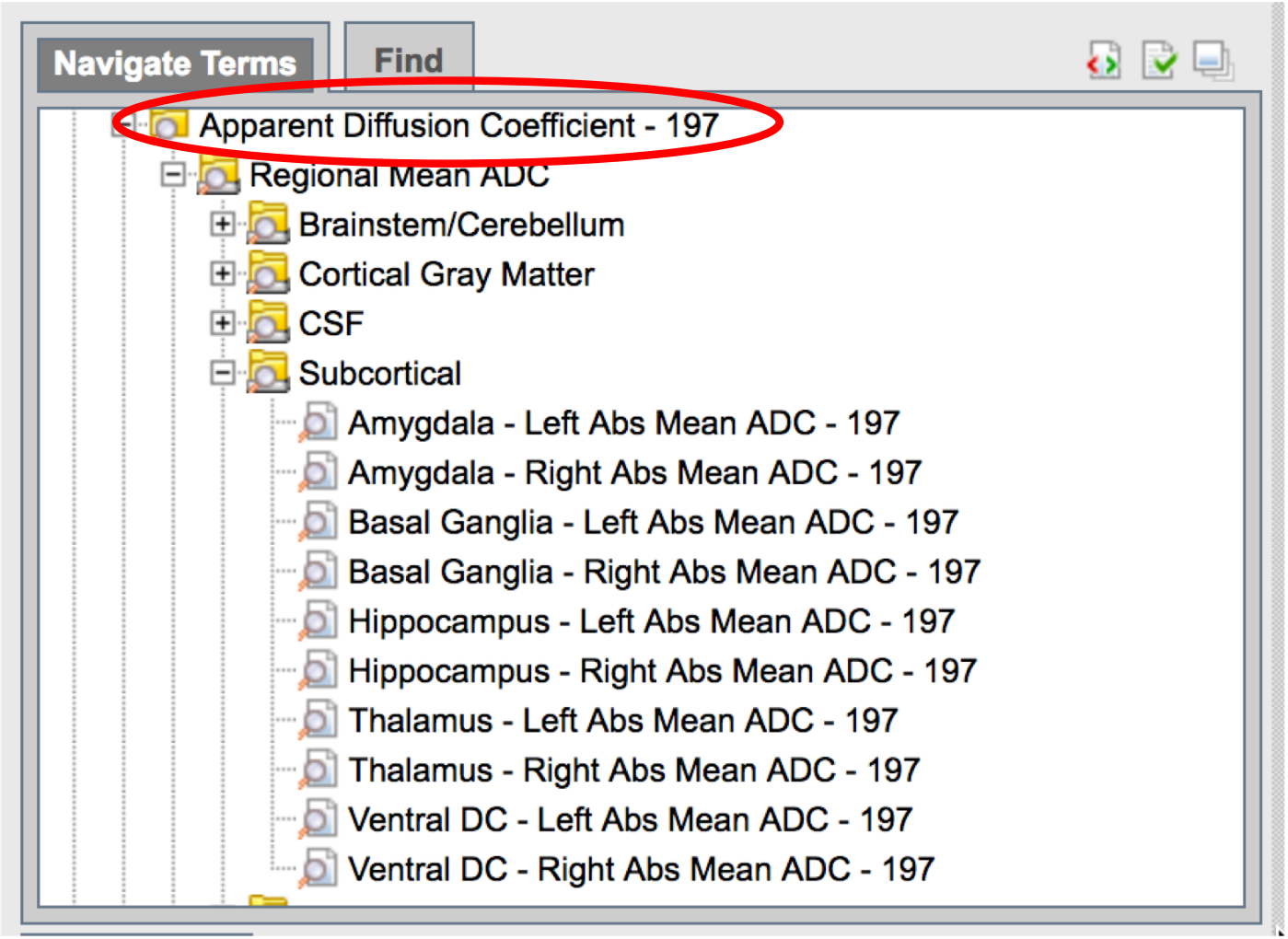
Detailed information on NICU care



CIB: Clinical outcome measures

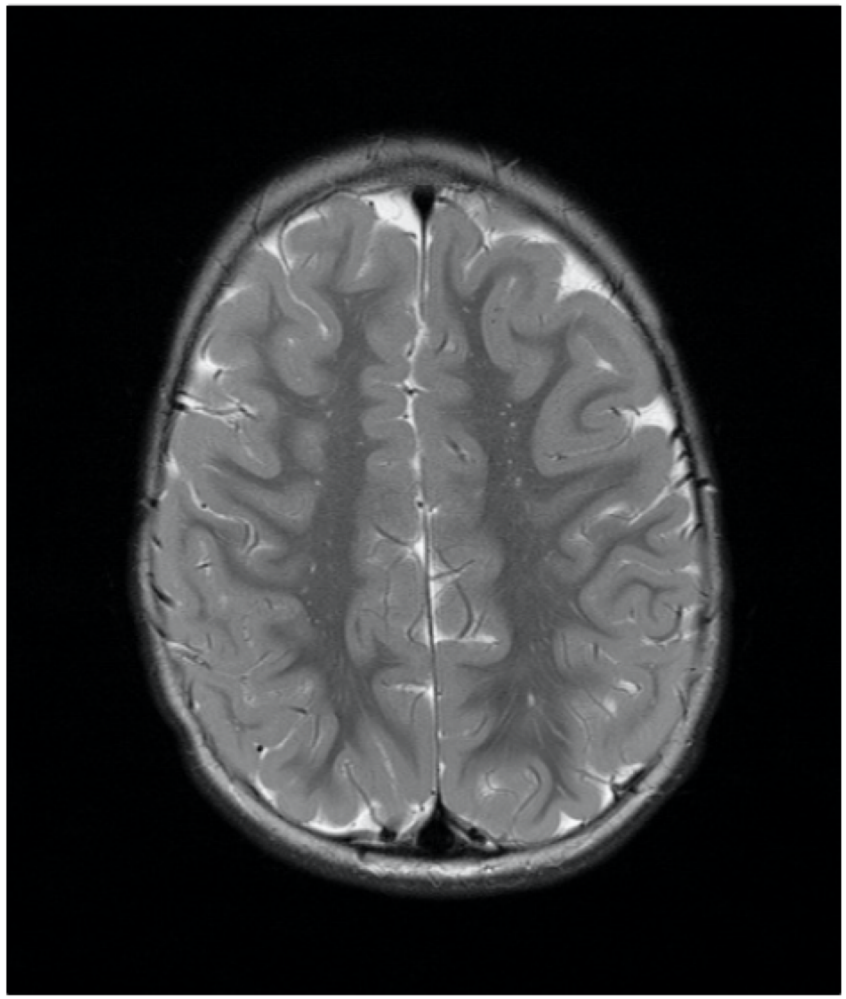


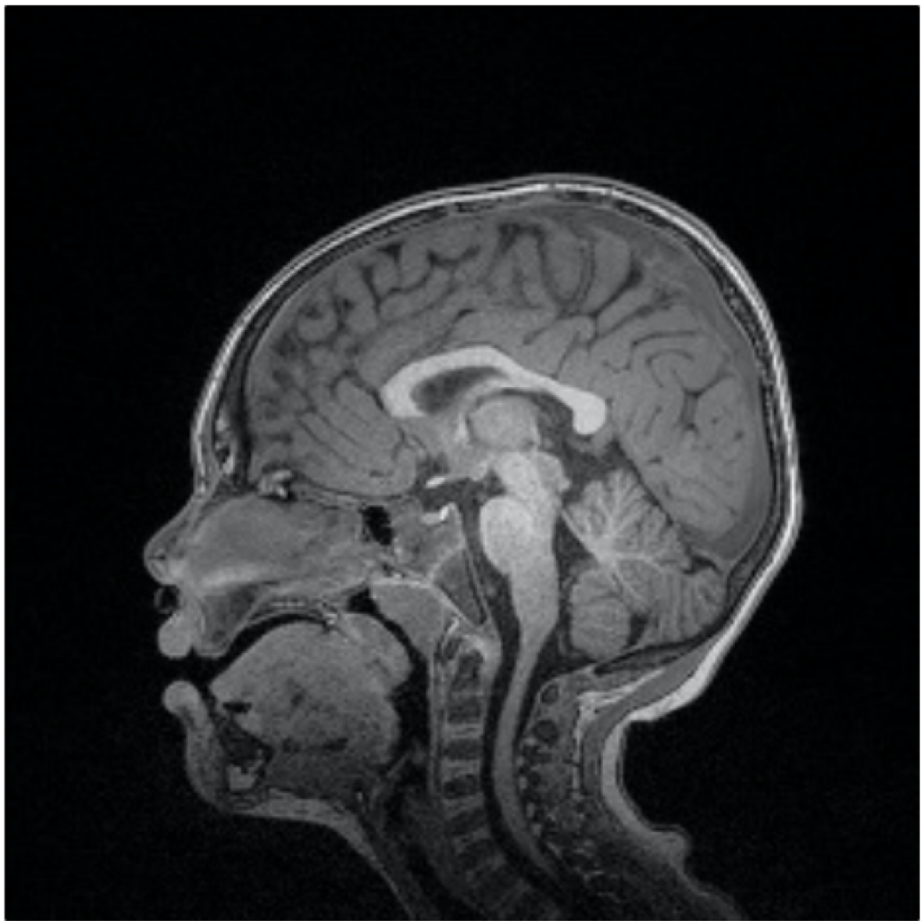
CIB: Quantitative Imaging Metrics



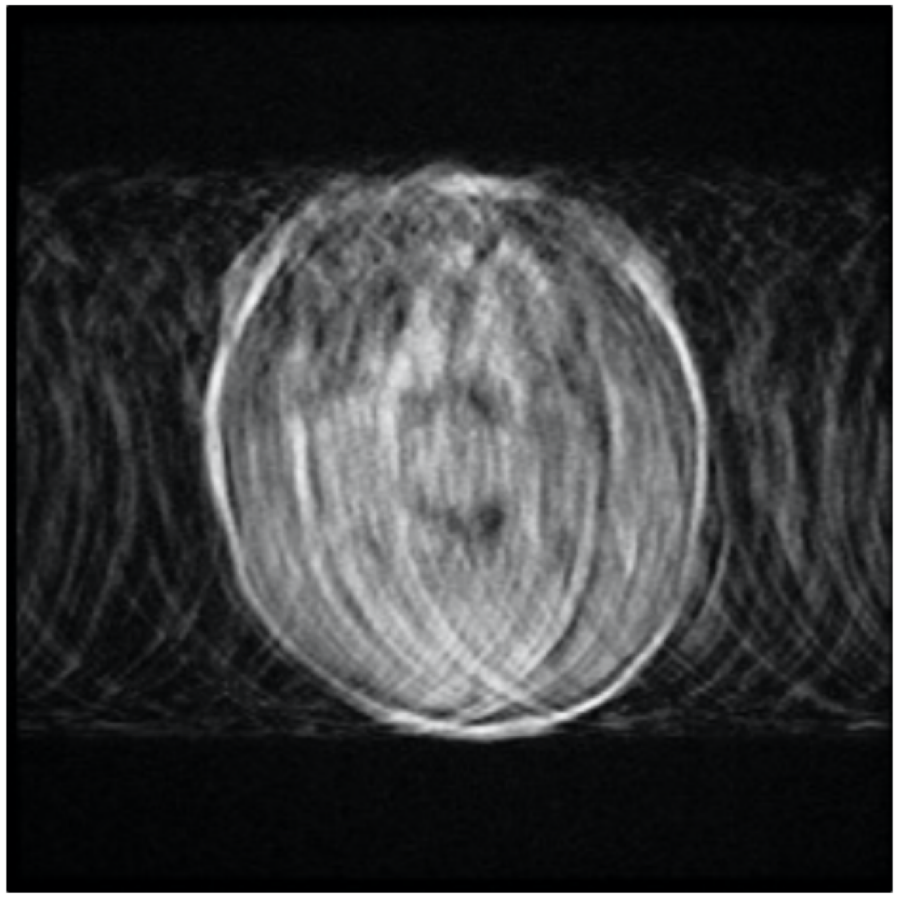
What kinds of images?

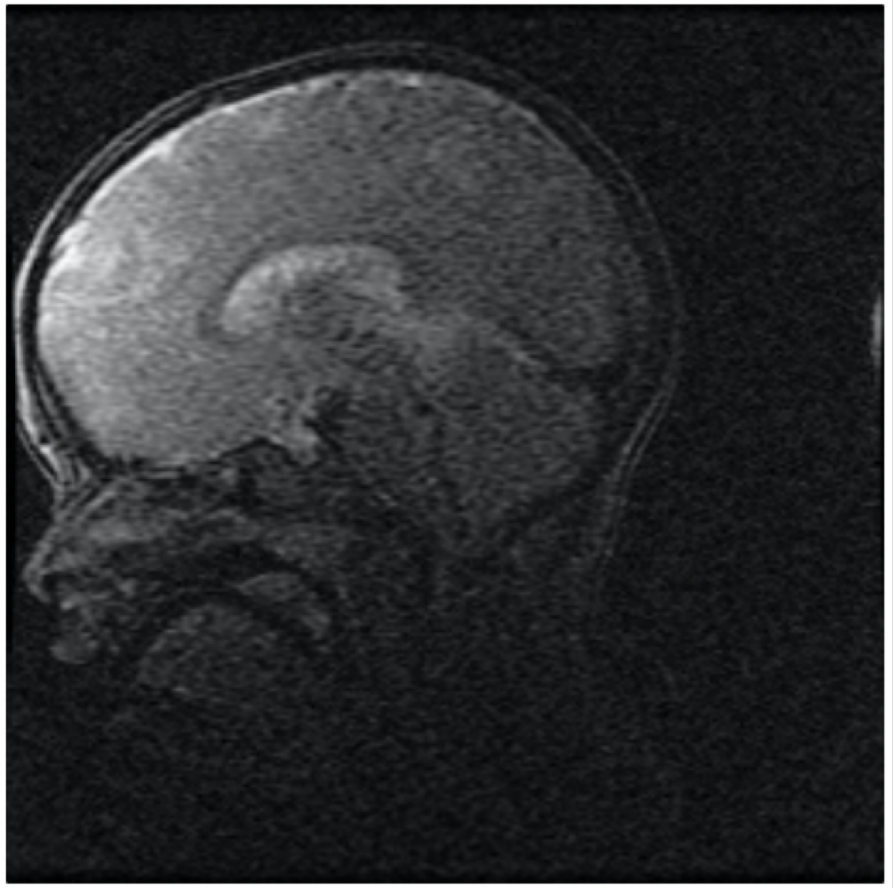
- Mostly brain MRI now (T1, T2, FLAIR, DWI/ADC)





Occasional scans are of poor quality





Approximately n=120 Non-Brain scans

- Mostly spine (n=99)
- Miscellaneous other MR (n=21)
- No way to consistently tell anything from file name

In addition there are MRS traces (n=2)

Identify Subjects / Request Data

Partners Biobank Portal

HIDE

Enterprise-wide da
for analysis or to g
researchers throu

A new initiative, th
with Epic. The spe
creating a distribu
specific integratio

Research Pat

Research Patient D

RPDR Daily Q

The RPDR has a ne

Partners Biol

Biobank Portal

mi2B2 Medic

mi2B2 Medical Ima

The **Partners Biobank Portal** is a tool that links consented subjects from the Partners Biobank with their healthcare data from the electronic medical record (EMR) and allows researchers to request clinical samples for these subjects. Users must have a valid Partners logon and be a registered Research Patient Data Registry (RPDR) user to use the Portal.

In addition to comprehensive electronic medical record data, the Biobank Portal includes:

- **Biobank Health Information Survey,** patient-reported lifestyle, environment and family history information.
- **Curated Disease Populations** sets of subjects within the Biobank population who have been statistically determined to have a particular disease such as Type 2 diabetes, rheumatoid arthritis, congestive heart failure and others. These cohorts are often called disease phenotypes.
- **Healthy Populations,** an index that statistically groups patients by co-morbidities (using the Charlson Index) in order to help select relatively healthy controls from the Biobank population.
- **Biobank Sample Types,** including DNA, plasma and serum. Both de-identified and identified samples may be requested from the Portal. Requesting identified samples requires a valid Partners IRB protocol.
- **Biobank Genomic Data**, genotyped and imputed genomic data are available for a subset of the Biobank population and may be requested via the Portal. Both de-identified and identified samples may be requested from the Portal. Requesting identified samples requires a valid Partners IRB protocol.
- **Querying by Genomic Data,** single nucleotide polymorphism (SNP) and insertion and deletion (indel) variants and their related annotations are available on a subset of genotyped subjects in the Biobank Portal and may be used to query for subjects within the Portal.

Researchers can use the Biobank Portal to identify eligible case and control subjects, request samples, and perform analyses related to using consented samples for research.

Please contact the Biobankportalhelp@partners.org mailbox with any questions or support.

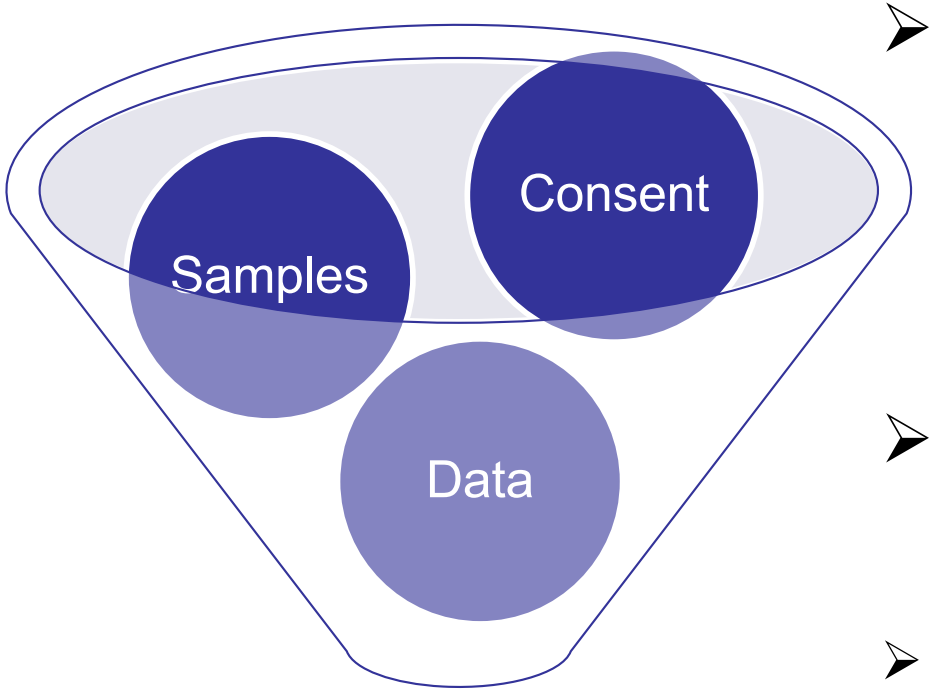
Biobank Portal Access

You must register to use the Biobank. If you are already an RPDR user, you are automatically registered.

- Request Access »
- Log in to the Biobank Portal »
- Biobank Portal Wiki »
- Help performing queries? Stacey Duey, (617) 759-8248 »
- Biobank Help Mailbox »

CONTACT BIOBANK SUPPORT »

The Partners Biobank



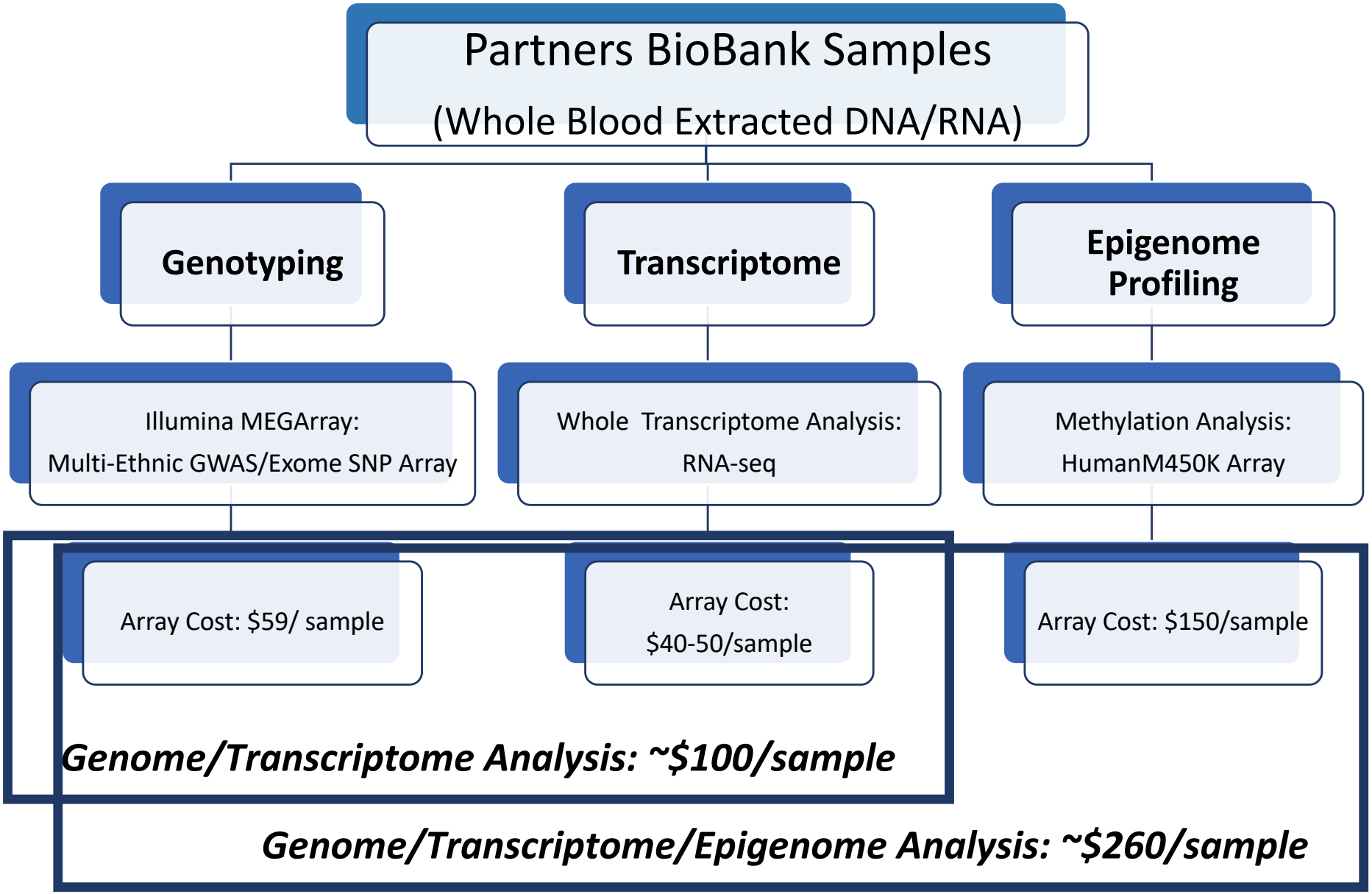
Research Discoveries

Improved Clinical Care for All Patients

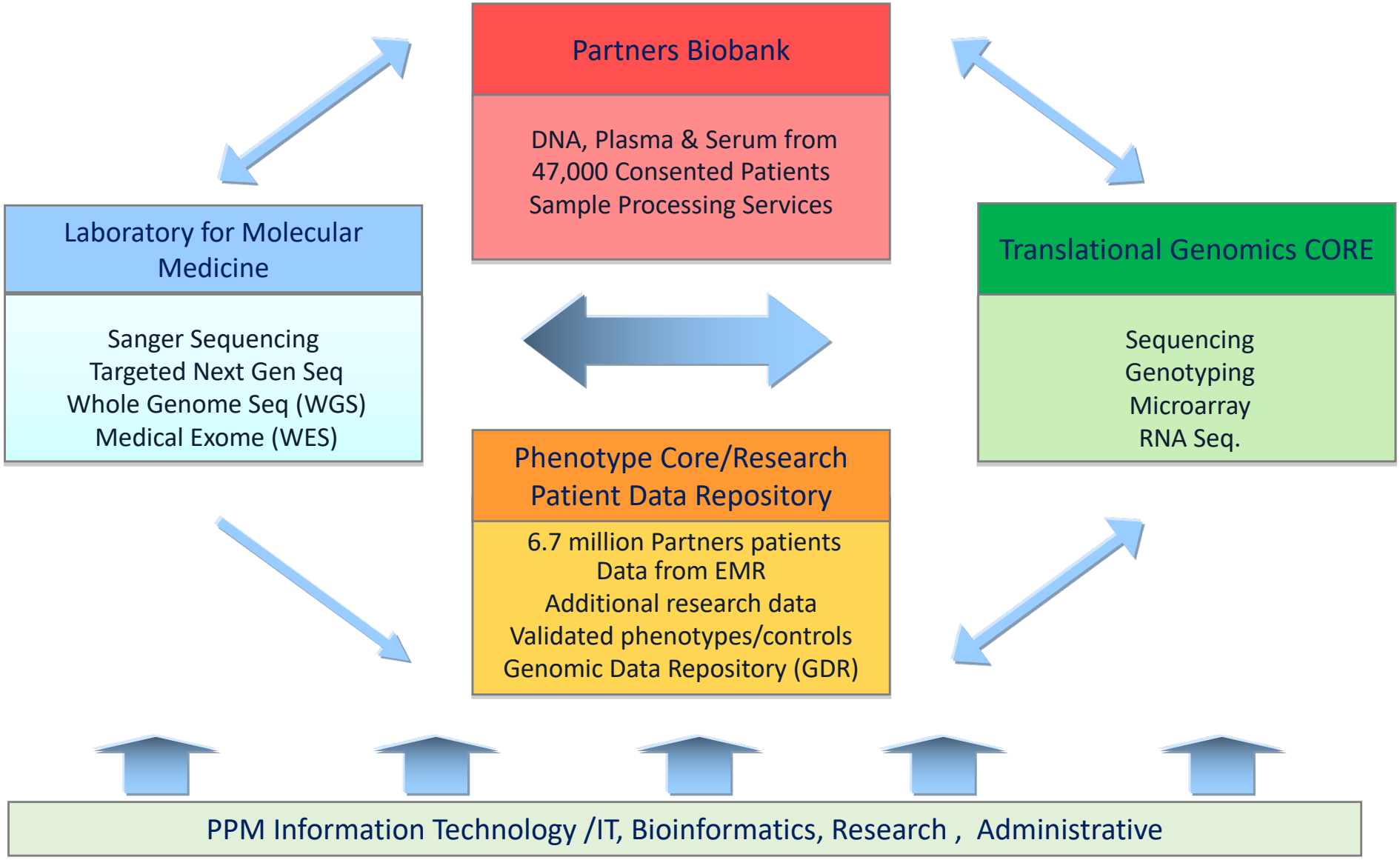
- The Partners Biobank provides samples (plasma, serum, and DNA) collected from consented patients.
- 80,000 patients have consented to date
- Samples are available for distribution to Partners investigators* to help identify novel Personalized Medicine opportunities that reduce cost and provide better care

**with required approval from the Partners Institutional Review Board (IRB).*

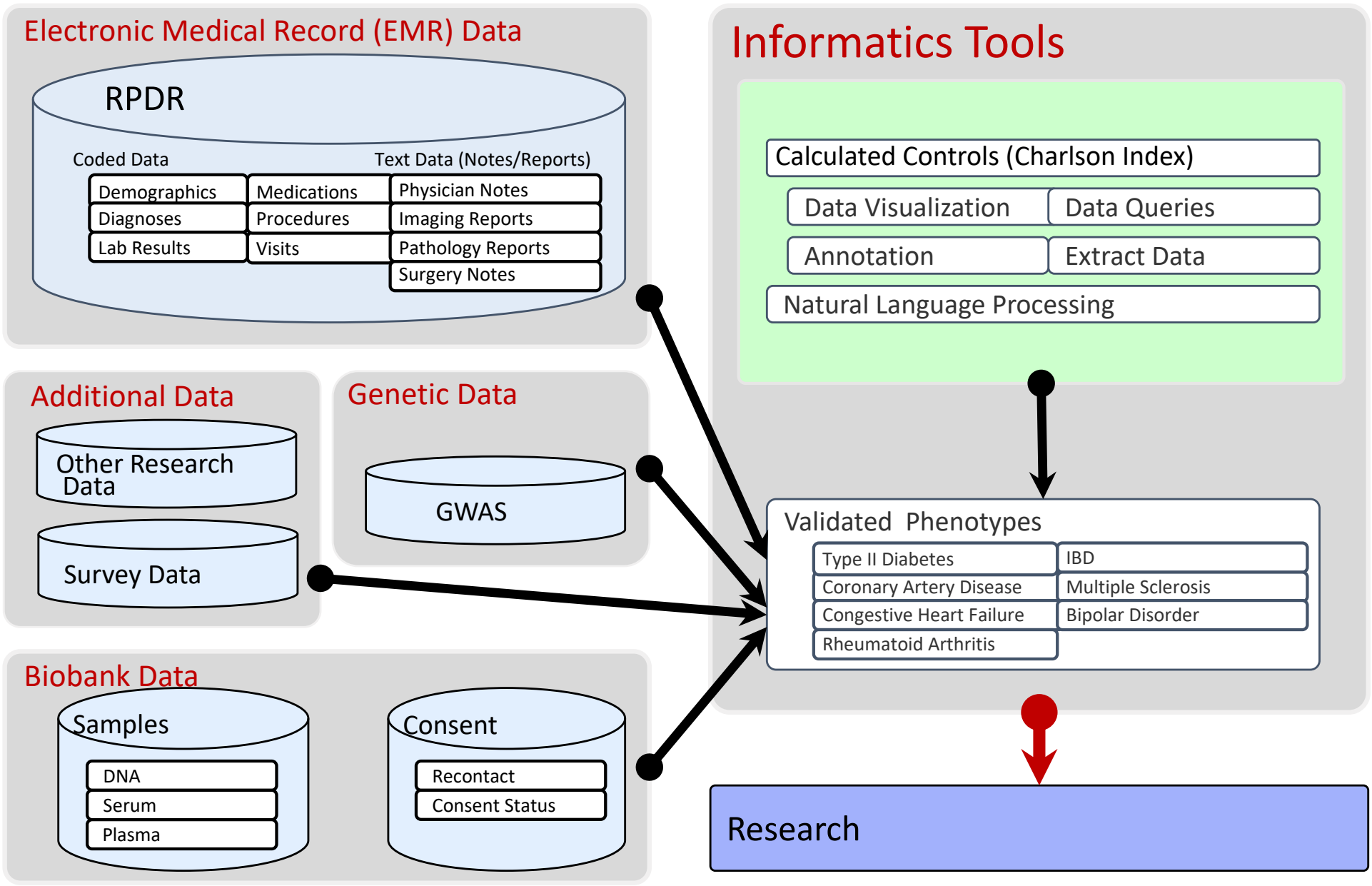
Biobank Integrative Genomics Strategy



Partners Personalized Medicine Components



Data Integration | Phenotype Discovery Center



Psychological Medicine (2012), **42**, 41–50. © Cambridge University Press 2011
doi:10.1017/S0033291711000997

ORIGINAL ARTICLE

Using electronic medical records to enable large-scale studies in psychiatry: treatment resistant depression as a model

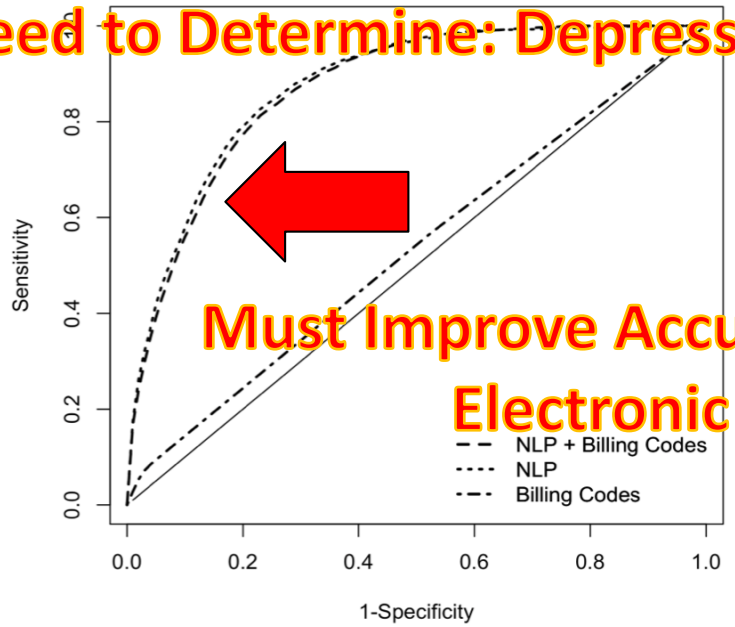
R. H. Perlis[1,2*], D. V. Iosifescu[1,3], V. M. Castro[4], S. N. Murphy[5], V. S. Gainer[4], J. Minnier[6], T. Cai[6], S. Goryachev[4], Q. Zeng[7], P. J. Gallagher[2], M. Fava[1], J. B. Weilburg[1], S. E. Churchill[8], I. S. Kohane[9] and J. W. Smoller[2]

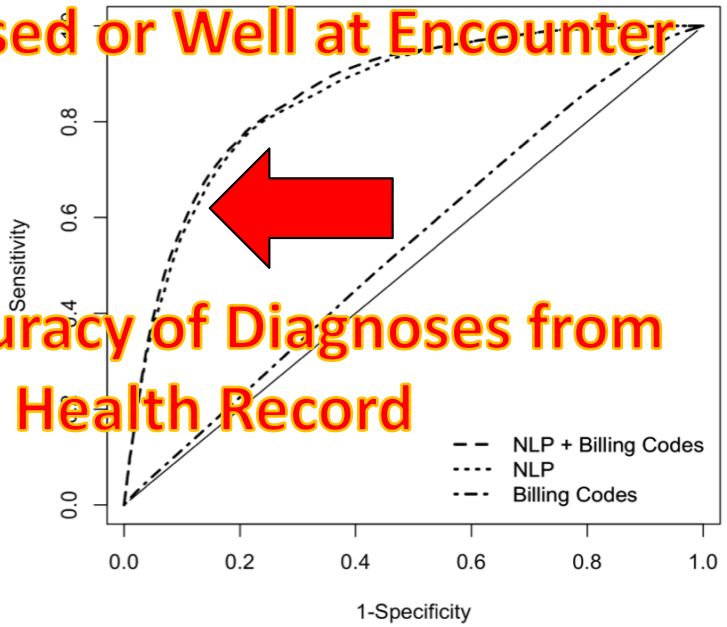
Use Phenotyping Algorithms to define cohorts of treatment-resistant and treatment-responsive depression

Need to Determine: Depressed or Well at Encounter

Initially:
AUC = 0.54

Finally:
AUC = 0.87





Initially:
AUC = 0.55

Finally:
AUC = 0.86

Must Improve Accuracy of Diagnoses from Electronic Health Record

Clinical Status	Model	Specificity	Sensitivity	Precision	AUC
Depressed	Billing Codes	0.95	0.09 (0.03)	0.57 (0.14)	0.54 (0.02)
Depressed	NLP	0.95	0.42 (0.05)	0.78 (0.02)	0.88 (0.02)
Depressed	NLP + Billing Codes	0.95	0.39 (0.06)	0.78 (0.02)	0.87 (0.02)
Well	Billing Codes	0.95	0.06 (0.02)	0.26 (0.27)	0.55 (0.03)
Well	NLP	0.95	0.37 (0.06)	0.86 (0.02)	0.85 (0.02)
Well	NLP + Billing Codes	0.95	0.39 (0.07)	0.85 (0.02)	0.86 (0.02)

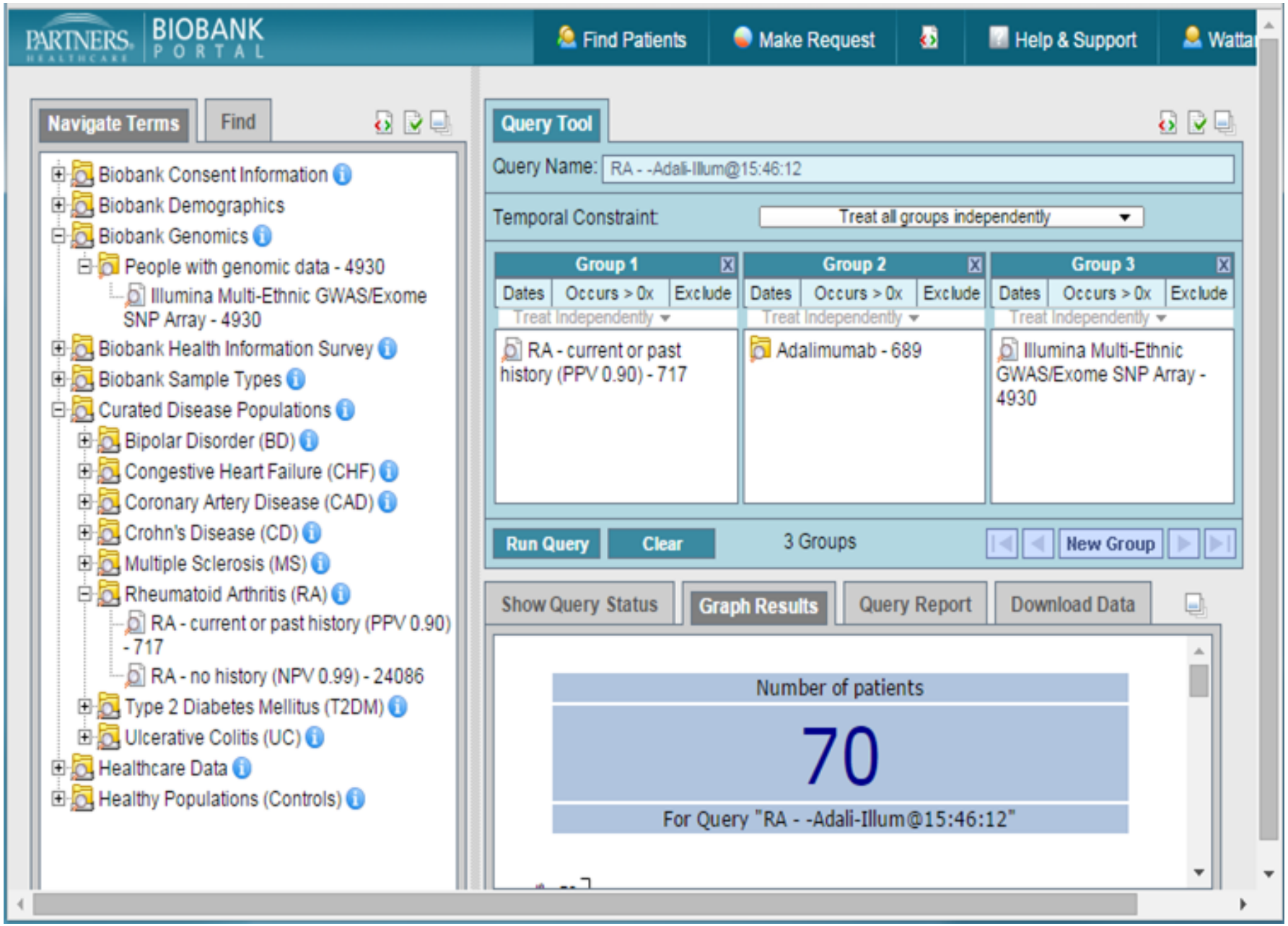
Biobank Portal | Curated Diseases w/genotype data

Validated Phenotype	Count*	Predictive Positive Value
Bipolar Disease	154	89%
Congestive Heart Failure	556	90%
Coronary Artery Disease	3476	97%
Crohn's Disease	566	90%
Multiple Sclerosis	190	90%
Rheumatoid Arthritis	885	90%
Type 2 Diabetes Mellitus	2712	97%
Ulcerative Colitis	392	90%

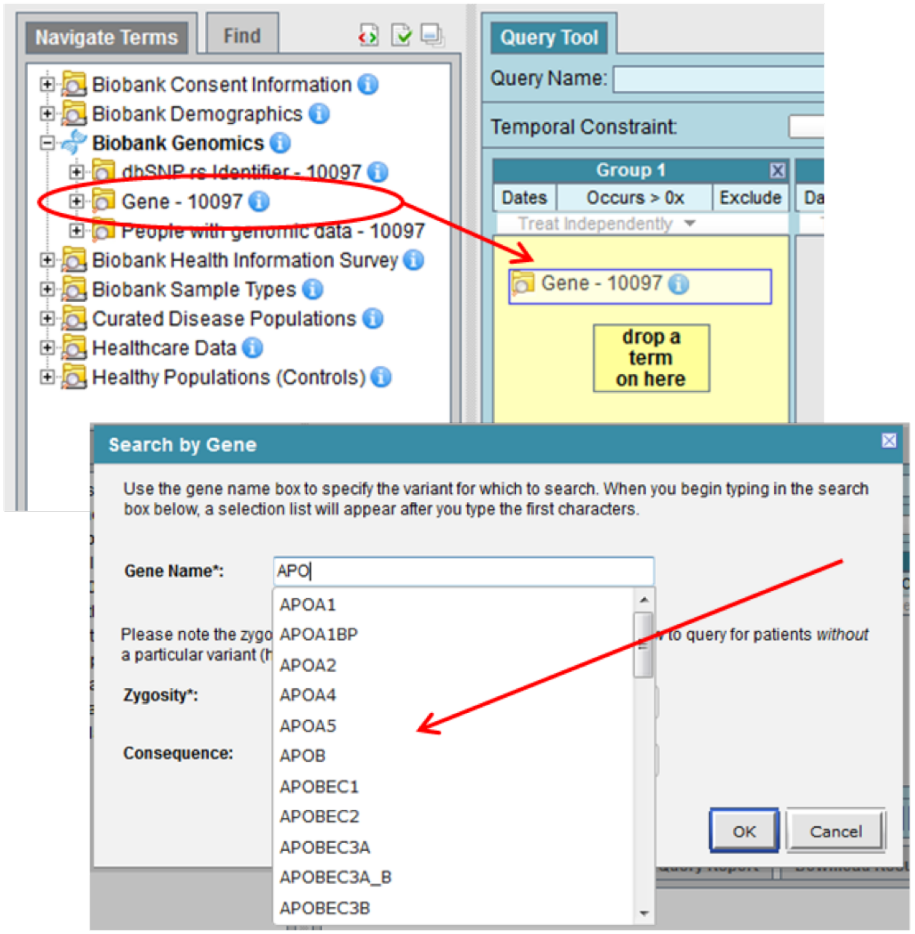
Healthy Controls based on Charlson Index	Count*
0 – 10-year survival probability is >98.3%	12,142
1 – 10-year survival probability is >95.87%	8,556
2 – 10-year survival probability is >90.15%	8,250

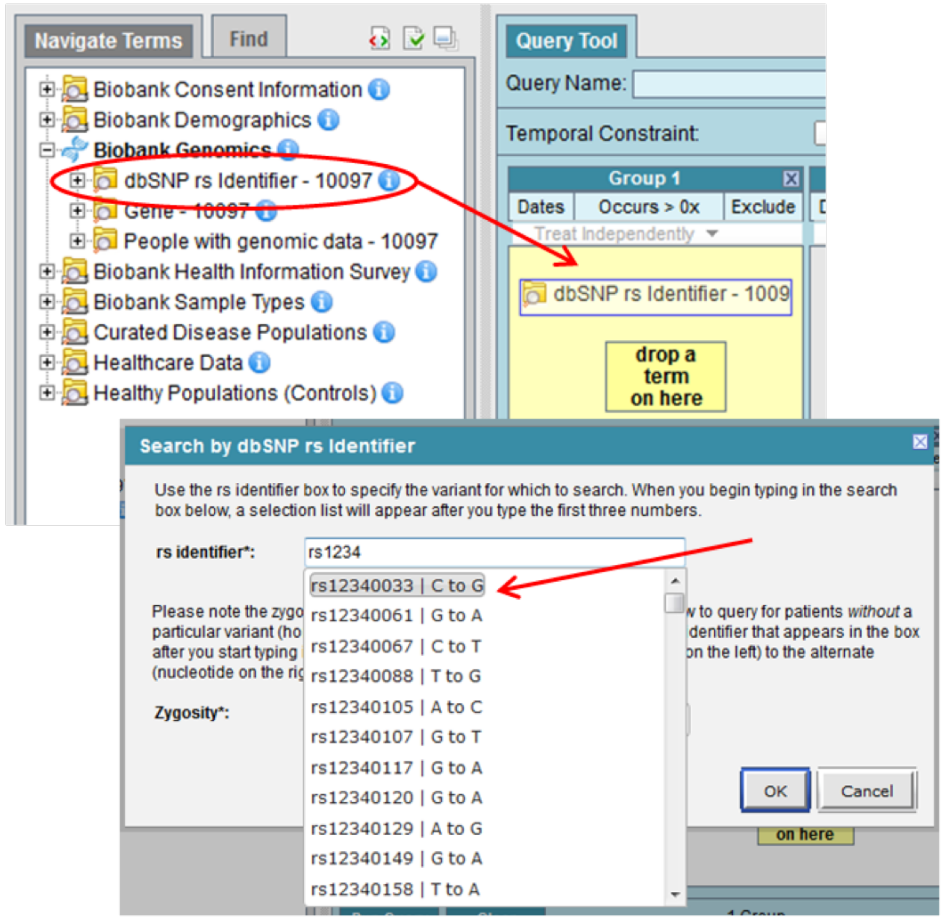
* Based on 20,086 patients

** Based on 79,834 patients


PARTNERS HEALTHCARE
BIOBANK PORTAL
Find Patients
Make Request
Help & Support
Navigate Terms
Find
Biobank Consent Information
Biobank Demographics
Biobank Genomics
People with genomic data - 4930
Illumina Multi-Ethnic GWAS/Exome SNP Array - 4930
Biobank Health Information Survey
Biobank Sample Types
Curated Disease Populations
Bipolar Disorder (BD)
Congestive Heart Failure (CHF)
Coronary Artery Disease (CAD)
Crohn's Disease (CD)
Multiple Sclerosis (MS)
Rheumatoid Arthritis (RA)
RA - current or past history (PPV 0.90) - 717
RA - no history (NPV 0.99) - 24086
Type 2 Diabetes Mellitus (T2DM)
Ulcerative Colitis (UC)
Healthcare Data
Healthy Populations (Controls)
Query Tool
Query Name: RA - -Adali-Illum@15:46:12
Temporal Constraint: Treat all groups independently
Group 1
Group 2
Group 3
Dates
Occurs > 0x
Exclude
Treat Independently
RA - current or past history (PPV 0.90) - 717
Adalimumab - 689
Illumina Multi-Ethnic GWAS/Exome SNP Array - 4930
Run Query
Clear
3 Groups
New Group
Show Query Status
Graph Results
Query Report
Download Data
Number of patients
70
For Query "RA - -Adali-Illum@15:46:12"

Genotype Data

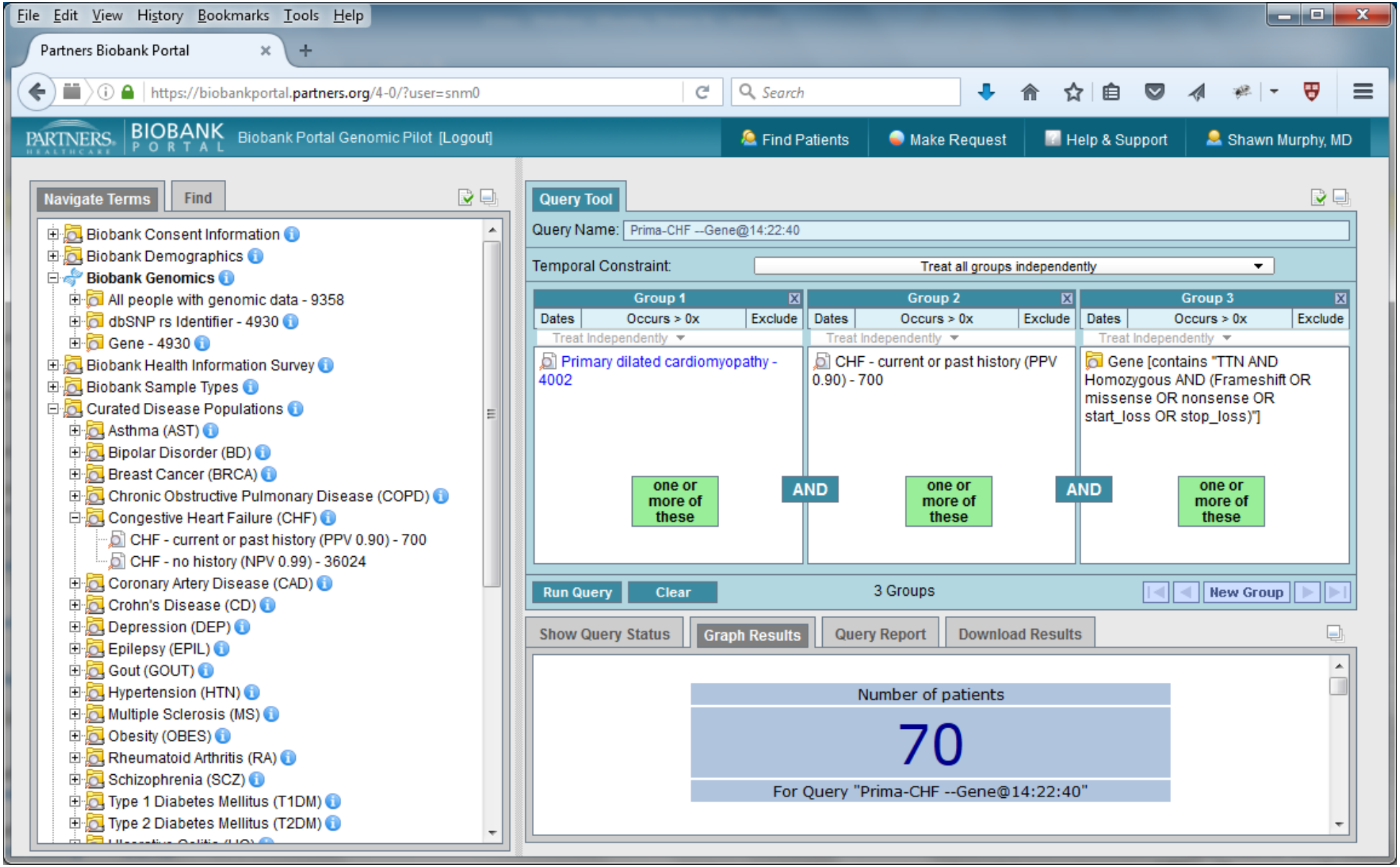




LDLR

- 141 SNP or indels (V1)
- 243 SNP or indels (V2)
- 1336 subjects with protein altering (frameshift, missense, nonsense, start loss, stop loss) variant

High Quality Phenotypes for Genetic Studies



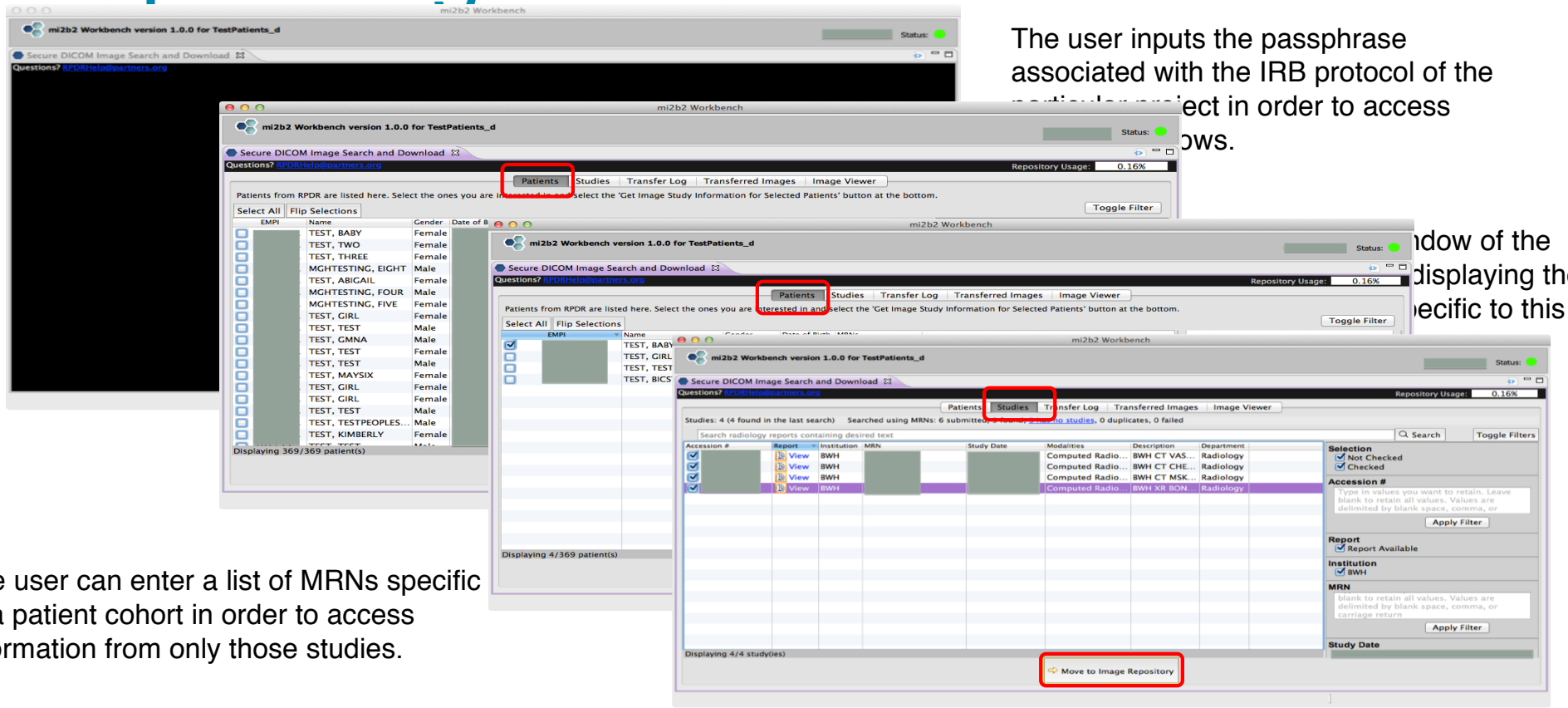
Acknowledgements

- RPDR
  - Shawn N Murphy
  - Christopher Herrick
  - Mariah Mitchell
  - Stacey Duey
  - Laurie Bogosian
  - Eugene Braunwald
  - Anne Klibanski
  - Henry Chueh
- CIB
  - Shawn N Murphy
  - Randy L Gollub
  - Vivian Gainer
  - Andrew Cagan
  - Nich Wattanasin
  - Christopher Herrick
  - Bill Wang
  - Reeta Metta
  - Rudolph Pienaar
  - Yangming Ou

- Mi2b2
  - Randy L Gollub
  - Shawn N Murphy
  - Christopher Herrick
  - Bill Wang
  - David Wang
  - Kathy Andriole
  - Darren Sack
  - P Ellen Grant
  - Nathaniel Reynolds
  - Kallirroi Retzepi
  - Rudolph Pienaar
  - Victor Castro
  - Steve Pieper
  - Lilla Zollei
  - Yangming Ou

Partners Healthcare, NIH/NCBC; /NIMH; /NCBI; /NCATS; /NIBIB
NIH RO1 EB014947
NIH R01 AT006364
NIH R01 AT005280
NIH P01 AT006663

Operating the mi2b2 Workbench



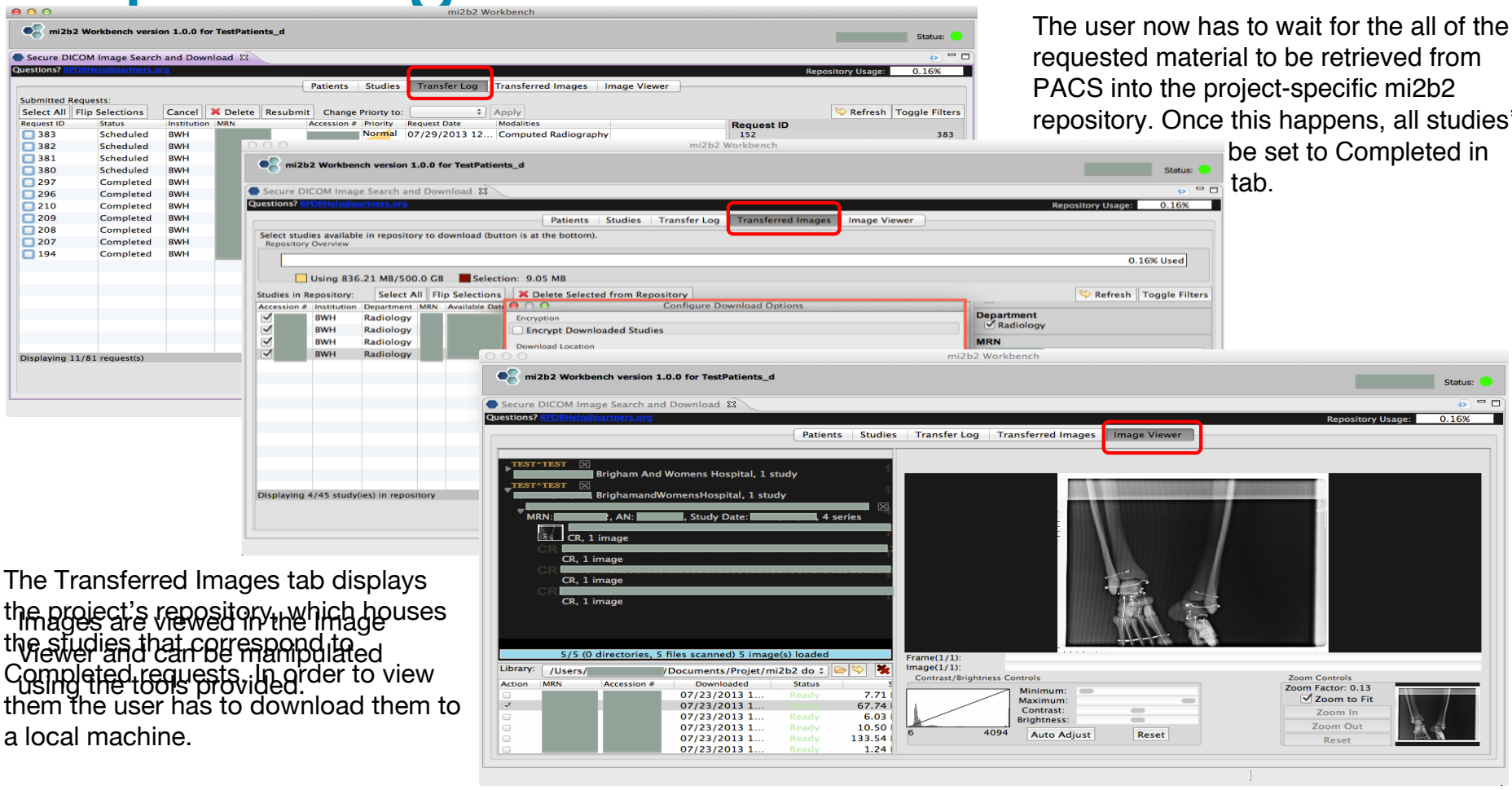
The user inputs the passphrase associated with the IRB protocol of the particular project in order to access ows.

ndow of the displaying the ecific to this

The user can enter a list of MRNs specific to a patient cohort in order to access information from only those studies.

After selecting the studies of interest under the Studies tab, the user requests them from PACS by clicking on the “Move to Image Repository” button

Operating the mi2b2 Workbench



The user now has to wait for the all of the requested material to be retrieved from PACS into the project-specific mi2b2 repository. Once this happens, all studies' be set to Completed in tab.

The Transferred Images tab displays the project's repository, which houses the studies that correspond to Completed requests. In order to view them the user has to download them to a local machine.

Images are viewed in the Image Viewer and can be manipulated using the tools provided.