Mouse models of GBM: MRI characterization and caBIG® tools

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CBIIT Seminar, February 29 2012

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Outline

- The ***Mouse GBM*** project
- How do caBIG® tools support ***Mouse GBM***?
  - Standardize MRI features (VASARI)
  - Archive and organize DICOM data (NBIA)
  - Integrate imaging and biology (caIntegrator)
- Summary and remaining challenges

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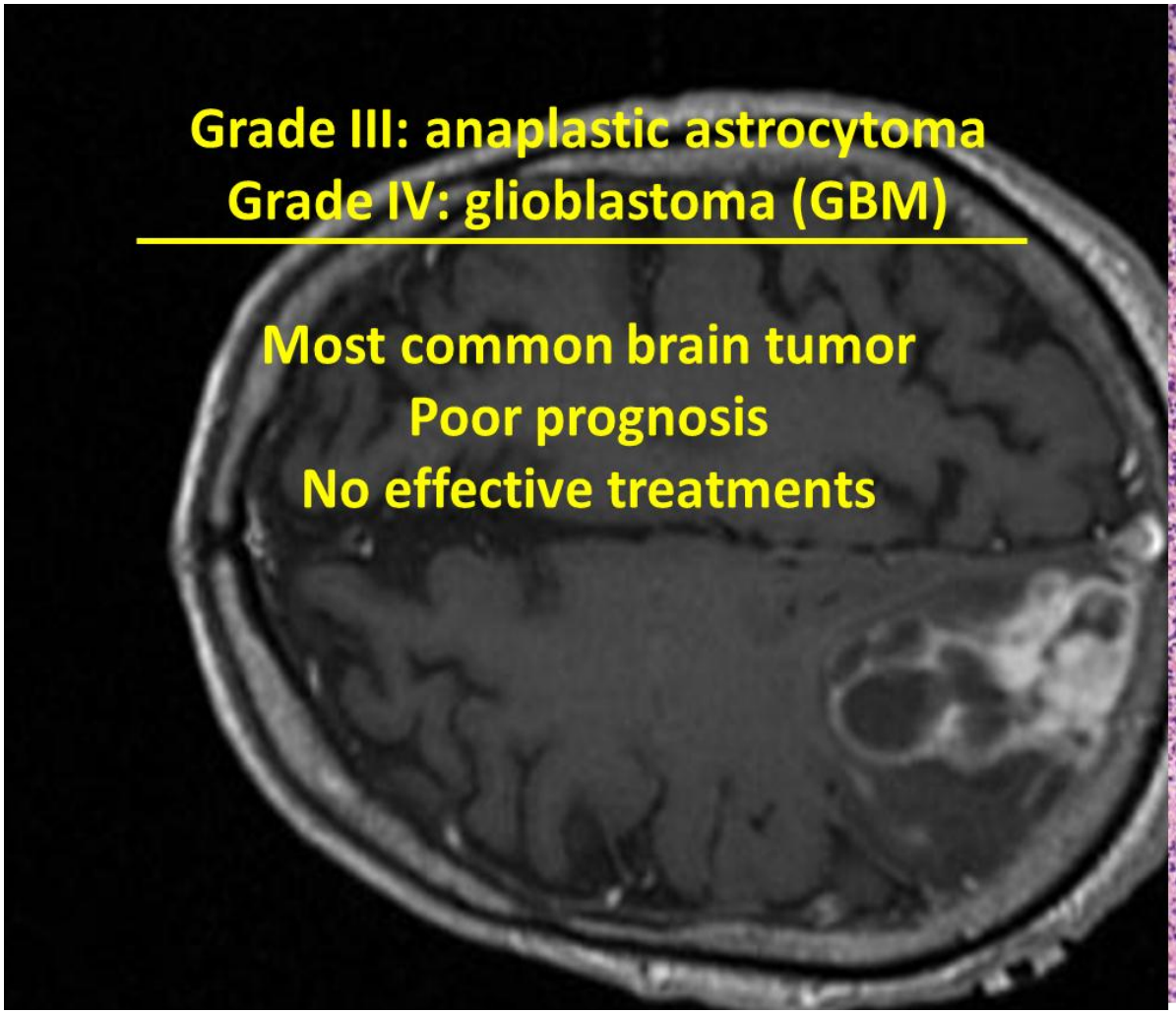
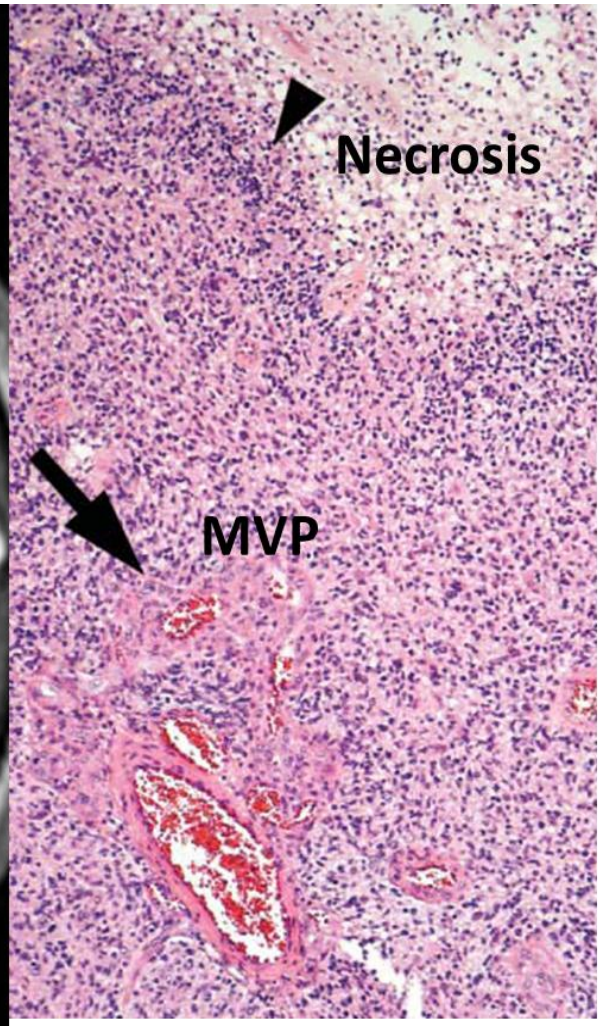
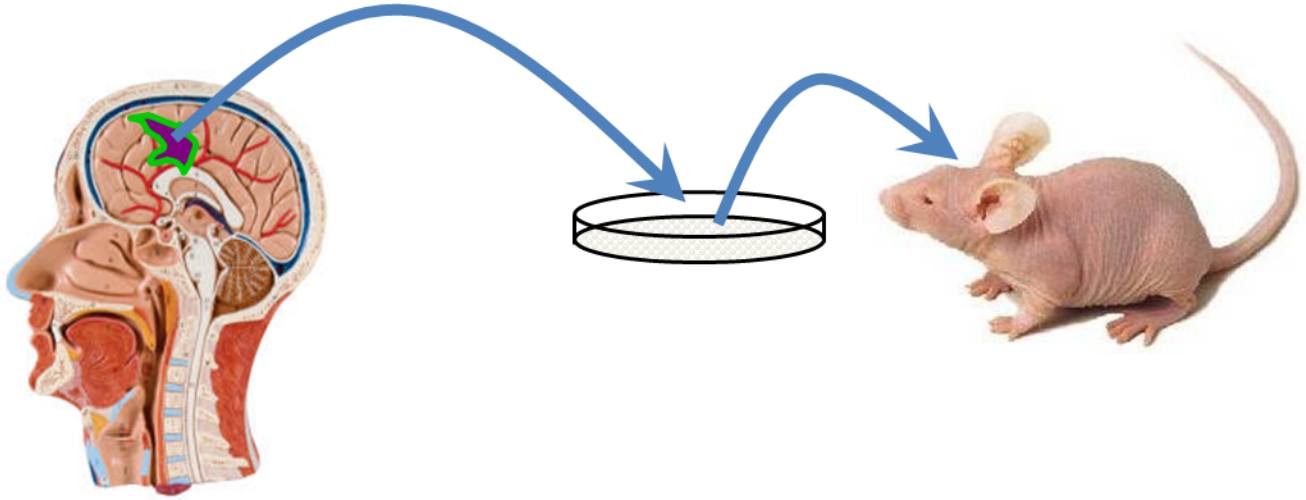
High grade astrocytoma



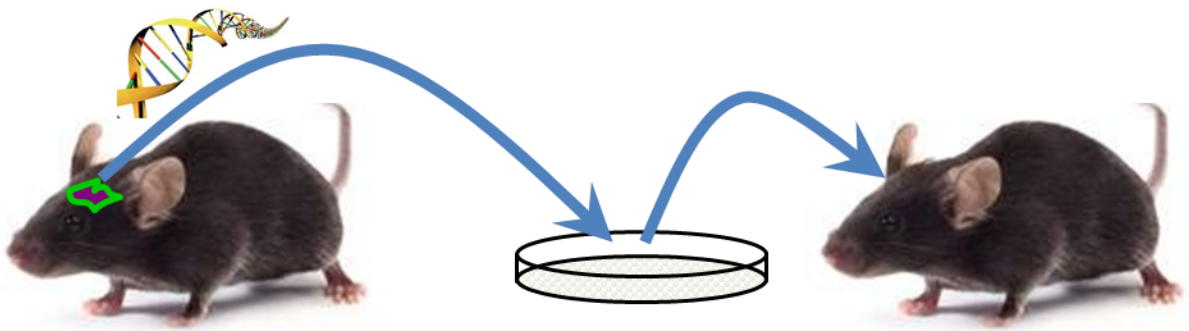


Mouse models of GBM



Established cell lines xenograft

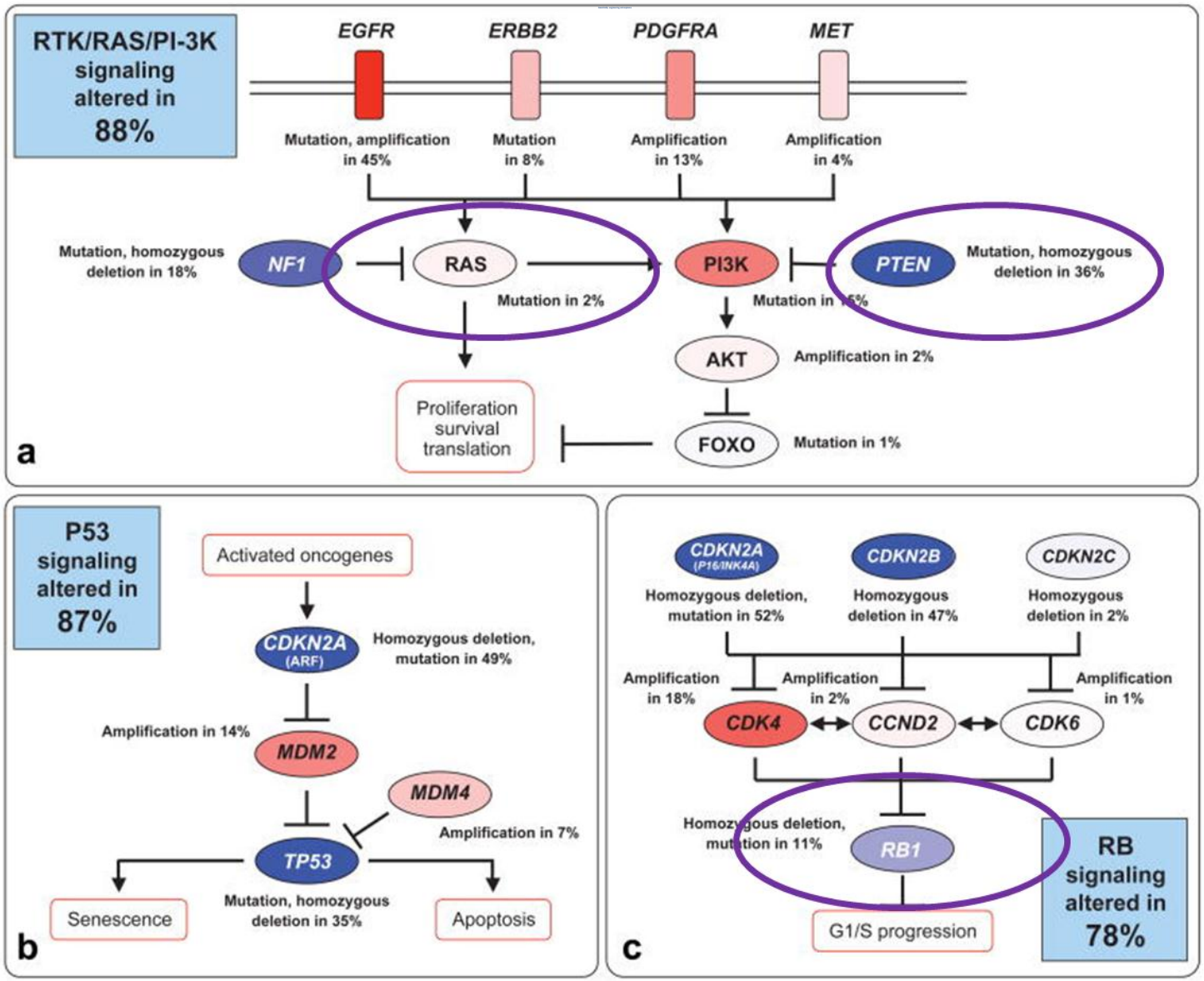
Patient derived xenograft



Genetically engineered mouse (GEM)

Syngeneic allograft

Core pathways altered in human GBMs



From Terry Van Dyke

The Cancer Genome Atlas (TCGA) 2008 Nature

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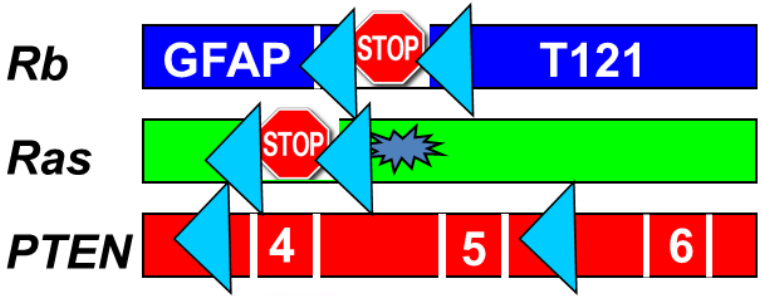
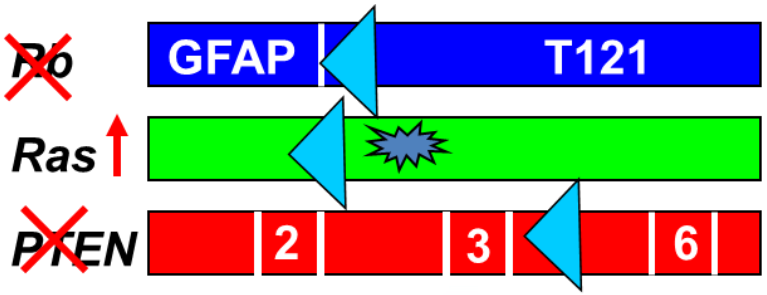
Genetically engineering astrocytoma





×

GFAP | CreER^{Tam}

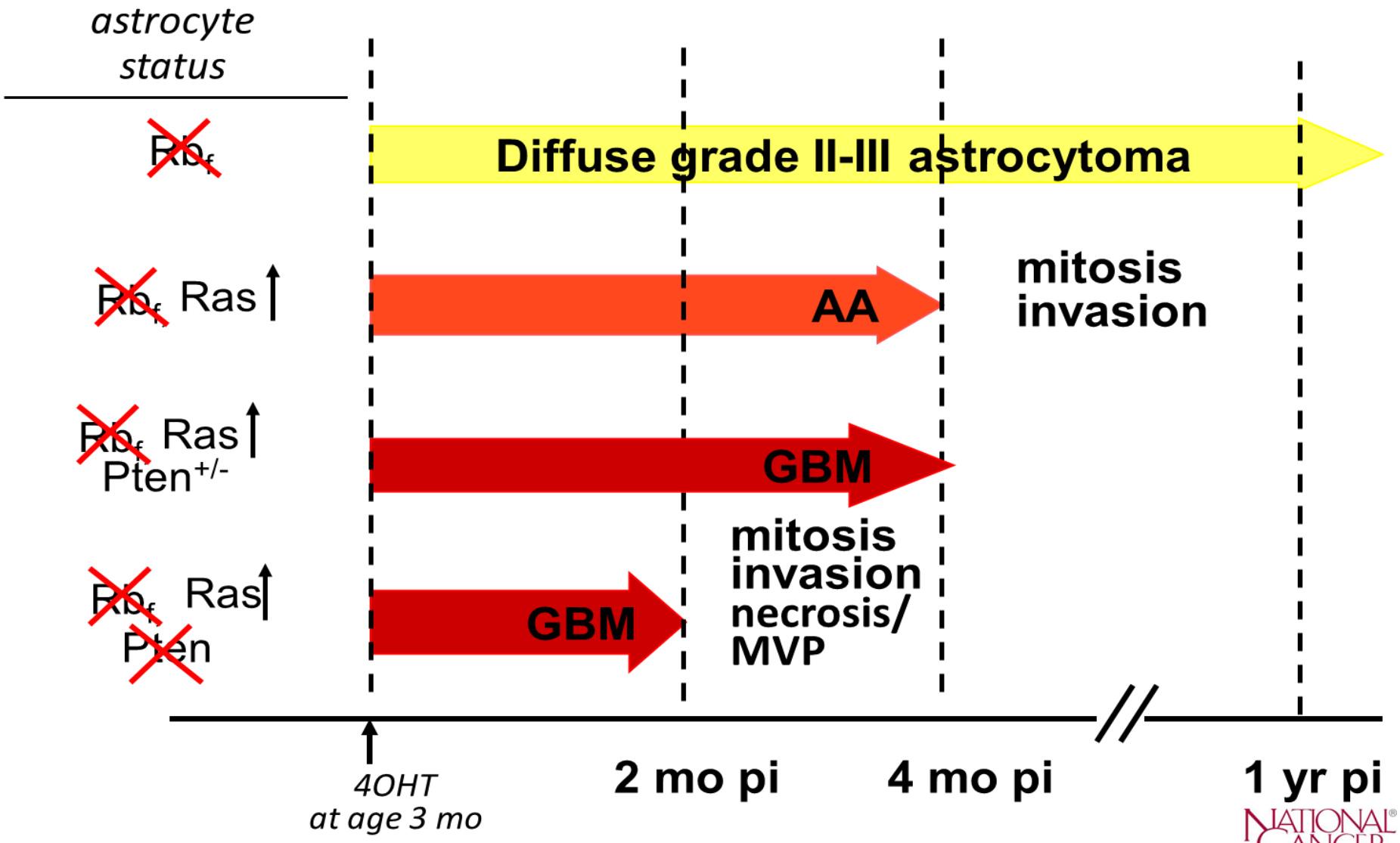
+

4-OH Tamoxifen

Germline genotype is normal

Adult/induced genotype is cancerous

Inducible astrocytoma GEM models



From Terry Van Dyke

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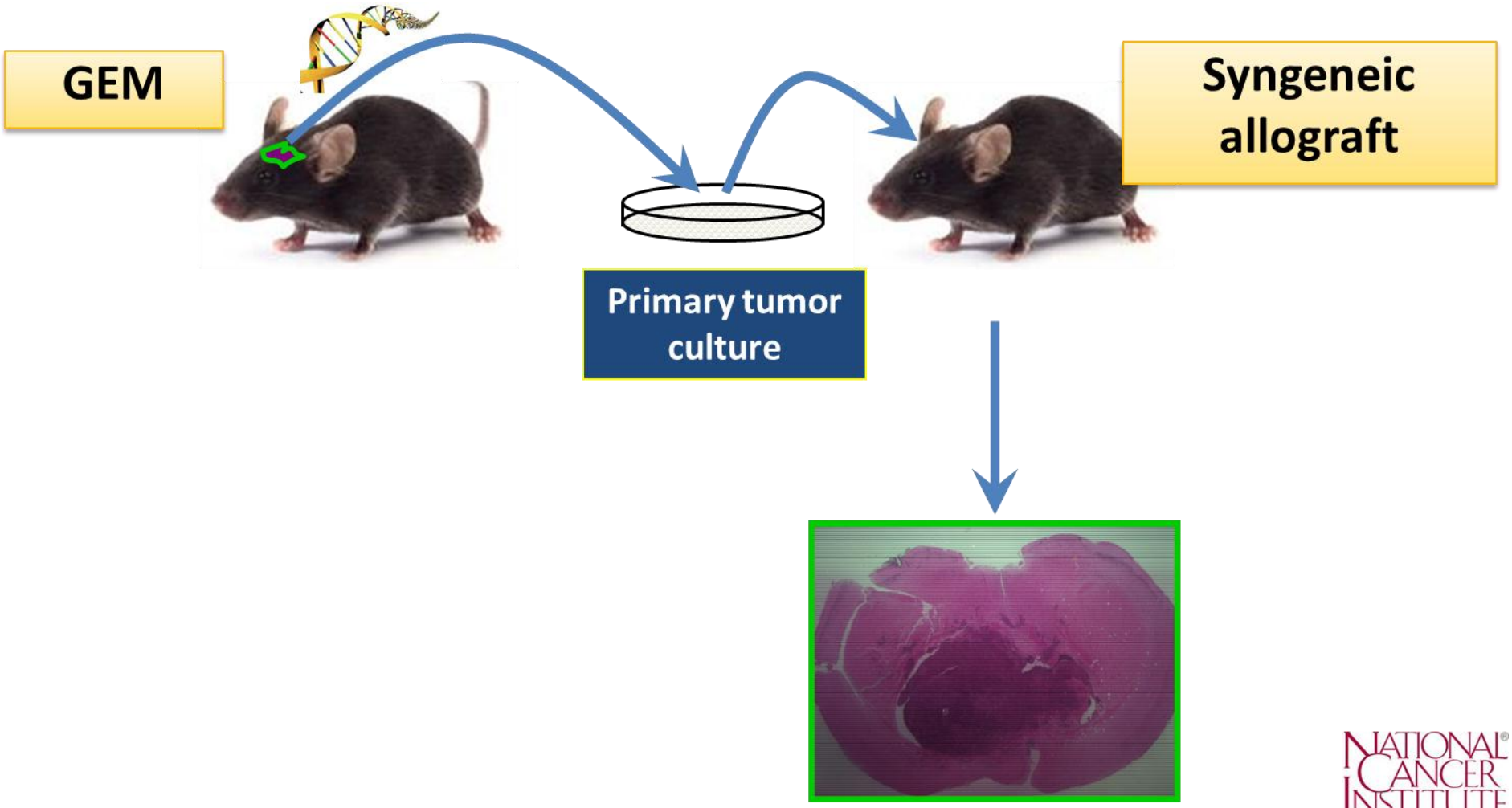
Mouse GBM

Syngeneic orthotopic transplant



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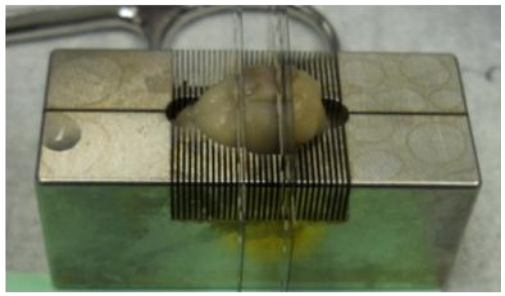
Mouse GBM

Brain imaging workflow

Four mice imaged
at once

Philips Intera Achieva
3.0T MRI clinical scanner
~1hour imaging time



Post imaging euthanize
and histology

MRI acquisitions

- Pre-contrast T_1 FFE
- Pre-contrast T_2 TSE
- Dynamic contrast enhanced MRI (DCEMRI)
- Post-contrast T_1 FFE

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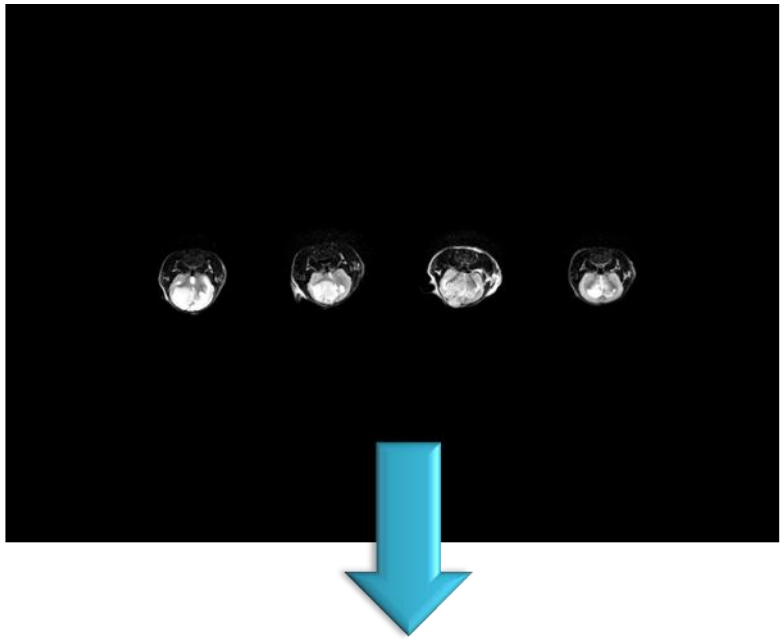
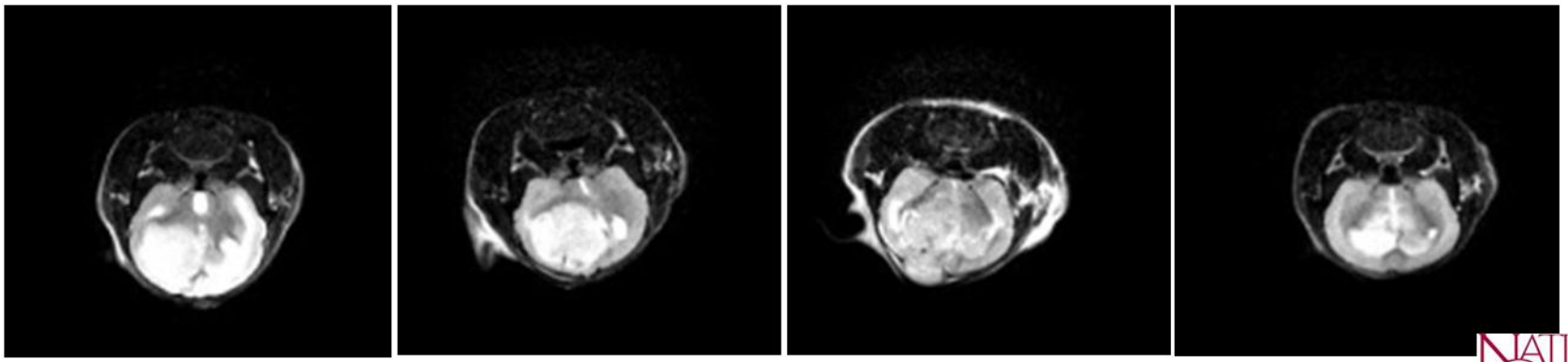
Mouse GBM

Challenge: cropping and splitting the data



Crop and split DICOM data and headers

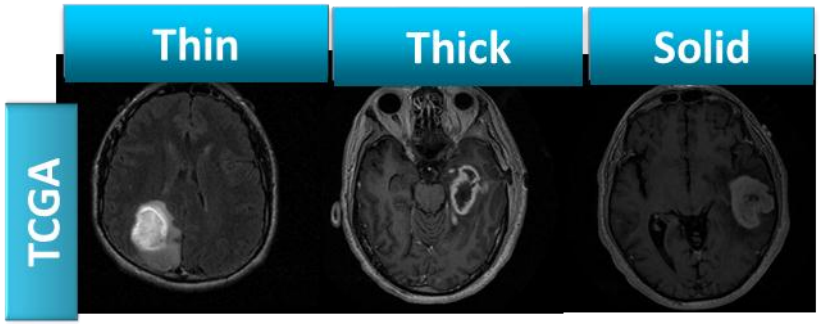


Mouse GBM

MRI features: mVASARI

- VASARI lexicon used for analysis of human GBM in TCGA

e.g.. Thickness of Enhancing Margin (F11)

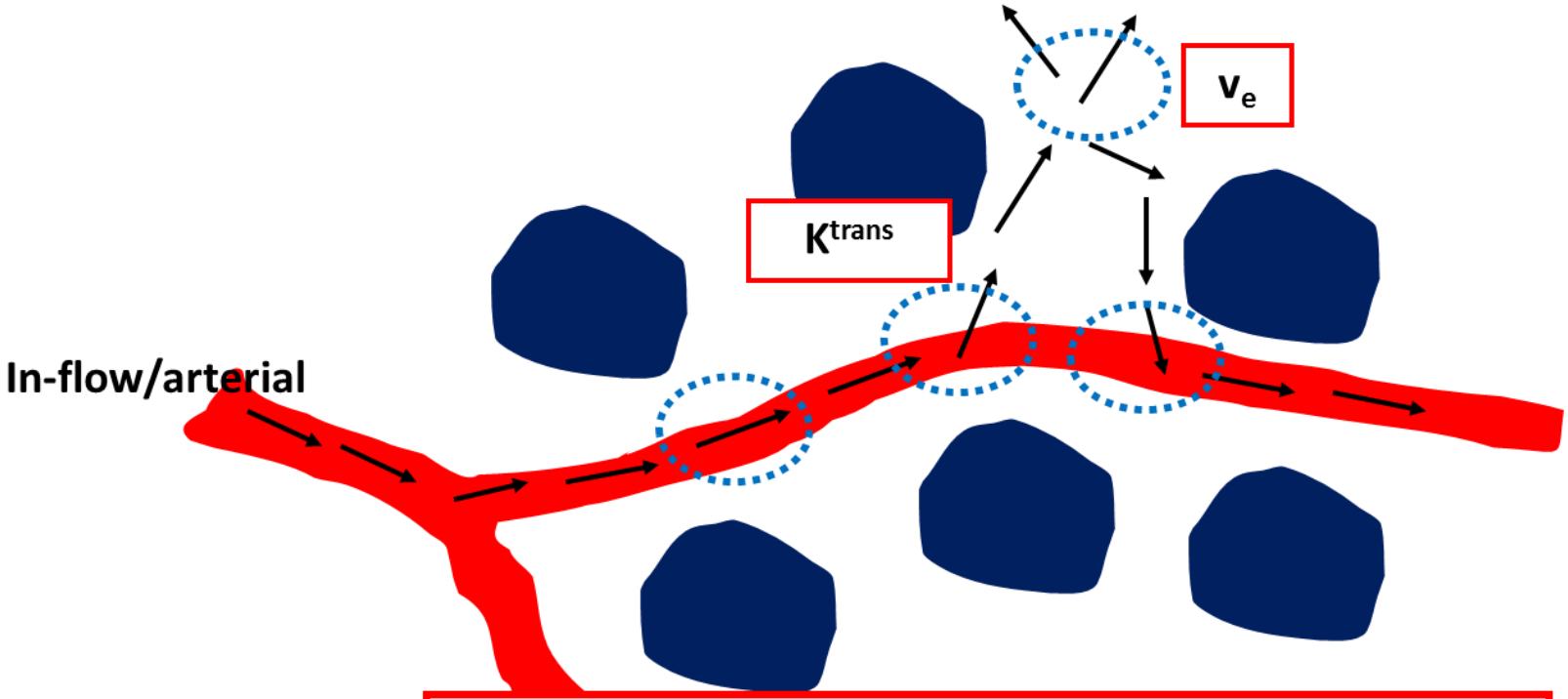


- Mouse VASARI=mVASARI
- Publically available VASARI features for human GBM from caIntegrator

Mouse GBM

MRI features: BBB permeability

- Quantifiable information on the blood brain barrier permeability is extracted from the pattern of contrast agent uptake

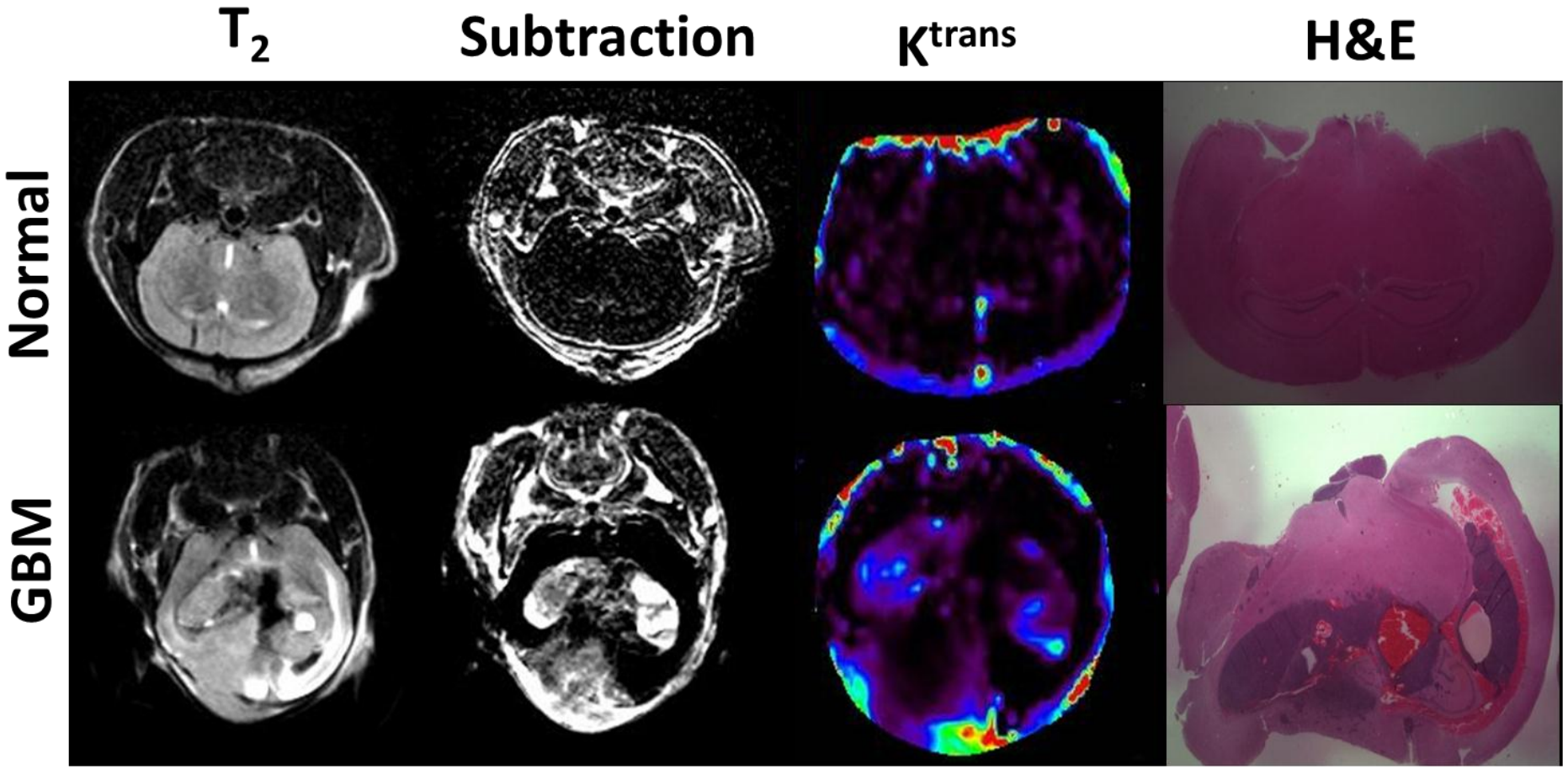


$$\frac{dC(t)}{dt} = K^{trans} \cdot \left(C_p(t) - C(t)/v_e\right)$$

From Cheng Yang

Mouse GBM

MRI reveals disease pathology noninvasively



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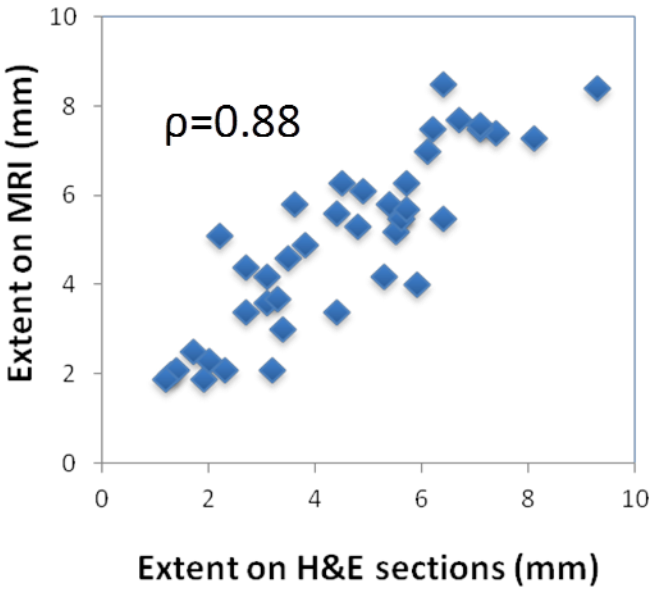
Mouse GBM

MRI reveals disease pathology noninvasively

A

Pathology Features	Categories	No.
Diagnosis	Normal	8
	Grade II	1 *MRI missed 1*
	Grade III	7 *MRI missed 1*
	GBM	36 *MRI missed 1*
Necrosis	No	8
	Yes, pseudopalisading	16
	Yes, not pseudopalisading	20
Microvascular Proliferation	No	42
	Yes	2

B



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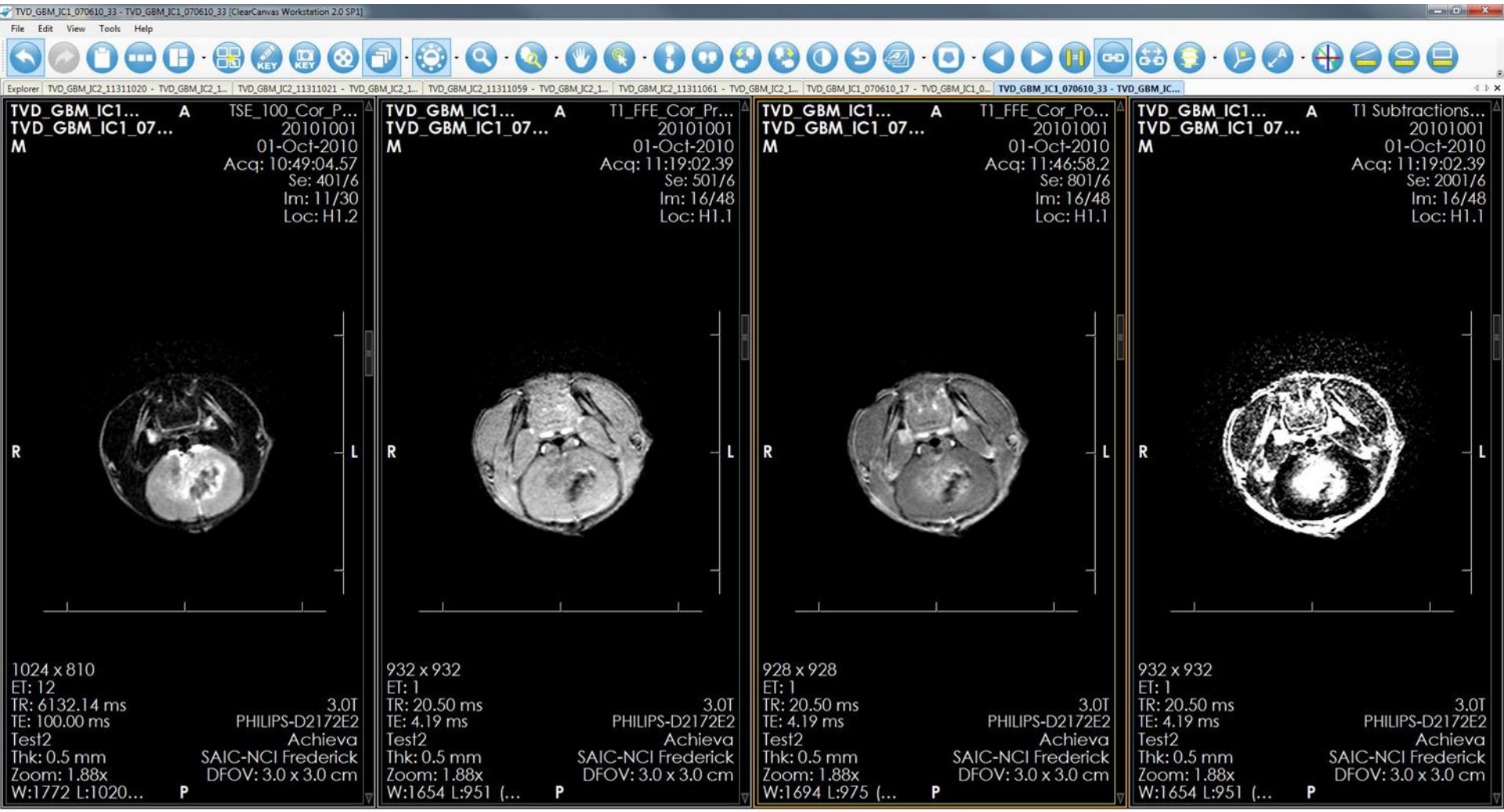

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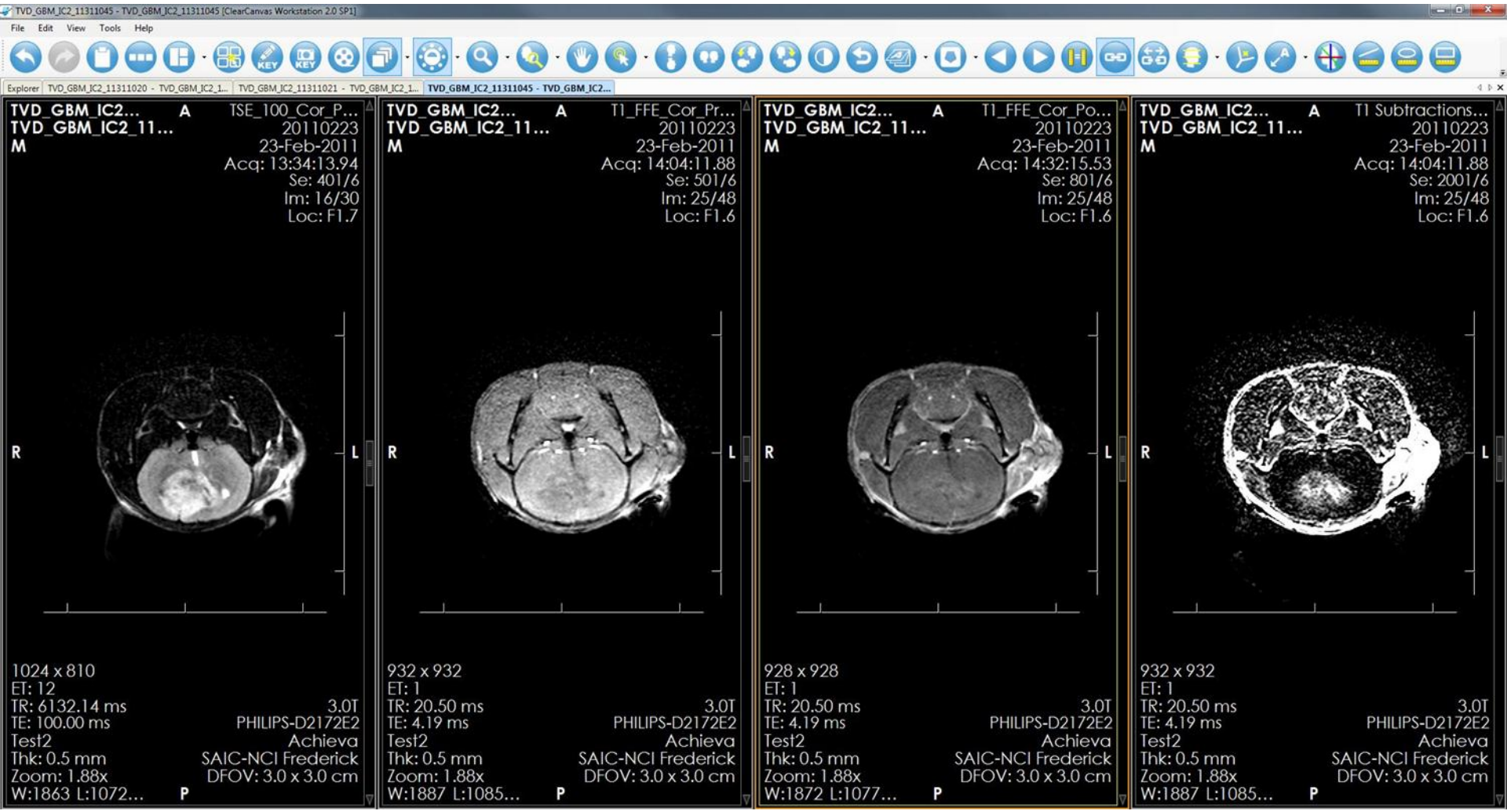

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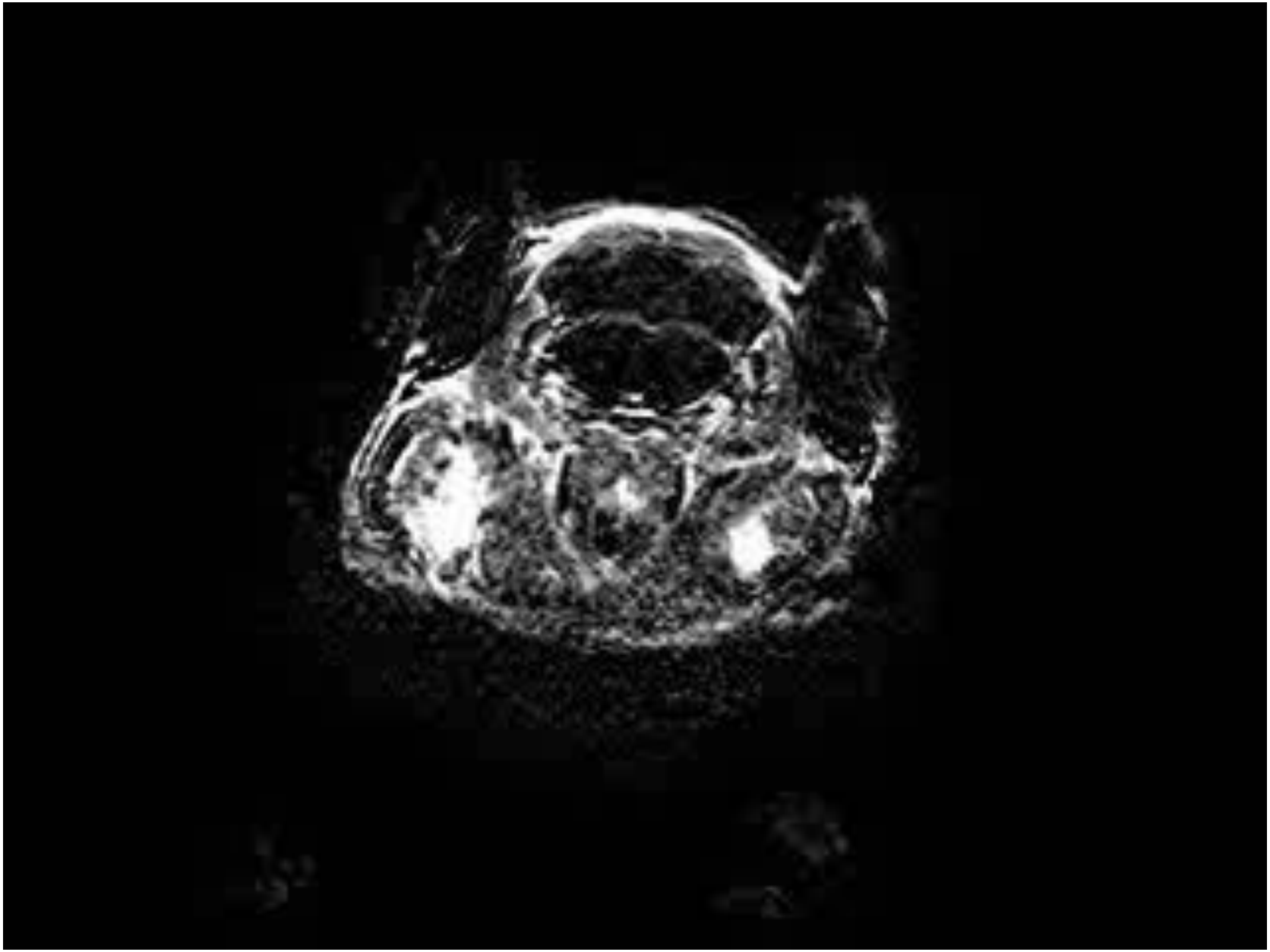

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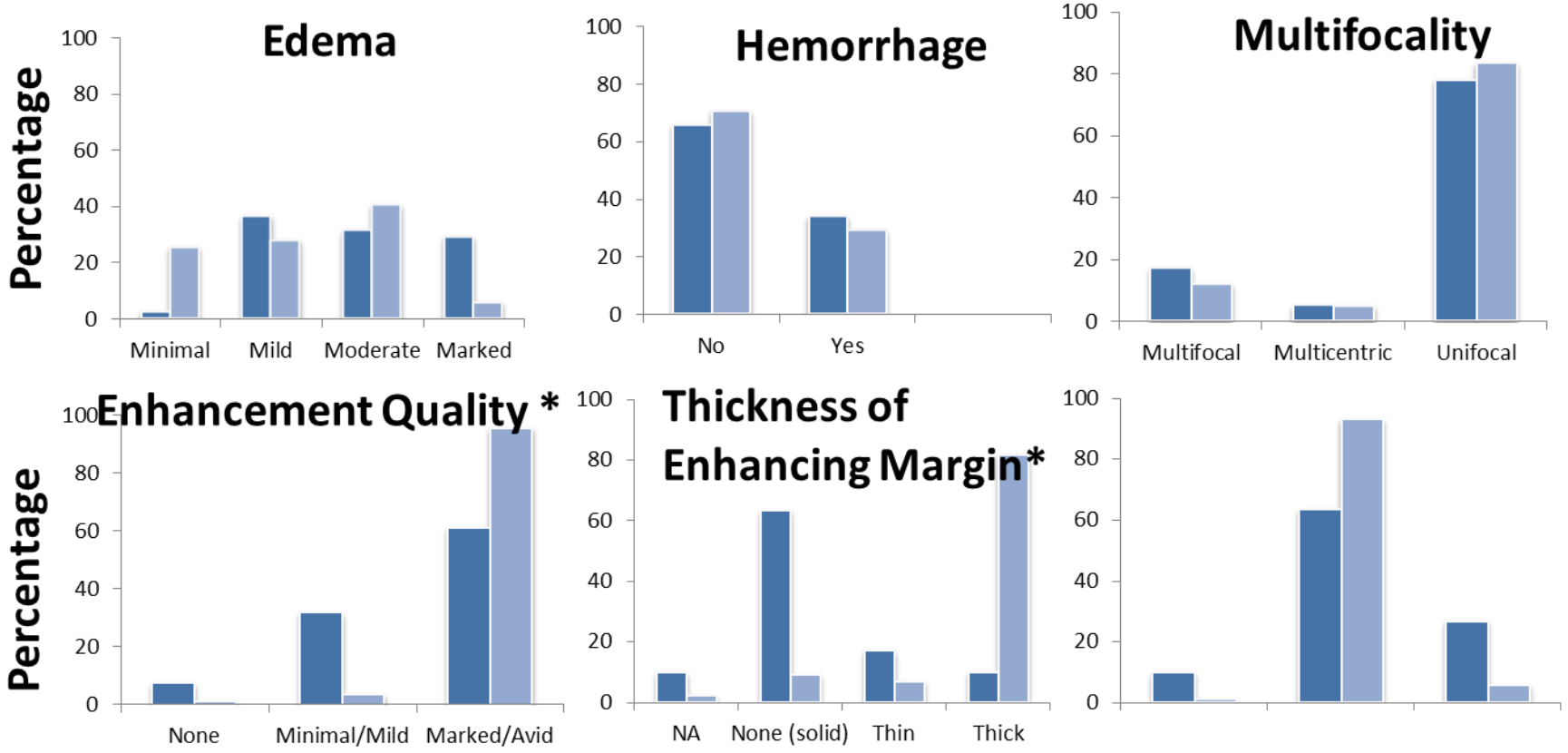
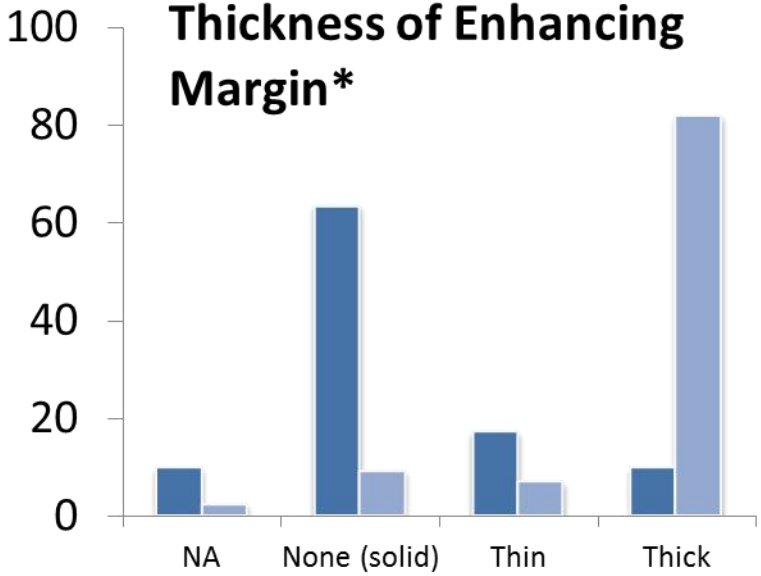
Mouse GBM

Mouse models can capture many features of human GBM…



Mouse GBM

… but not the necrosis?



- ***Thick*** enhancing margin rarely seen in mice

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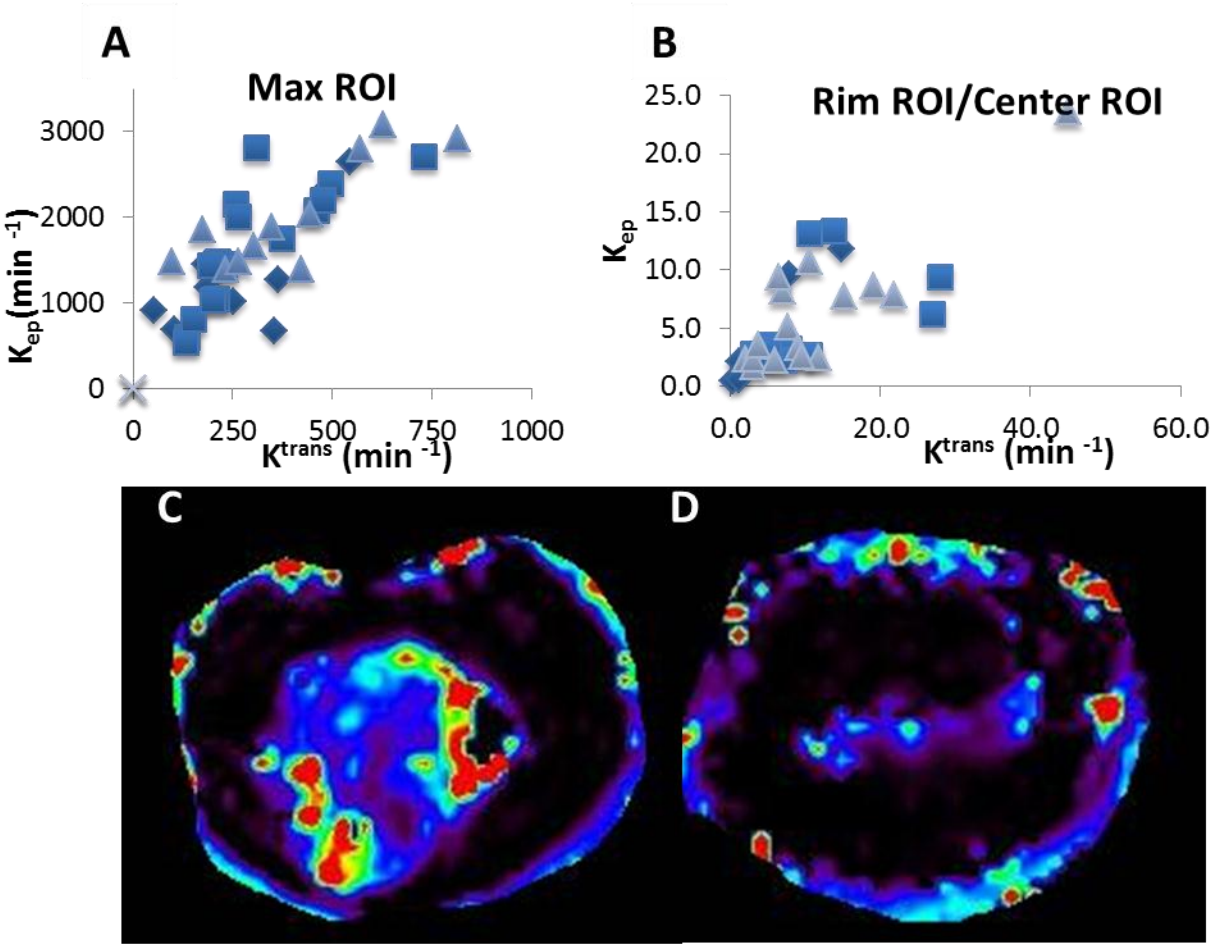
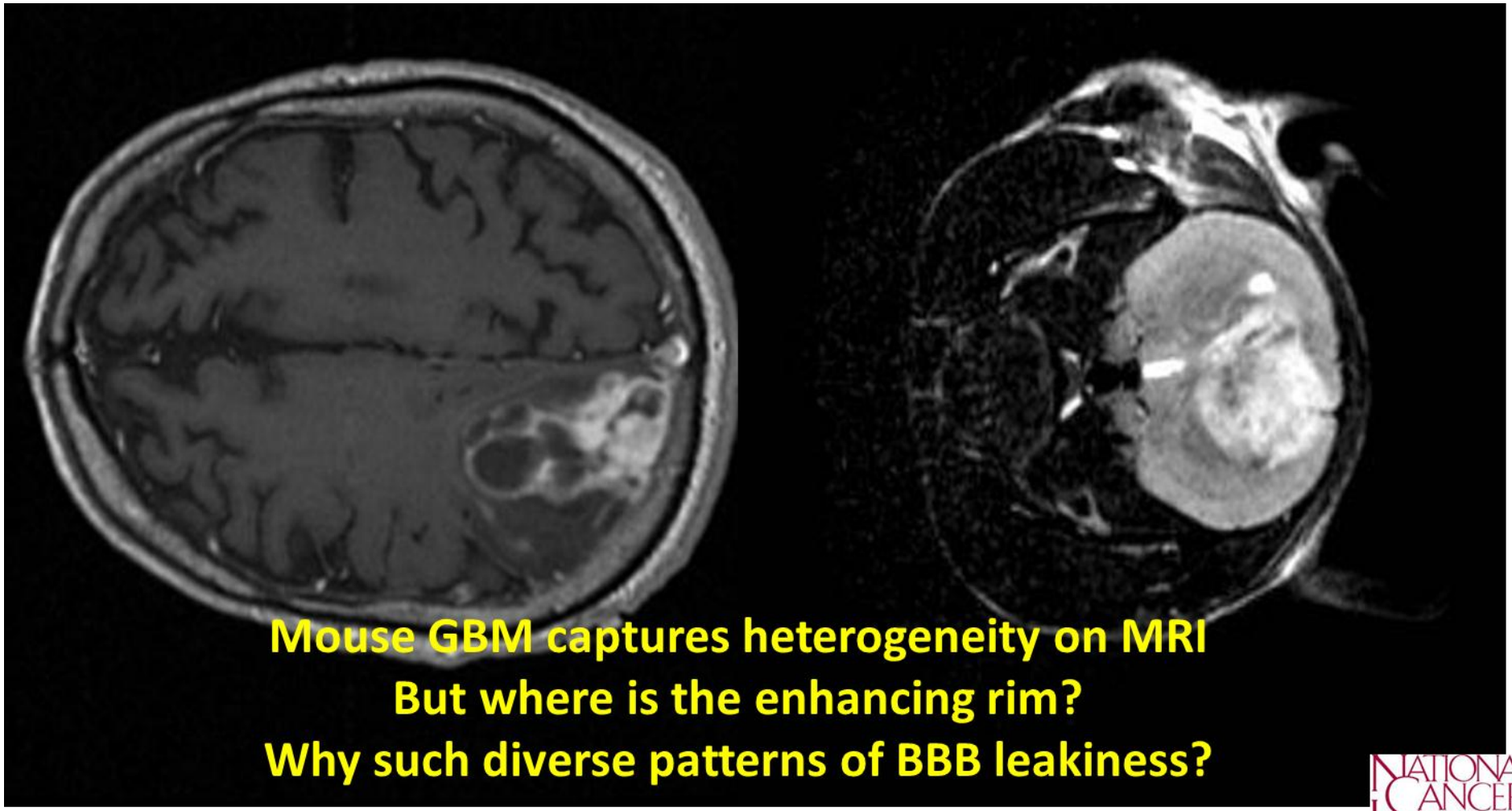
Mouse GBM

Heterogeneous patterns of BBB permeability



Mouse GBM

Summary



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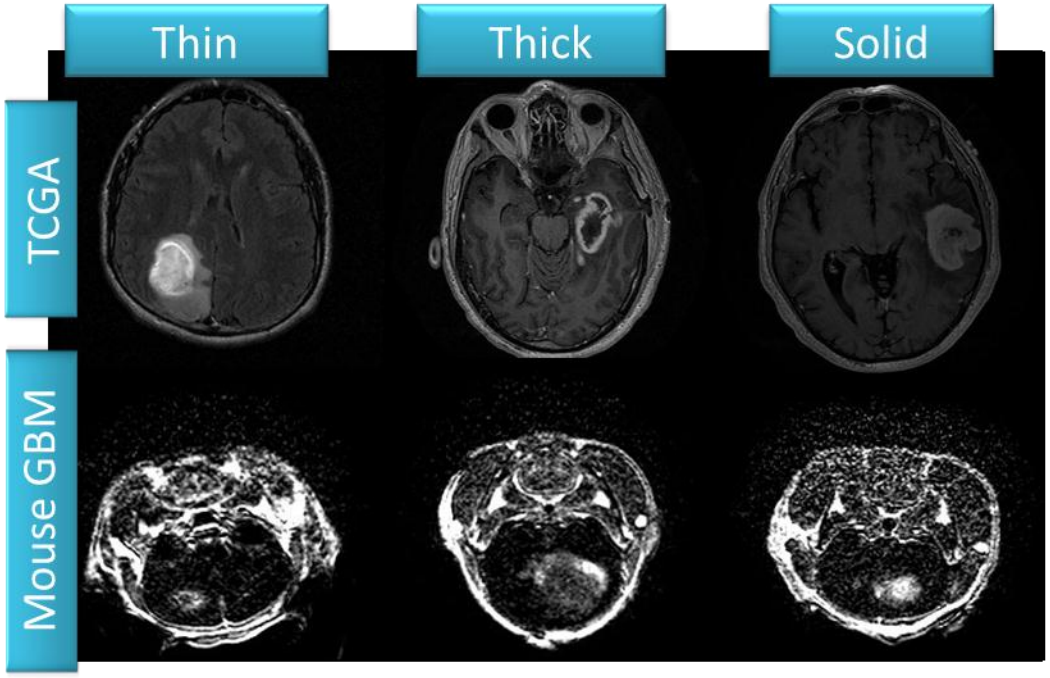
caBIG® tools support *Mouse GBM*

Standardized lexicon: mVASARI features

Thickness of the Enhancing Margin (VASARI feature 11)



VASARI features essential for comparing ***Mouse GBM*** to human GBM

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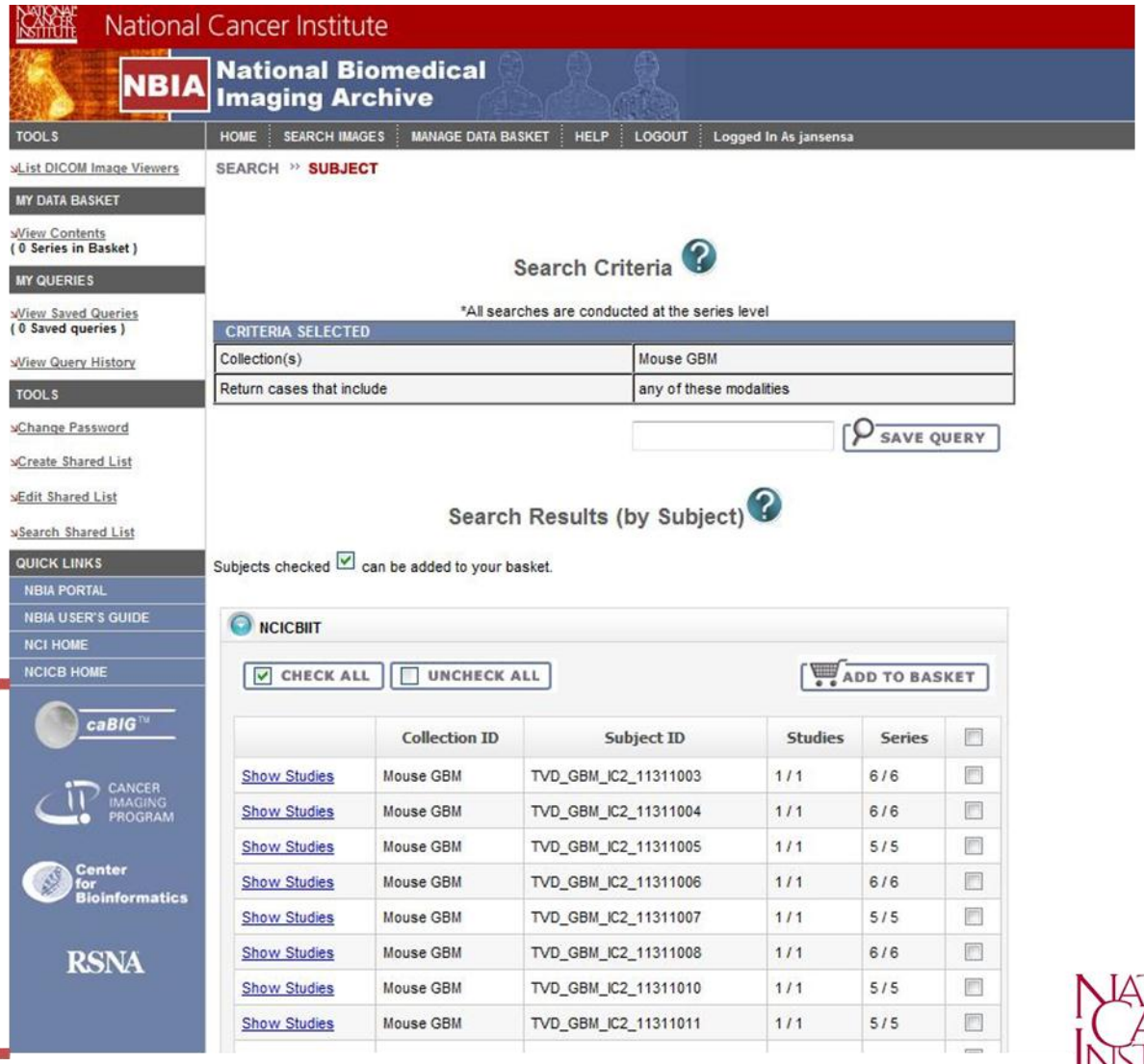
caBIG® tools support *Mouse GBM*

NBIA: Demo

Images from ***Mouse GBM*** stored in NBIA



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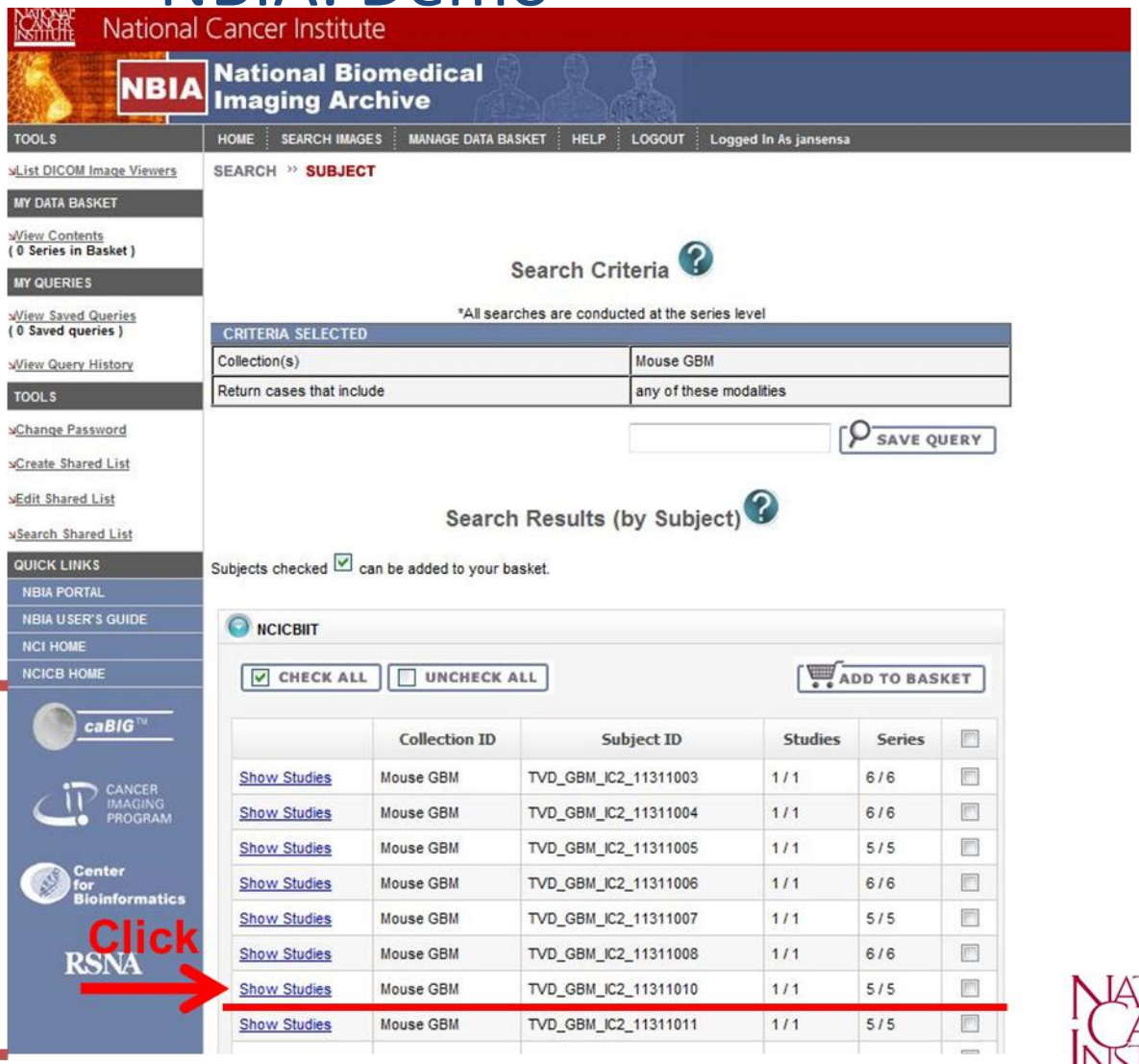

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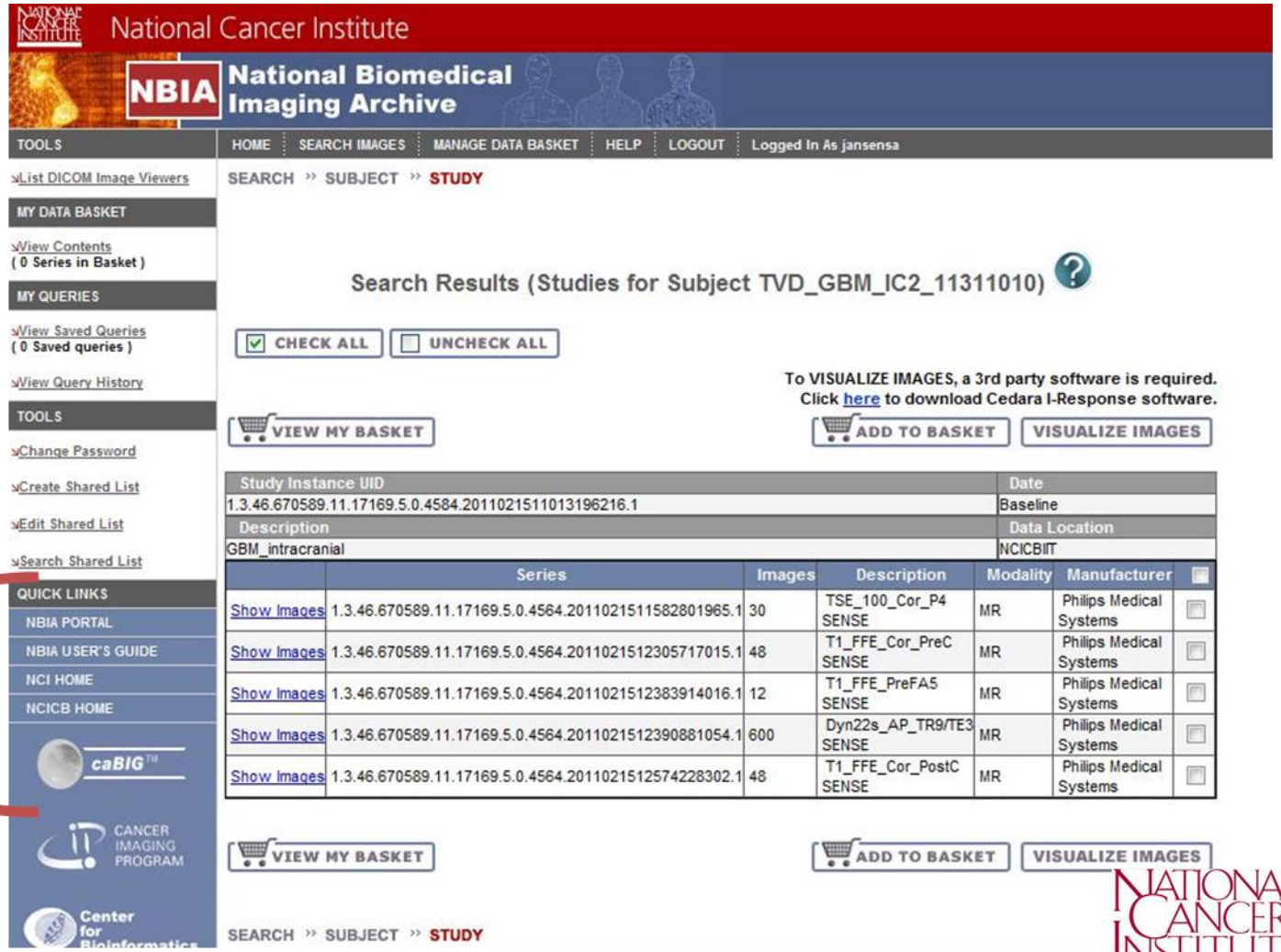
caBIG® tools support *Mouse GBM*

NBIA: Demo

Image series organized



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caBIG® tools support *Mouse GBM*

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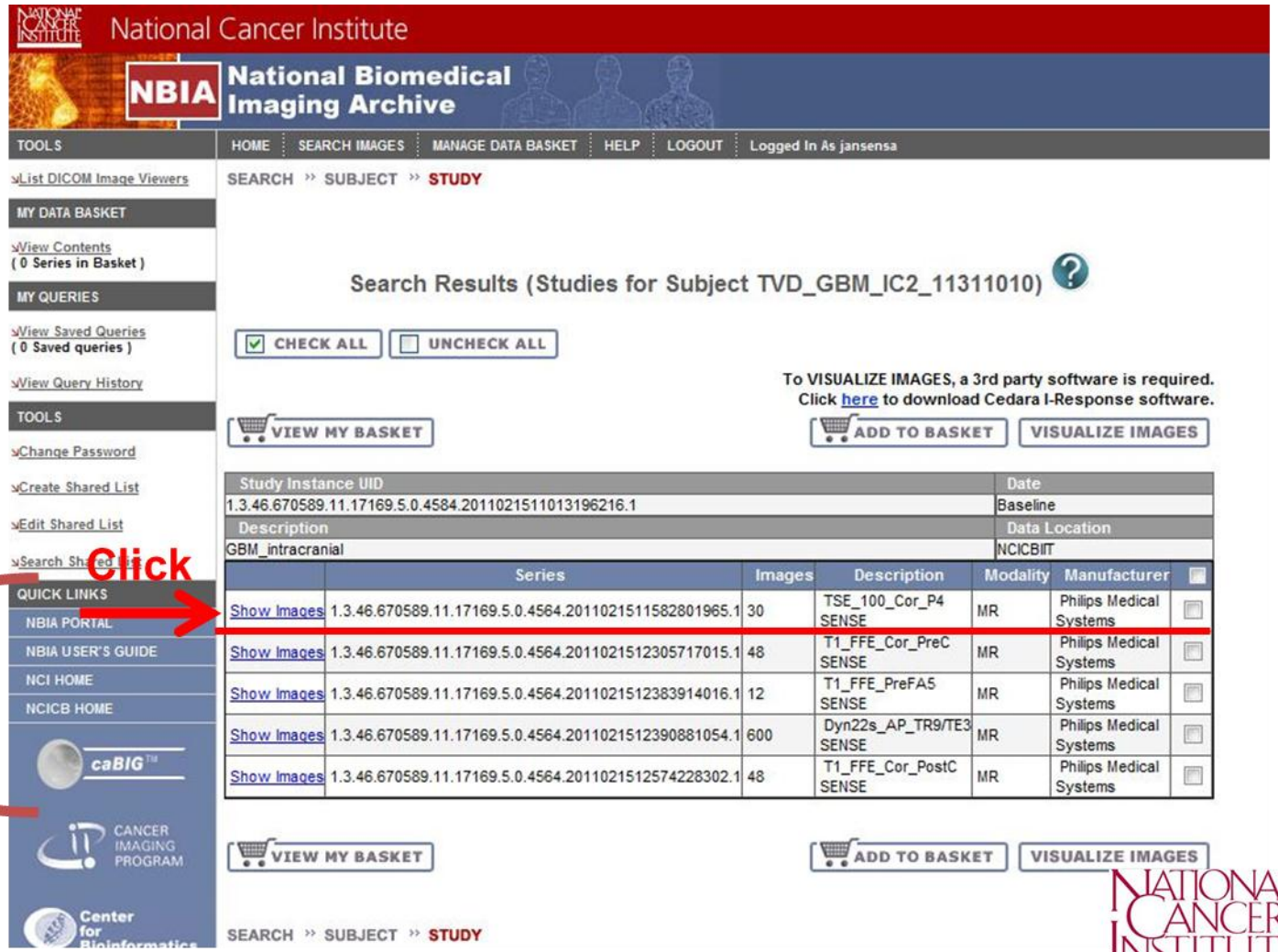

caBIG® tools support *Mouse GBM*

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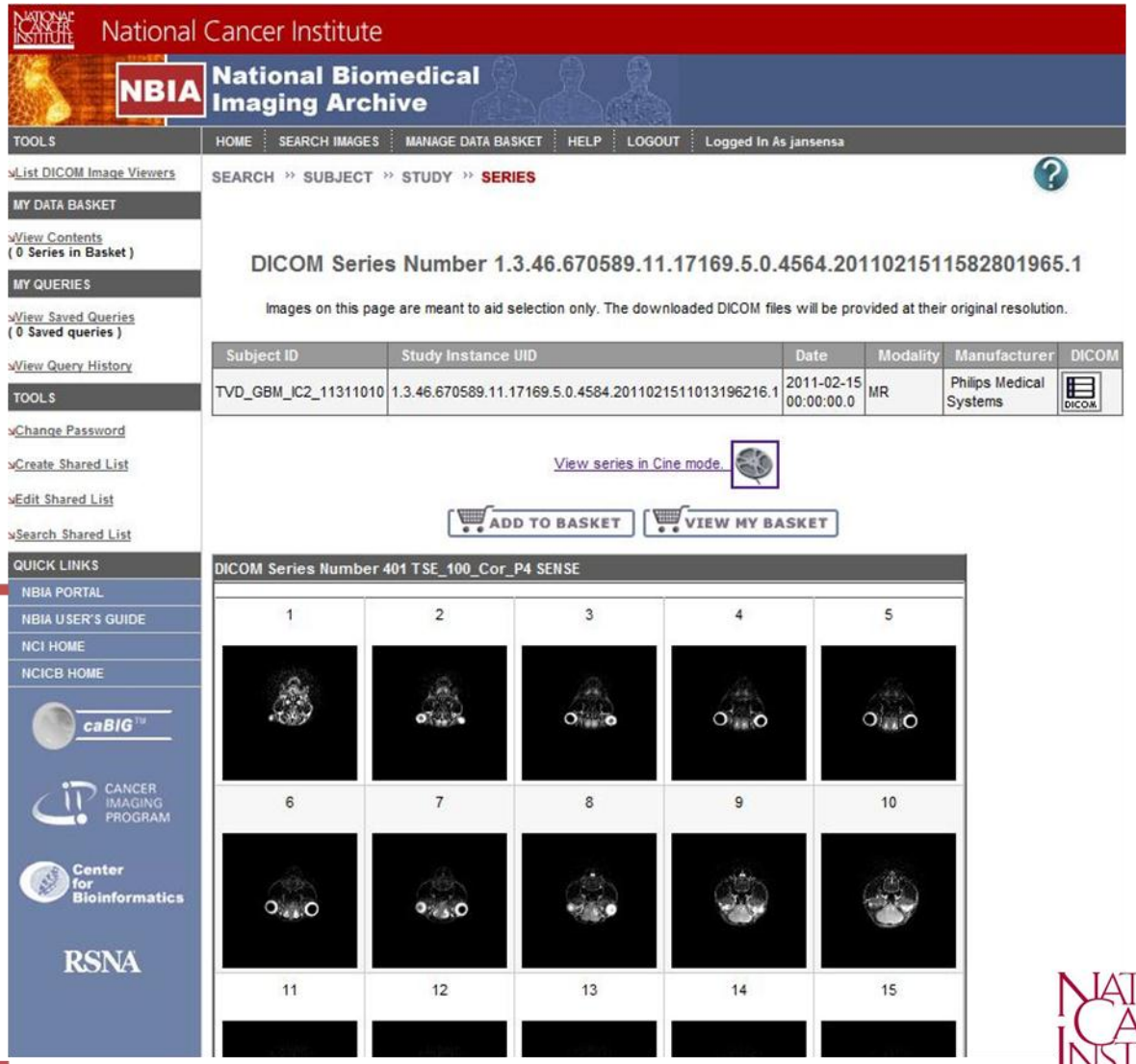

Images from series are displayed

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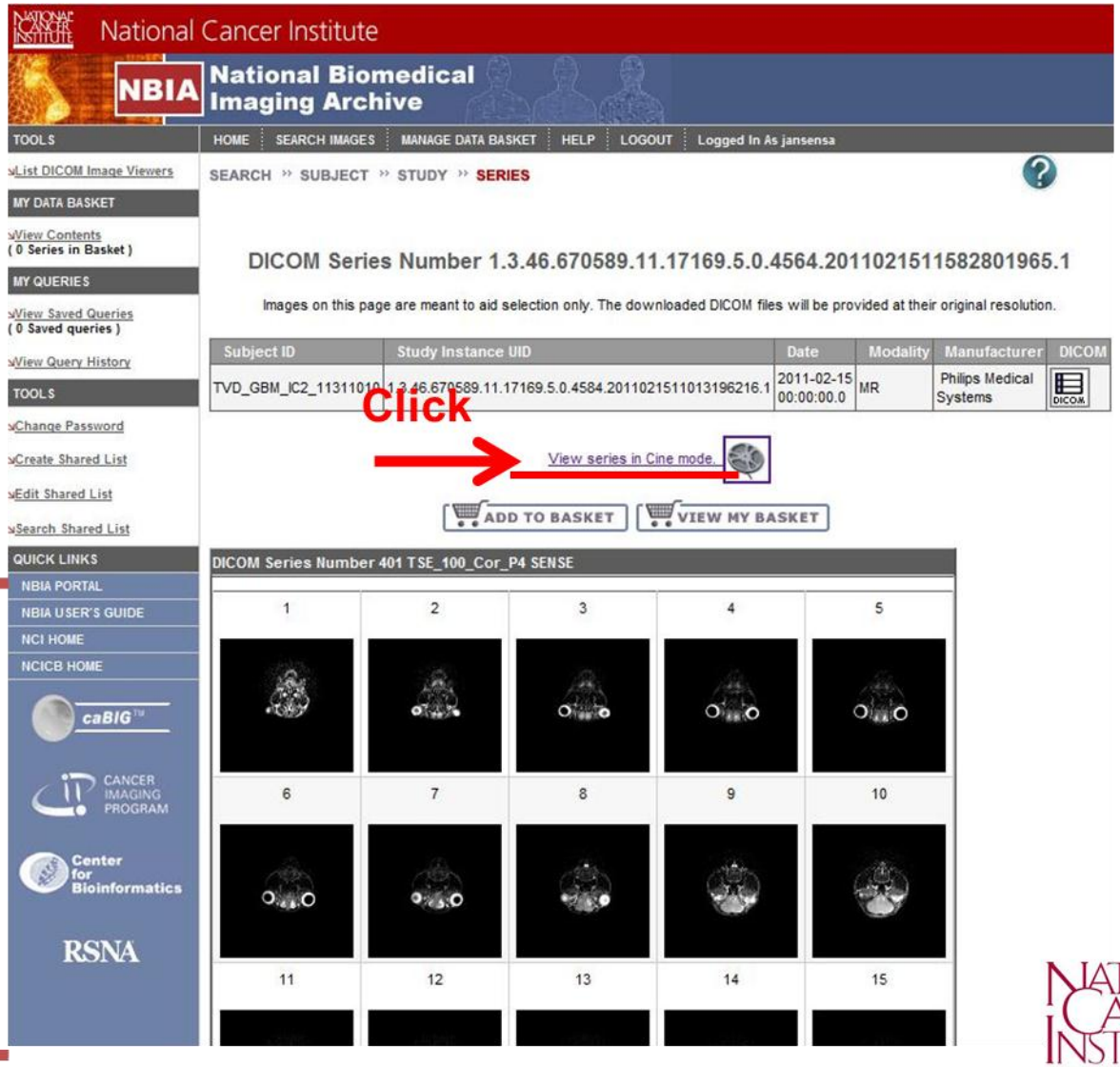
caBIG® tools support *Mouse GBM*

NBIA: Demo



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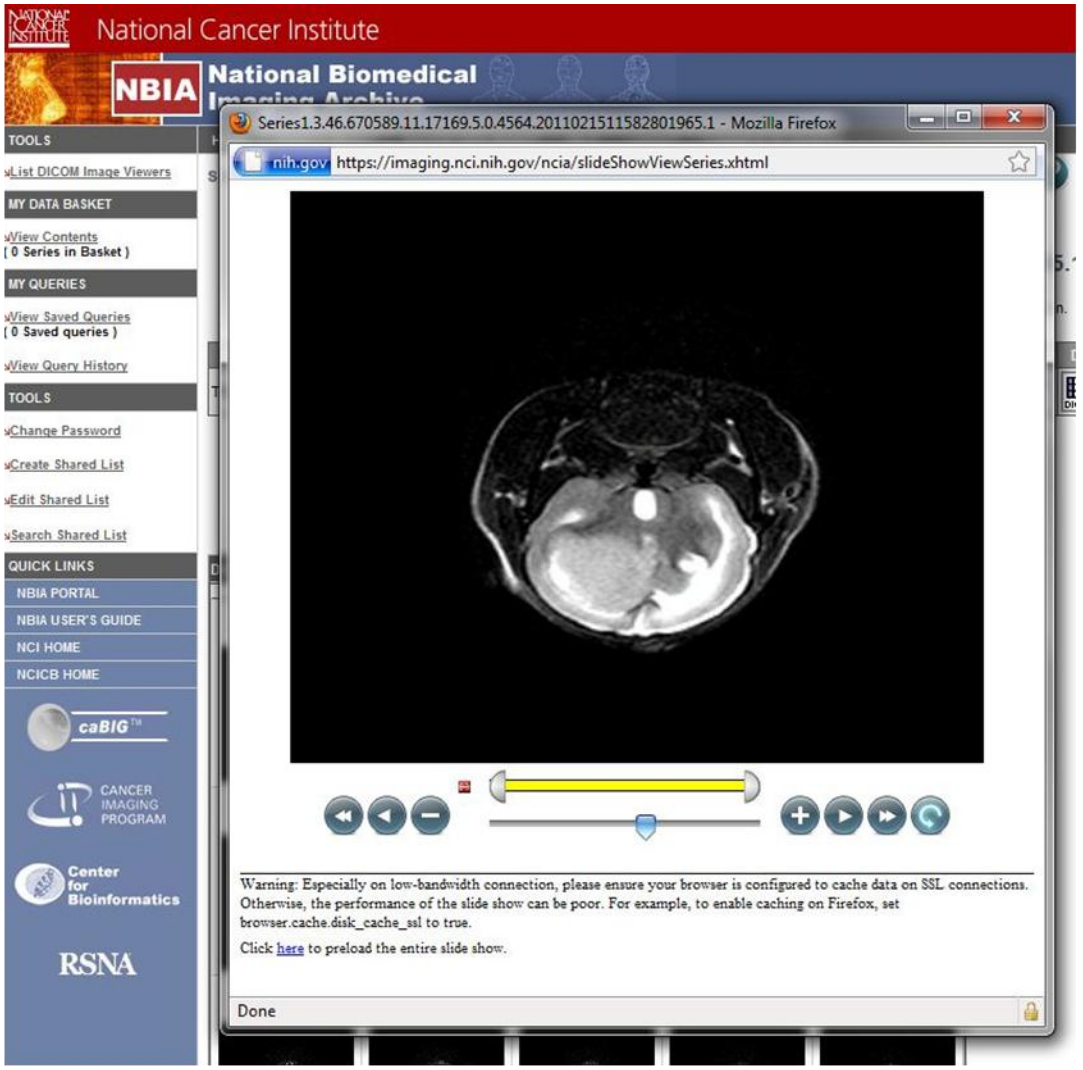
caBIG® tools support *Mouse GBM*

NBIA: Demo

Images can be viewed in Cine mode



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caBIG® tools support *Mouse GBM*

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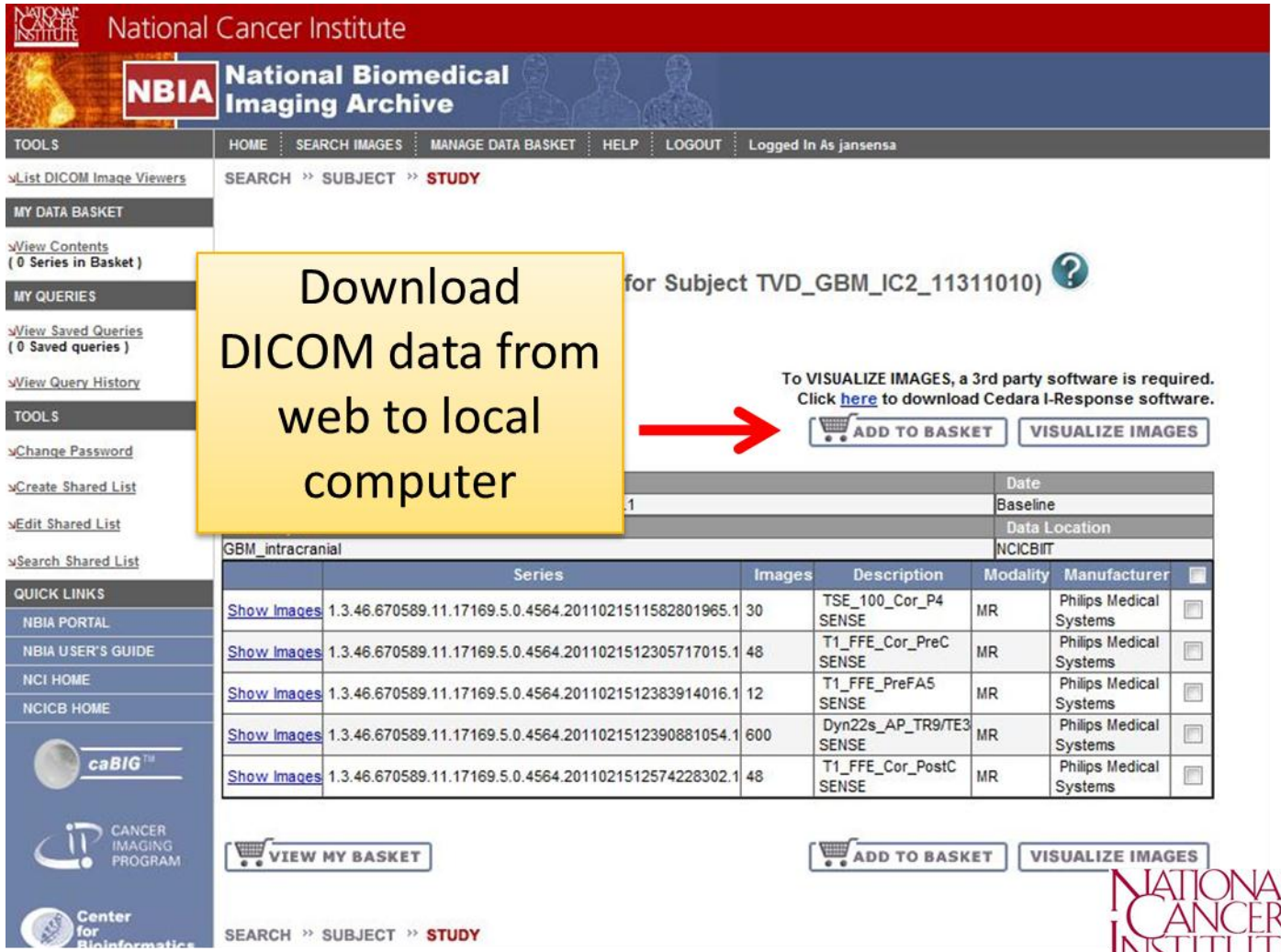
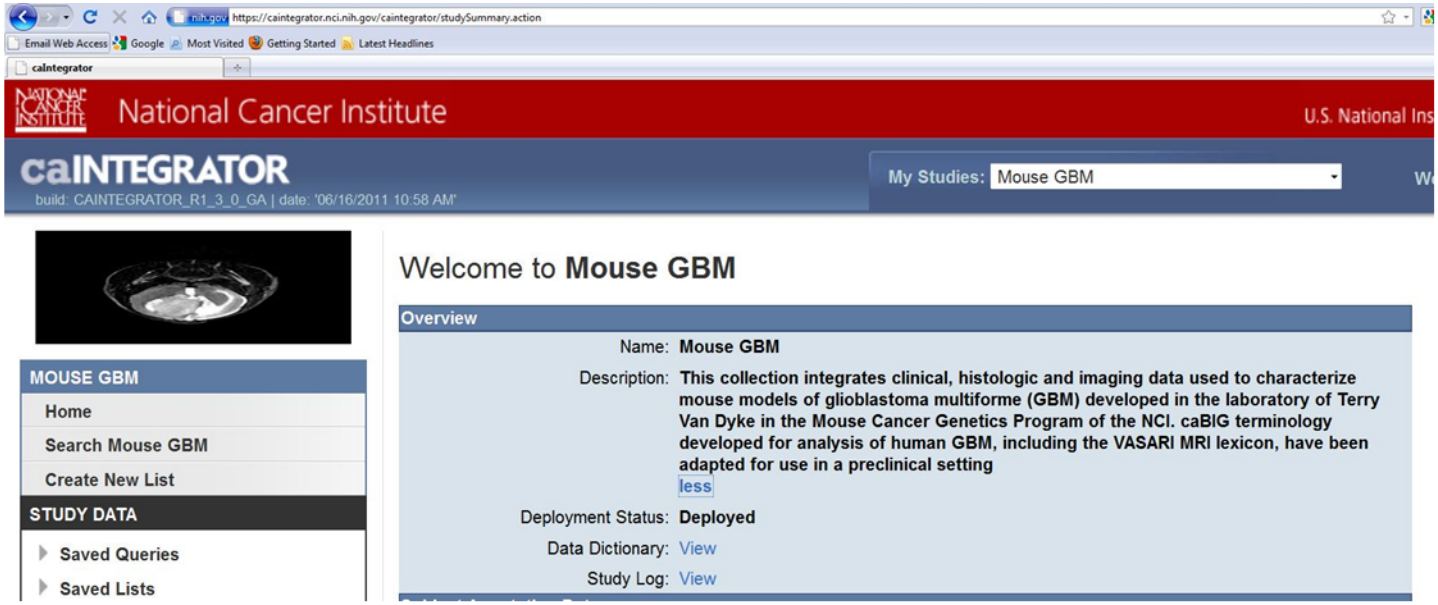


caBIG® tools support *Mouse GBM*

caIntegrator: Demo

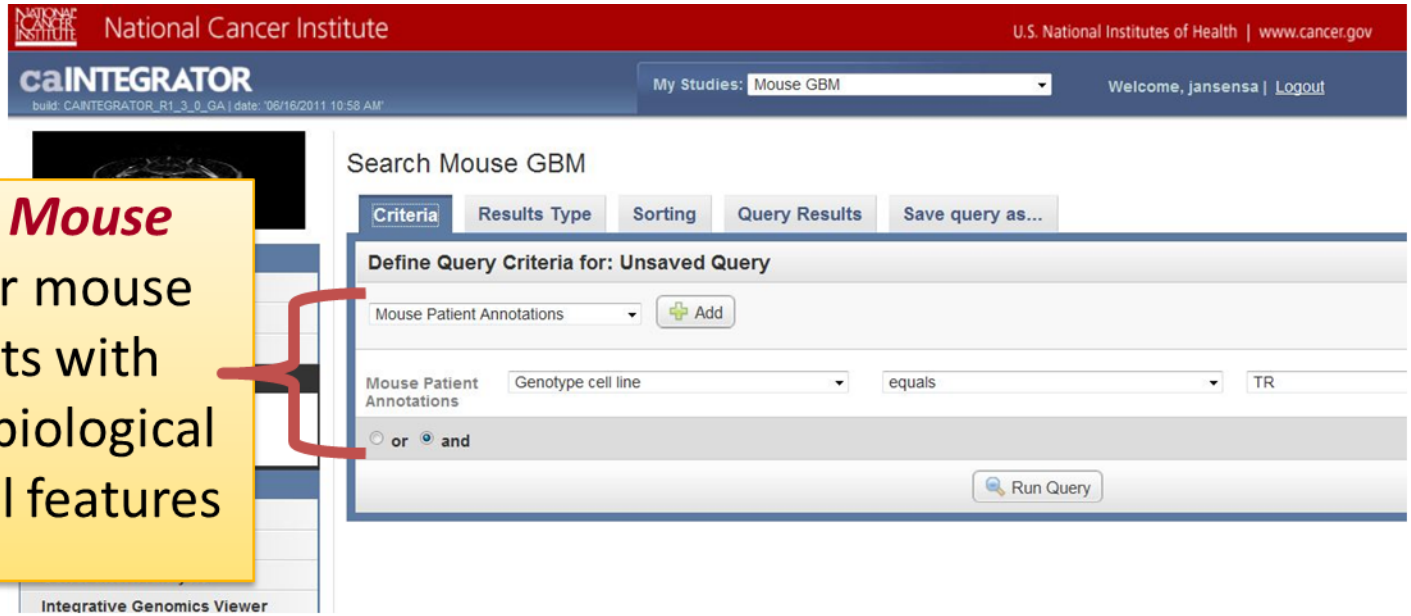
Data from ***Mouse GBM*** stored in caIntegrator



caBIG® tools support *Mouse GBM*

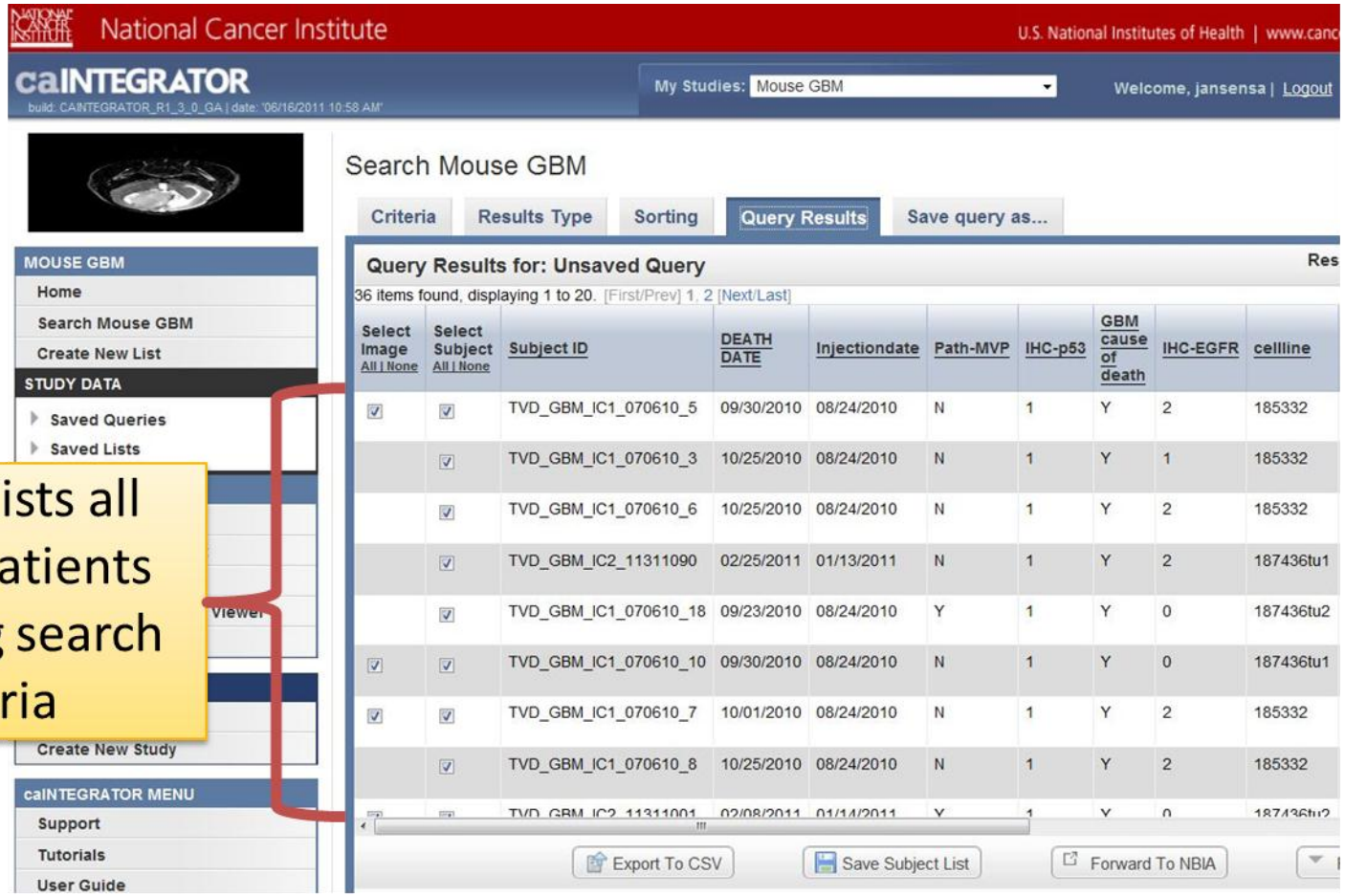
caIntegrator: Demo

Search ***Mouse GBM*** for mouse patients with defined biological or clinical features



caBIG® tools support *Mouse GBM*

caIntegrator: Demo

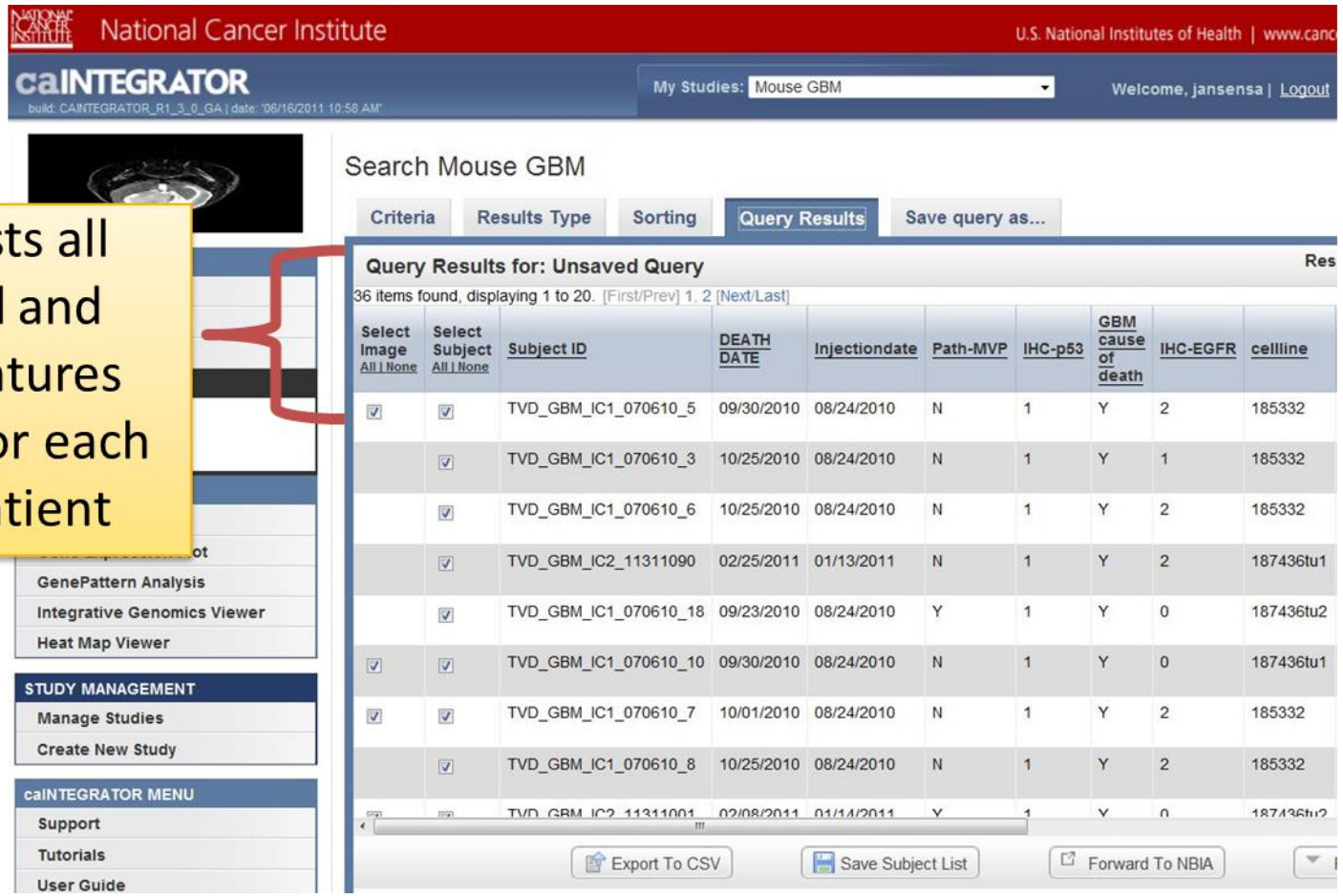


Results lists all mouse patients satisfying search criteria

caBIG® tools support *Mouse GBM*

caIntegrator: Demo

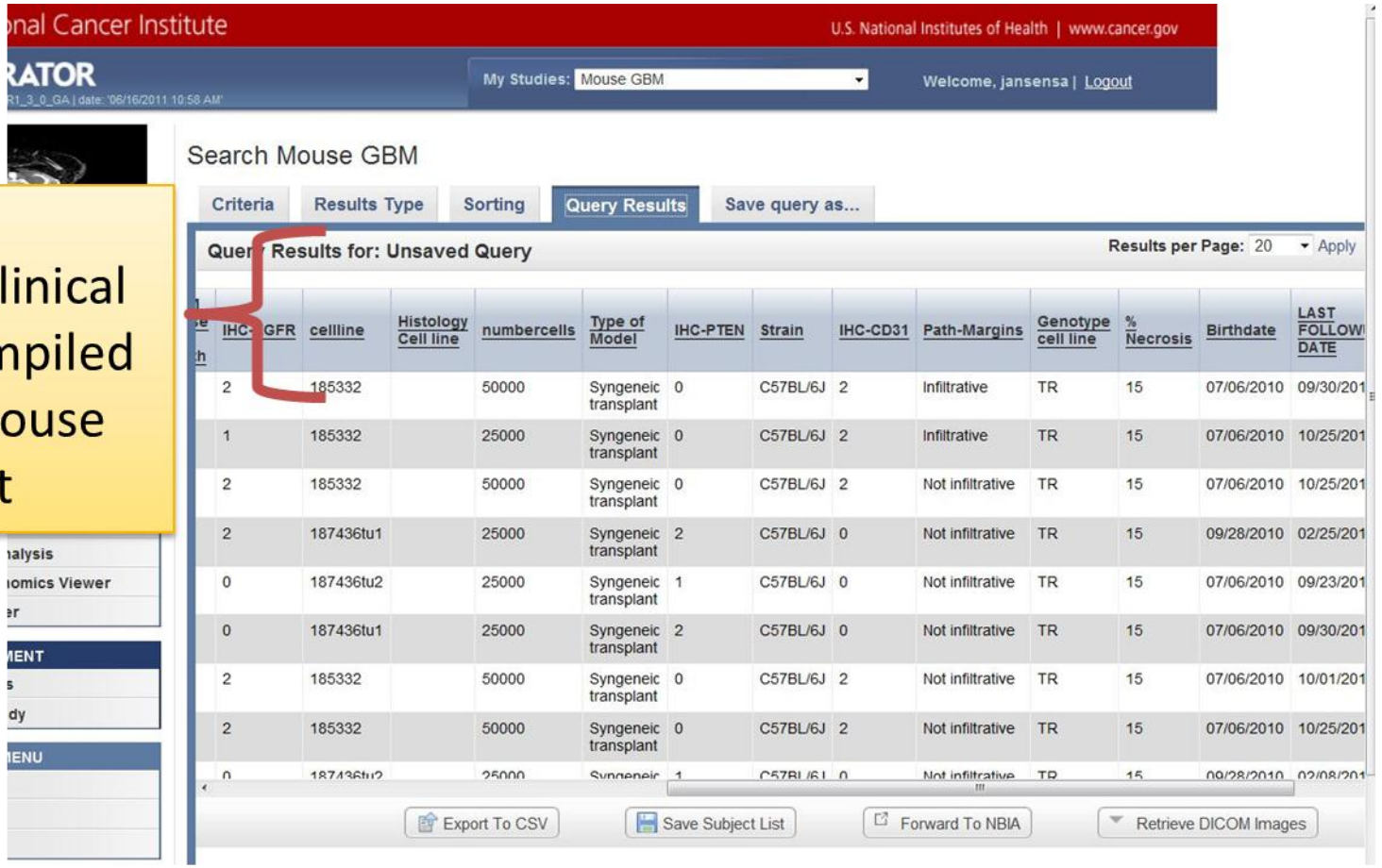
Results lists all biological and clinical features compiled for each mouse patient



caBIG® tools support *Mouse GBM*

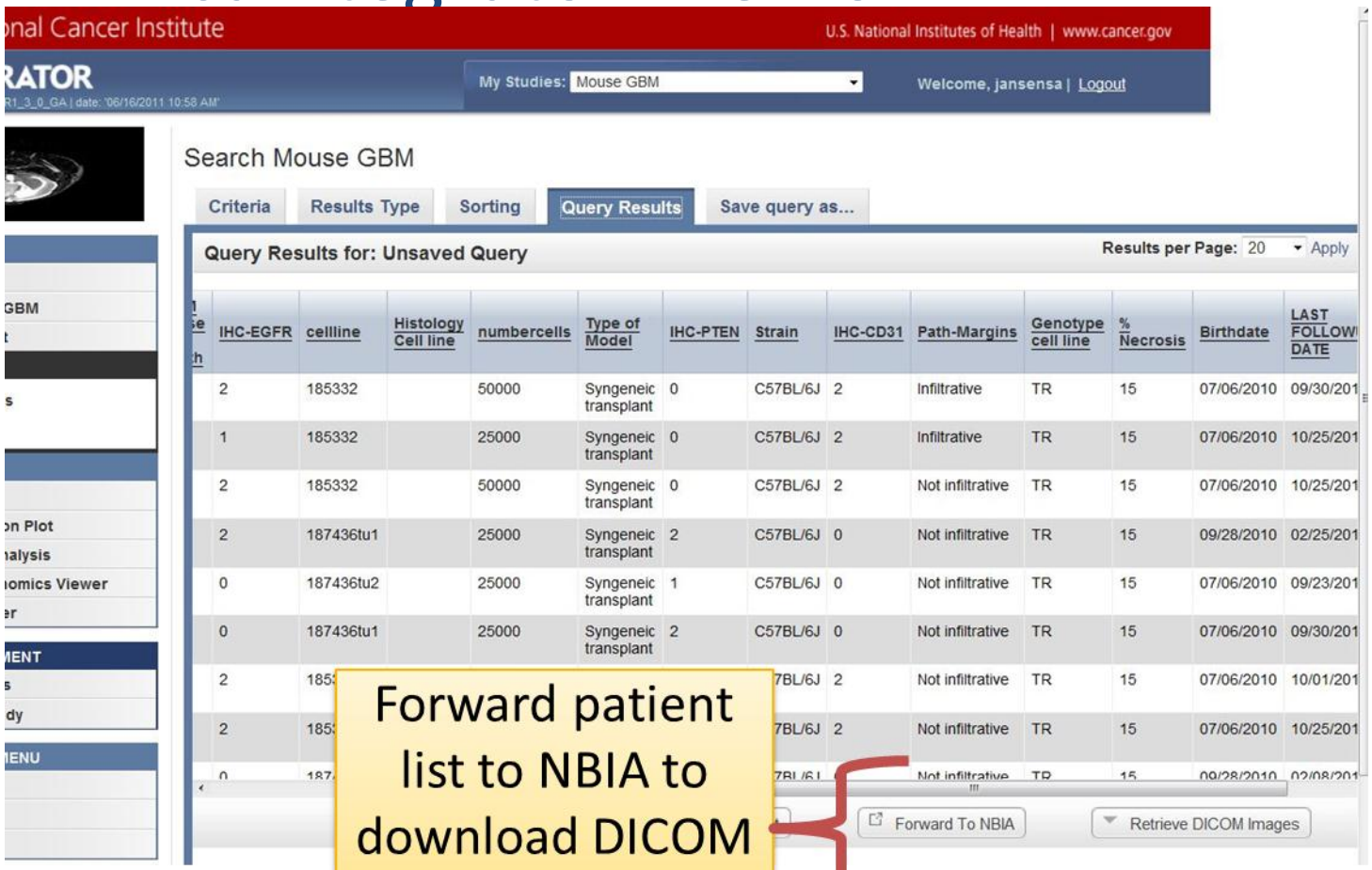
caIntegrator: Demo

More biological/clinical features compiled for each mouse patient



caBIG® tools support *Mouse GBM*

caIntegrator: Demo



Forward patient list to NBIA to download DICOM images

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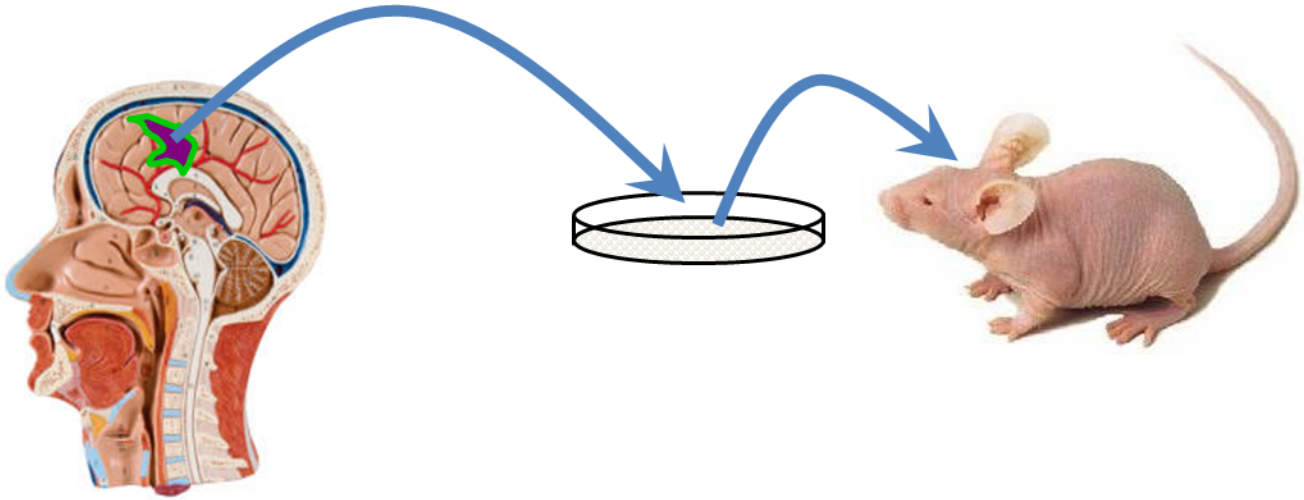
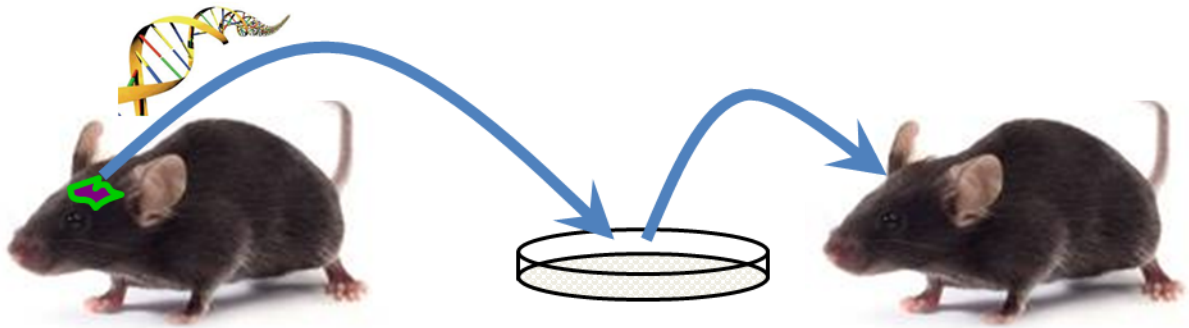


Established cell lines xenograft

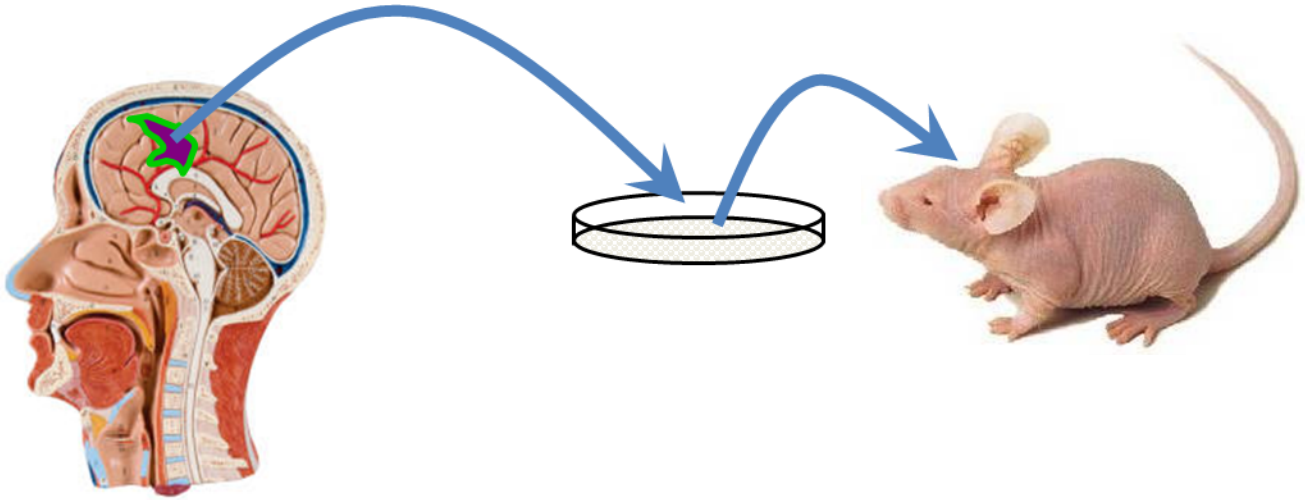
Patient derived xenograft



Genetically engineered mouse (GEM)

Syngeneic allograft

Mouse models of GBM



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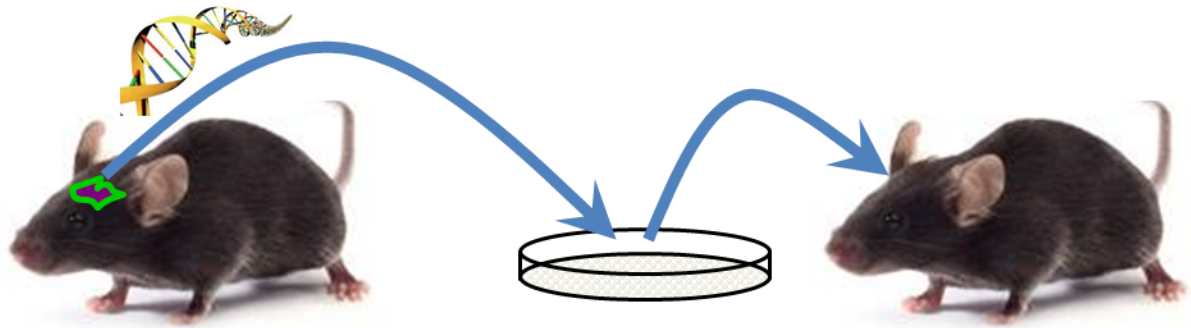

Genetically engineered mouse (GEM)

Syngeneic allograft

caBIG® tools for preclinical research

Remaining challenges

- Standardized features for mouse vs. human comparison
- NBIA: Non-DICOM images
- caIntegrator: Archiving vs. integrating

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Preclinical research for caBIG® tools

- Data stream is similar to humans!
  - Multimodality imaging
  - Chemotherapy (novel), radiation therapy
  - Histology, molecular and genetic analysis
- Large numbers with standardized data
- Full access to tissue
- Tumors at different stages

Acknowledgements

TVD Lab
Terry Van Dyke
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Terry Sullivan
Debbie Gilbert
Linda Cleveland
Sophie Wang
Stephanie Henderson

SAIP
Joe Kalen
Lily Ileva

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Brian Hughes
Eliot Siegal
Carl Jaffe
Adam Flanders
Joseph Chen
Debra Hope
caBIG Imaging Workspace

PHL
Jenn Matta
Tammy Beachley

CAPR
Philip Martin

LASP
Dan Logsdon

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