









The Biomedical Informatics Research Network:

Experiences with Cyberinfrastructure in a Biomedical Research Community

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BRIITE - IT SUPPORT FOR MULTI-INSTITUTION COLLABORATIVE RESEARCH November 4, 2005





### **Biomedical Informatics Research Network**



A Shared Biomedical IT Infrastructure to Hasten the Derivation of New Understanding and Treatment of Disease through use of Distributed Knowledge

- Connect distributed multi-scale biomedical data and researchers
- Open access to data and tools
- Bring Transparent GRID Computing to Biomedical Research
- Grow Interdisciplinary Biomedical Informatics Workforce >Translation



# Challenges



### Overview of the BIRN Roadmap

- Be the vehicle for bringing advanced cyberinfrastructure to the larger biomedical community
- Deliver and maintain a robust and scalable PRODUCTION Grid for the collaborative sharing, analysis and interrogation of biomedical data
- Provide integrated solutions for core domain science requirements
- Provide a consistent and scalable delivery mechanism

BIRN has developed an "End-to-End" Production Infrastructure in the context of distributed biomedical research projects.

### BIRN-CC Enables Test Bed Science

- A stable, robust, shared network and distributed database environment
- Extensible tools and IT infrastructure that can be reused.
- Established cyberinfrastructure for data grid and large scale data integration effort
- High performance connectivity between distributed resources (computation and data storage)
- Seamless access to distributed high performance computing resources

# Changing the use pattern for research data from the individual laboratory/project to shared use.

### The BIRN Collaboratory Today

Edinburgh

Enabling collaborative research at 28 research institutions comprised of 37 research groups.

RIRN

BIOMEDICAL INFORMAT





# **BIRN Testbeds - Overview**

- Morphometry BIRN
  - Brain Structure in AD, MCI, Depression
- Function BIRN
  - Activation Differences in Schizophrenia
- Mouse BIRN
  - High Resolution Imaging and Animal Models of Human Diseases

### BIRN-CC

 Coordinating Center for Cyberinfrastructure



# Morphometry **BIRN**

 Anatomical Correlates of Psychiatric Illnesses

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BIR

- Unipolar Depression, Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI)
- Site and Platform Independent Acquisition and Analysis for Pooling Data
  - Multi-Site Clinical Studies
  - Increase Statistical Power for Rare Populations or Subtle Effects
- Advanced Image Analysis and Visualization
- MGH, BWH, Duke, UCLA, UC San Diego, Johns Hopkins, UC Irvine, Wash U, MIT



**Normal Elderly Control** 



Alzheimer's Individual



### SASHA Project

### Semi Automatic SHape Analysis (SASHA)





# Large Deformation Diffeomorphic Metric Mapping (LDDMM) using the TeraGrid

- Each LDDMM comparison takes about 3 to 8 hours
- Completed analysis of scaled run of 45 subjects
  - Examining hippocampus clustering and disease detection in senile dementia (control, Alzheimer's, semantic dementia)
  - 30,000 CPU hours, 4 TB data
- Being applied in Mouse BIRN test bed Fragile X mouse model

Successful classification of the different subject groups through the utilization of non-invasive imaging methodologies potentially provides clinicians with new tools to assist them in their daily work

# **Function BIRN Overview**

- Calibration Methods for Multi-Site fMRI
  - Study Regional Brain Dysfunction and Correlated Morphological Differences
  - Progression and Treatment of Schizophrenia
- Human Phantom Trials
  - Common Consortium Protocol
  - 5 Subjects Scanned at All 11 Sites
  - Add'l 15 Controls, 15 Schizophrenics Per Site Per Year
- Statistical Techniques
  - Identify Cross-Site Differences
  - Develop Corrections to Allow Data Pooling
- Develop Interoperable Post-Processing
- UC Irvine, UCLA, UC San Diego, MGH, BWH, Stanford, UMinnesota, Ulowa, UNew Mexico, Duke/UNorth Carolina, MIT





# fBIRN Multi-Site Data Example





# FBIRN Stability QA Portal





and Visualization Data Manar

### MDI Stability

Institution	Scanner	FS	mean	stdDev	SNR	SFNR	%-Fluct	drift	count	csv
			20000	20	300	225	.30	3		
duke-unc	GE mr5c	4.0	1607.92	3.92	351.62	258.73	0.24	-0.53	46	CSV
duke-unc	GE MR6C	1.5	655.39	0.55	87.92	87.69	0.08	-0.39	126	CSV
harvard-bwh	GE LMRC	3.0	19066.82	15.22	178.57	176.98	0.09	-0.46	6	CSV
harvard-mgh	SIEMENS bay4oc	2.9	984.45	0.95	183.85	182.20	0:10	0.38	2	c
minnesota-cmrr	SIEMENS trio	2.9	780.69	1.15	221.67	211.07	0.14	0.53	30	c
newmexico-hsc	SIEMENS MRC21262	1.5	666.63	1.06	74.75	74.10	0.16	0.47	191	C
stanford-lucas	GE LMR3	3.0	819.52	0.92	223.60	223.38	0.11	-0.67	13	c
uci-bic	PICKER ba187_ws	1.5	4174.62	8.20	126.66	120.22	0.19	-0.76	30	C
ucsd-fmri	SIEMENS MRC14109	1.5	677.10	0.93	79.30	76.70	0.14	2.33	1	c
ui-mhoro	GEMRCV	1.5	2007.02	1.62	201.07	189.40	0.08	-0.29	6	c

#### Mean Trimming Percent: 0

MRItotal csv GA Pivot xlt

back to QA Protocols

#### QA Analysis Description

Sampling Region: The sampling region is a 20x20 voxel region centered in the volume's central slice (slice #18).

Mean: Simple mean calculated from the average of each sampling region over 198 volumes. The first 2 volumes are skipped to allow for signal instabilities during ramping of the gradient electronics.

Standard Deviation (stdDev): Calculated in the same fashion as the mean.

Signal-to-noise ratio (SNR): The noise measurement is calculated by subtracting the average of the even numbered volumes from the odd numbered volumes using the sampling region. The signal measurement is calculated from the sampling region applied to the mean image. The SNR is calculated from the ratio of these.

Signal-to-noise fluctuation ratio (SFNR): The SFNR measurement is calculated by dividing the sampling region from the mean image by the sampling region of the standard deviation image.

Percent fluctuation (% fluc): Percent fluctuation or root mean square stability is calculated from the sampling region after applying a second order detrending fit.



Tue Oct 12 11:24:31 2004

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### Community Database Development



► <u>Qu</u> ► <u>Lo</u> BIRN

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# **fBIRN Analysis Infrastructure**



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# Mouse **BIRN**

Studying animal models of disease across dimensional scales to test hypothesis with human neurological disorders

- Experimental Allergic Encephalomyelitis (EAE) mouse models characteristic of Multiple Sclerosis (MS)
- Dopamine Transporter (DAT) knockout mouse for studies of schizophrenia, attention-deficit hyperactivity disorder (ADHD), Tourette's disorder, and substance abuse
- Using an alpha-synuclein mouse to model the symptoms/pathology of Parkinson's Disease
- Cancer animal models consortium with astrocytoma mouse model: NCI supported with Terry Van Dyke @ Duke
- Cal Tech, Duke, UCLA, UCSD, Univ. Tenn





# Multiscale Data Integration



1. Databases at each site



2. Create conceptual links to a shared ontology



4. Use mediator to navigate and query across data sources



3. Situate the data in a common spatial framework





# Spatial Registration of Data



Volume and slice data brought into register in order to correlate cellular and subcellular changes with noninvasive imaging Processing stream for spatial registration of brain volumes using the LONI pipeline, UCLA: David Rex, Allan MacKenzie-Graham



# The Smart Atlas: Spatial Integration over Distributed Data



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### Autosegmentation- Morph- Mouse BIRN



# Human-Mouse integration



# Driving **Big Science** where it Didn't Exist Before

- Encouraging Collaboration
- Removing Barriers to Multi-Site Collaborative Research
  - Calibration
  - Compute / Storage Resources
  - Databases
  - Common Protocols
  - Post-Processing Tools
  - Governance



**RN** Testbeds

### **Challenges: Creating a New Culture**

- How to get competitors to cooperate
  - Will this project decrease the RO1 \$ pool
  - How to share glory, work and \$
  - Governance who makes and keeps the rules
- How to avoid data-mine-ining
  - "What's mine is mine and what's yours is mine"
- How to communicate across fields efficiently:
  - Clinician scientists
     Computer scientists
  - Experimental psychologists MRI physicists
  - Statisticians
     Database engineers
- How to show a clear scientific benefit from cooperation
  - Efficiency of multiple studies in parallel; quick revisions
  - Different perspectives create new ideas or achieve the lowest common denominator "designed by committee"



### Working Groups BIRN



Ad hoc working groups created by the test beds meet according to their needs

# **BIRN IRB/HIPAA Working Group**

- One member from each BIRN site required to participate
- Each member is required to review BIRN consents, waivers and procedures with local IRBs
- Regular video conferences among members to coordinate information and activities

- Produce BIRN template language for subject consent, IRB waiver for data upload and IRB waiver for data download
- Produce guidelines and procedures for data sharing across institutions taking into account Common Rule, HIPAA and state regulations
- Develop procedures to allow for longitudinal studies within BIRN



### BIRN Toolkit



### **BIRN** Cyberinfrastructure

### We Began with Standard Hardware



- Jumpstarted BIRN for functionality
- Software footprint managed by the BIRN-CC
- Integration of domain tools, middleware, OS, updates, and more
- Expansion/upgrade of existing sites have more generic (and fewer \$\$) hardware
  - e.g. Opteron, New Xeon, Multi-vendor

### Software Problem in a Nutshell

- Enable Analysis of Distributed Biomedical Data in a National-Scale Production Facility
  - Data Sets are Large Data Sets are Many
  - Enable New Queries that Integrate Multiple Sources
  - Specialized Application Codes (from Test Beds) need to work on BIRN-accessible Data
- Some Analysis Pipelines Require Significant Computation
  - Privacy, Patient Anonymity Required

Data & Network

Security

- Institutional Ownership of Originals
- Easily Replicate Entire Software Stack (Including Centralized Services) for other Groups



### Major System Components

### **Collaborating Groups of Biomedical Researchers**

Application Portal

Command/Batch

Access





### Specific Implementations

### Mouse, Function, Morphometry (+ New Areas and Users )



Command/Batch Access



### System Deployment

- Utilizing Rocks grid management software
- BIRN specific extensions to Rocks, also under CVS, means automated, repeatable deployment of any version of the BIRN system
- We've created BIRN "rolls" that integrate
  - BIRN domain tools (e.g. 3DSlicer, LONI Pipeline, FreeSurfer)
  - Database (Oracle) and SRB Configuration
- Rocks, with BIRN extensions, includes automated deployment mechanism for
  - Middleware (Security, Computational, Data)
  - Data mediation/integration
  - Application codes
  - Portal and other Workflows

### Software Integration Cycles



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# BIRN Toolkit



### **BIRN** Cyberinfrastructure

INFORMATICS RESEARCH NETWORK BIOMEDICAL

### **BIRN** is Enabling Secure Collaboratories



Welcome to the Morphometric BIRN Public Alzheimers Disease Human Imaging Database web interface

The site currently provides the following features:

- building a fairly generic assessment guery and navigating through its results
- · exporting the full set of search results in comma separated value (CSV) format to be used with statistical packages like
- SPSS viewing visits (both scan and clinical) of a selected subject from the query results. dowloading the structural MRI mage series for the subject as tared spped AFNE brik from SPB Univariate and Rivariate stratistics via SIPM fortal integration.

To start using this web interface, you need to get an account by contacting the webmaste

The BIRN Coordinating Center is deploying a common authentication and security infrastructure. •Provides for Single Sign-On to access all portal, data and computational resourcees •Available to all BIRN applications •Will provide access to external resources (e.g. **OptiPuter and TeraGrid**)

### Enabling Large Scale Data Sharing

- BIRN Data Grid: a Distributed Data Handling System built utilizing the Storage Resource Broker (SRB)
- Data has more than doubled in the last year

 Provides a scalable and distributed solution for distributing publicly available data



From outliers in univariate statistics, launch 3DSlicer to view anatomical data and use Query Atlas tool

### /home/BIRN/Human/Clinical

/home/Public/MorphAD\_p0001/009007669326

Launch 3D Slicer

Browse Data

/home/Public/MorphAD\_p0001/009022174223

Launch 3D Slicer

Browse Data

/home/Public/MorphAD\_p0001/009134330441

Launch 3D Slicer

Browse Data

/home/Public/MorphAD\_p0001/009157526843

Launch 3D Slicer

Browse Data

### /home/Public/MorphAD\_p0001/009196266232

Launch 3D Slicer

Browse Data



### Integrating the Local Desktop

 Java Grid Interface (JGI) provides wrapper for applications on a users desktop

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Ih:

PR

- Brokers communications and information/data transfer between the application and BIRN resources (e.g. BIRN Data Grid)
- Allows for domain applications to be integrated with the BIRN infrastructure in a straightforward way
- Improved version being developed in collaboration with Telescience for GridSphere Portal

## Integrating Data using the BIRN

BIOMEDICAL INFORMATICS RESEARCH NETWORK Mediator



![](_page_37_Picture_0.jpeg)

# Expert Knowledge

![](_page_37_Figure_2.jpeg)

"Find proteins located in cerebellar cortex"

![](_page_38_Picture_0.jpeg)

### Semantic (Glue) Knowledge for BIRN

![](_page_38_Figure_2.jpeg)

### Ontological Tools

![](_page_39_Figure_1.jpeg)

### **UMLS Browser**

Concept :	cerebellum
CUI:	C0007765
Semantic Type(s) :	Body Part, Organ, or Organ Cor
Definition :	

- Part of the metencephalon that lies in the posterior cranial fossa b stem. It is concerned with the coordination of movement. (MSH)
- The portion of the brain in the back of the head between the cere stem. The cerebellum controls balance for walking and standing, complex motor functions. (PDQ)

Synonym(s) :

- cerebellums
- · cerebellum, nos
- cerebellum <1>
- tissue of cerebellum
- corpus cerebelli <2>
  corpus cerebelli
- corpus cerebellum
   cb cerebellum
- co cerebellum
  epencephalon-1
- a60 cerebellum

concepts Lookup

concept	conceptid	conceptontology	language
CA3	C0694600	UMLS	ENG
CA3-field CA3 of hippocampus	C0694600	UMLS	ENG
CB	BF_C000202	BONFIRE	ENG
Cg/Rs	BF_C000203	BONFIRE	ENG
IPI	BF_C000272	BONFIRE	ENG
KF	C0175530	UMLS	ENG
Kolliker-Fuse nucleus	C0175530	UMLS	ENG
LAcbSh	BF_C000273	BONFIRE	ENG
LDDM	BF_C000279	BONFIRE	ENG
LDTg	BF_C000280	BONFIRE	ENG
LDTgV	BF_C000281	BONFIRE	ENG
LDVL	BF_C000282	BONFIRE	ENG
LEnt	BF_C000283	BONFIRE	ENG
LHbL	BF_C000284	BONFIRE	ENG
LHbM	BF C000285	BONFIRE	ENG

4 7

Done

RIRN

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![](_page_40_Picture_0.jpeg)

### **Distributed Computation**

 Enhanced job management functions provide detailed job information for execution on remote resource

![](_page_40_Picture_3.jpeg)

BIOMEDICAL INFORMATICS RESEARCH NETWORK

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Data Management Analysis and Visualization Collaboratory Tools Advanced Data Integration

#### BIRN Grid Job Status

\$5

BIRN

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4 .

LDDMM Jo	b
Start Time	Fri Sep 10 16:41:44 2004
User	jegrethe
Execution	/opt/birn/ldmm/bin/ldmm -d 3 -A srbfile:/home/BIRN/Human/Dev/lddmm/human/hippocampus/renewal_demo_2004/registered_80_96_80/XJJ_lh.hippocampus_96.img -T srbfile:/home/BIRN/Human/Dev/lddmm/human/hippocampus/renewal_demo_2004/registered_80_96_80/XSP_lh.hippo
Resource	jhu-gpop.nbim.net
Status	PENDING

application which aims to onal Anatomy thereby ges in shapes. As part of develop techniques to not

![](_page_40_Picture_9.jpeg)

![](_page_40_Picture_10.jpeg)

![](_page_41_Picture_0.jpeg)

### **BIRN Toolk**

![](_page_41_Figure_2.jpeg)

**BIRN** Cyberinfrastructure

The BIRN shared information technology infrastructure for basic and translational research is available to all researchers from any internet capable location.

The BIRN is developing a shared information technology infrastructure for basic and translational research that is available to all researchers from any internet capable location.

![](_page_42_Picture_2.jpeg)

![](_page_43_Picture_0.jpeg)

#### **Choose Your Testbed**

<u>Function</u> - studying regional brain dysfunctions related to the progression and treatment of schizophrenia.

Morphometry - examining unipolar depression, mild Alzheimer's disease and mild cognitive impairment.

<u>Mouse</u> - studying animal models of multiple sclerosis, schizophrenia, Parkinson's disease, ADHD, Tourette's disorder, brain cancer.

**NAMIC** - The National Alliance for Medical Imaging Computing (NAMIC) is a multi-institutional, interdisciplinary team of computer scientists, software engineers, and medical investigators who develop computational tools for the analysis and visualization of medical image data.

<u>BIRN CC</u> - supports these projects and the overall information technology (IT) infrastructure of the BIRN

#### **BIRN Announcements**

#### May 13, 2004

The BIRN CC released the <u>BIRN Grid Portal API</u> for use on the production BIRN portal.

#### March 22, 2004

BIRN test bed participants presented a **"Building on the BIRN"** workshop at the National Institutes of Health. View <u>presentations</u> from and <u>photos</u> of the event.

#### March 3-5, 2004

UCI hosted a Function BIRN All Hands Meeting at the Beckman Center of the National Academy of Sciences, Irvine.

BIRN Grid Statu	5				
Grid Host	Data Grid R	esources			
UCSD - NCMIR	nas0:88%	nas1:92%			
UCSD - FMRI	nas0:75%	nas1:88%	nas2:88%	nas3:54%	nas4:57%
UCLA - LONI	nas0:11%	nas1:4%	nas2:4%	nas3:3%	
Caltech - BIC	nas0:36%	nas1:61%			
Duke - CIVM	nas0:75%	nas1:46%	nas0:75%		
Duke - UNC	nas0:3%	nas1:2%	nas2:3%	nas3:3%	
Harvard - BWH	nas0:81%	nas1:31%			
Harvard - MGH	nas0:23%	nas1:21%	nas2:45%		
UI - MHCRC	nas0:21%				
UMN - CMRR	nas0:12%				
UNM - HSC	nas0:10%	nas1:7%			

### **BIRN Portal**

•Application environment that provides transparent and pervasive access to the BIRN infrastructure (i.e. tools, applications, resources) with a **Single Login** from any Internet capable location

•Provides simple, intuitive access to distributed resources for data storage, distributed computation, and visualization

•Support for dynamic collaborative projects

•Built on standard Portal framework

### Providing an Intuitive Interface to the BIRN Collaborative Environment

![](_page_44_Figure_2.jpeg)

### **BIRN Supports Grid Portal Technology**

Project Memberships ID Username

akolasny

Role

Owner

Started

10-29-2004

Status

Active

Emailalert

akolasny@ihu.edu

![](_page_45_Picture_1.jpeg)

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The BIRN-CC is supporting development of the leading open-source standards-based grid portal.

#### gridsphere portal framework open-source / portlet jsr168 compliant GridSphere Download Documentation Developers Projects Consulting About Home News Events Contact Welcome to the GridSphere Project! News The GridSphere portal framework provides an 7/6/2005 Grid Portlets 1.1 open-source portlet based Web portal. GridSphere enables is now available for developers to quickly develop and package third-party download! portlet web applications that can be run and administered within the GridSphere portlet container. Here you will find 6/13/2005 Grid Portlets the GridSphere portal framework available for download 1.0.3 is now available for and documentation related to the installation and download! development of portlets using GridSphere. 5/27/2005 Grid Portal Workshop, hosted gridsohere Portal - Mozilla Firefox Australian Partner File Edit View Go Bookmarks Tools He 🗸 🗿 Go 💽 Advanced Comput 🛶 - 🛃 🖸 😭 📢 http:/ Apache Tomcat-5.0.28 🗳 local-oridsphere 🛸 GridSphere Portal - dev 🚥 Biomedical Inform open for registratio BIRN Project Info : Analysis, Visualization and Interpretation Project ID Members: 3 Project Na Access: Private pment, integration, and d ent of a suite of freely available software to Public Info estigation of the mo ation of the morphological bases of dysfunction through increasingly sophisticated image analysis ngly large subject populations acquired at multiple research sites. Type: Norma and development, integration, and deployment of a suite of treely available software to e pation of the morphological bases of dysfunction through increasingly sophisticated image ingly large subject populations acquired at multiple research sites. **Private Descript** Accessible Private SRB Group Nam avi 0004 Lines: thion 10-29-2004 09:31:54 Founded Number of P Role: Membe **Current Activities** loined: Oct 29, 2004 Status: Artive Contract All | Expand All Select Project(15) Analysis, Visualia Memberships Portal Te

### Integration with BIRN Services

•Portal provides Intuitive user interfaces to access commonly used functionality

• With authentication service there is seamless interaction with Portal services

Univariate Analysis		
Structure		
Brain Hippocampus.Volume	Laterality Total ^ Left Right v	
Demographic Factors	·	
Continuous	Dichotomous	

Lontinuous		Dichotomous	
MMSE.MMSE.Score	^	Demographics.Gender	^
Demographics.Age		Diagnosis.Diagnosis	
Demographics.Years.of.Education	~		~

#### **Output Selection**

- 🗹 Mean, Standard Deviation
- 📃 Stem & Leaf Plot
- 🗹 Plot Histogram
- Emperical Cumulative Distribution Function
- 🔲 Quartile-Quantile (Q-Q) Plot
- 🔲 Shapiro-Wilk Normality Test
- 🗹 Box Plot

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Export CSV										<< (1) >
										Results 1-20 of 2
Subject ID	Site ID	MMSE	Dem	ograph	nics	Diagnosis	CYLT	VFT	Left Hippocampus	Right Hippocampus
		MMSE Score	Age	Gender	Years of Education	Diagnosis	Discriminability raw score	"Animals" correc responses	t Volume	Volume
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009015726375										
Visit: 2 Seg: 1	SITE1	30								
Visit: 1 Seg: 1	SITE1		71	F	14	Control			3760.0	3650.0
Visit: 3 Seg: 1	SITE1						.93	22		
009016532513								_		
Visit: 2 Seg: 1	SITE1	17		_			.41	7		
Visit: 1 Seg: 1	SHEI		60	F	16	Alzheimer			3565.0	3435.0
<u>009022174223</u>	CITE1	20					00	10		
Visit: 2 Seg: 1	SITE1	30	71	м	10	Control	.93	19	4774.0	4405.0
13IC 1 3EG. 1	SITEI		71	141	10	Control			+//+.0	4493.0
Visit: 2 Sec: 1	SITE1	24					.8	g		
Visit: 1 Seq: 1	SITE1	2.	77	F	13	Alzheimer		ž	2852.0	2979.0
009042378934										
Visit: 2 Seg: 1	SITE1	29								
Visit: 1 Seg: 1	SITE1		70	F	12	Control			3313.0	3466.0
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		<i>c a</i>					.39	4		
	Analysis li	nformatio	on			eimer			2932.0	2907.0
	This is a pro	ototype fo	or univa	riate sta	tistical					
	summary a	nalysis of	f morph	ometric	data. It is a	in .	.75	14		
	example of	some of t	the bas	ic statis	stical feature	es eimer			2961.0	3335.0

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### Case Study:

that we need for accomplishing our Morph BIRN

clinical specific aims.

Human Imaging Database integration with Authentication Services and Portal Environment

1

.93

.84

.59

15

22

6

3754.0

3990.0

3267.0

4260.0

4152.0

3386.0

![](_page_47_Picture_0.jpeg)

### http://www.nbirn.net

![](_page_47_Picture_2.jpeg)