UAB SAIF ISSUE 10 2021
SMALL ANIMAL IMAGING FACILITY

NEUROIMAGING

Preclinical orthotopic models of brain imaging have emerged as a popular method to follow disease progression longitudinally. Molecular imaging with position emission tomography (PET) and optical imaging provides an avenue to quantify tissue level functional and metabolic characteristics. Further, anatomical imaging with magnetic resonance imaging (MRI) provides high resolution imaging of soft tissue in the brain. Brain imaging is a key component of research in neurology, neurooncology, and a variety of additional diseases.

Optical imaging provides one avenue to evaluate the progression of disease, targeted treatment of tumors using novel particles. New brain disease models can be developed by taking advantage of the sensitive detection of bioluminescence (as seen in Figure 1). When paired with PET or MR, information about these brain diseases can be revealed at the molecular or functional level. Tumor response to treatment can be determined in multiple ways. Most commonly, brain tumor cells expressing luciferase as injected orthotopically into a mouse and imaged longitudinally following drug treatment. This allows a researcher to follow tumor growth patterns by quantifying signal from viable tumor cells. Alternatively, a drug may be conjugated to a fluorescent probe or a virus may express luciferase, allowing the researcher to determine both the in vivo distribution of the drug or virus as well as it's ability to target the tumor. Further, in vivo imaging can be done on a second modality to track the changes in tumor growth. More recently, nanoparticles conjugated to a fluorescent agent have been used in brain research. New model development is particularly useful, especially for metastatic models. Using luciferase expressing cells, cell growth, cell tracking, and model induction methods can be perfected prior to investigation of drug treatment.

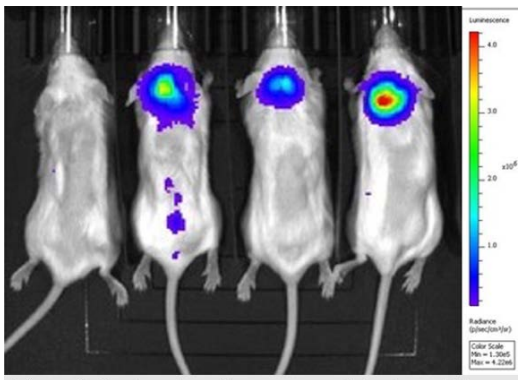


Figure 1: Confirmation of new metastatic brain model induction using luciferase positive tumor cells. Mice were implanted with tumor cells and followed longitudinally to optimize technique to increase metastasis. (Courtesy: J. Clements/Dr. Markert, Neurosurgery)

The SAIF 9.4T preclinical MRI scanner is located in the basement of Lister Hill Library and has been used in many studies of rodent neurological disease models including traumatic brain injury, epilepsy, Alzheimer's, and cancer. High resolution imaging (as seen in Figure 2) can assist in detecting anatomical (structure) or functional (vasculature) changes within the brain. The MRI system is undergoing a major upgrade in 2021 including new hardware electronics and amplifiers, new imaging coils, as well as new software and pulse sequences. One specific hardware improvement is a 4-channel receiver which along with new phased array coils will enable the use of parallel receive methods such as GRAPPA. The parallel receive methodologies use coil sensitivity profiles to interpolate imaging data allowing faster acquisition of data for higher spatial or temporal resolution scanning. Software improvements include a new operator interface which will simplify training for MRI users, and updated pulse sequences comparable to those used in clinical MRI research. Popular neuro imaging methods including EPI, DTI, DWI, ASL, DCE, and MRS will be available on the upgraded system.

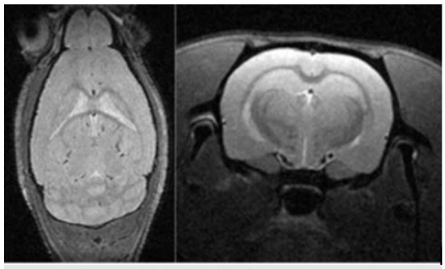
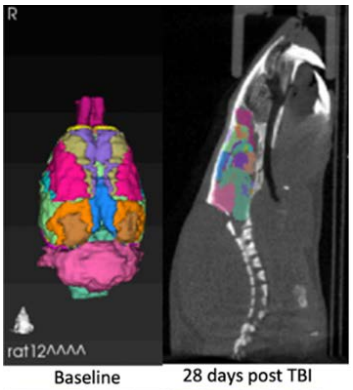


Figure 2: Anatomical T2-weighted imaging of mouse (left) and rat (right) brains with 9.4T MRI. High resolution anatomical imaging can help identify CSF, brain volume and edema



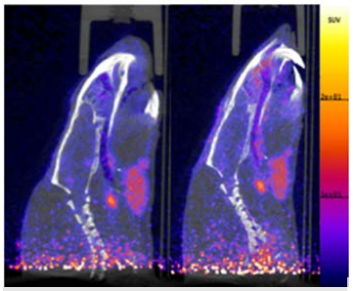
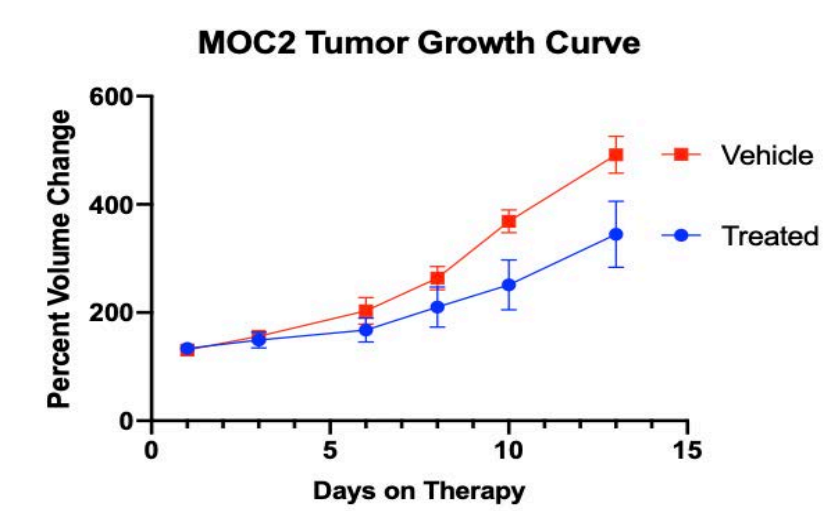


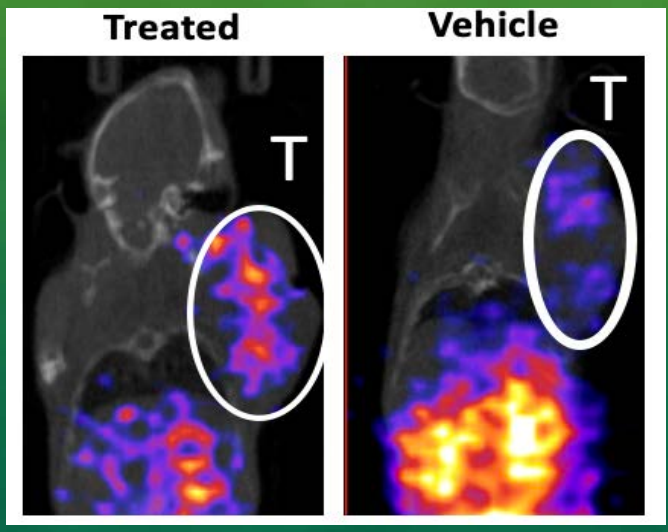
Figure 3: Top: Example of the brain atlas tool used in brain imaging analysis. Bottom: PET-CT imaging of a rat brain using [^{18}F] at baseline and at 28 days post traumatic brain injury (TBI). Courtesy of Dr. Bibb, Department of Surgery

PET is one of the most sensitive tools for studying brain function in vivo. It enables determination of a wide variety of processes using appropriate tracers that can be radiolabeled, including neurodegernative diseases. The most widely used of these tracers is [^{18}F]FDG (Fluorodeoxyglucose), a glucose analog, which has been extensively applied to map changes in brain metabolism in human neurodegenerative diseases. [^{18}F]DPA-714 (dimethylpyrazolo pyrimidine acetamide) is another radiotracer that is increasing in popularity. This radiotracer binds to the translocator protein 18 kDa (TSPO) which is overexpressed during microglia activation and therefore has been adopted as a biomarker for neuroinflammation. The UAB Cyclotron Facility also produces other radiotracers which can be available for preclinical studies, such as [^{11}C]PiB (binds to beta-amyloid plaques) and [^{18}F]AV1451 (binds to TAU protein). Imaging analysis is also an important aspect of a high-quality study. SAIF has implemented top-tier analysis software and specialized tools for brain analysis (as seen in Figure 3).

FEATURED IMAGE OF THE QUARTER

UAB GRANZYME B PET IMAGING





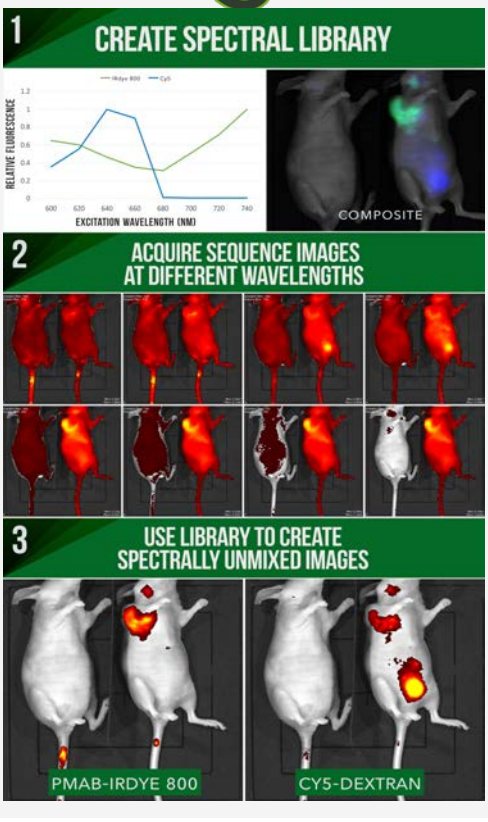
Granzyme B PET (GZP-PET) imaging in poorly immunogenic MOC2 head and neck tumors provides sensitive quantification of immune cell activation that corresponds changes in tumor volume.
Courtesy of Dr. Larimer, Department of Radiology

FEATURE SPOTLIGHT

Spectral Unmixing on the IVIS Lumina Using IRDye 800 and Cy5

Fluorescence imaging can be used to evaluate different molecular tracers simultaneously. The IVIS Lumina III has spectral unmixing capabilities that allow investigators to identify and analyze separate fluorescence sources injected in the same subject. Spectral unmixing can be performed by first creating a spectral library (panel 1) dependent on the individual spectral characteristics of each fluorophore. Researchers can also create spectral graphs to observe relative fluorescence intensities (panel 2) of each fluorophore across the utilized spectrum. This allows separation and quantification of individual signals generated from multiple fluorophores into composite and/or spectrally unmixed images.

The diagram to the right (panel 3) shows a HER2+ tumor bearing mouse imaged following the injection of two fluorescence agents, Panitumumab-IRDye 800 (Pmab-IRDye 800) and Cy5-dextran (10 kDa). Pmab-IRDye 800 targets the epidermal growth factor receptor (EGFR) while Cy5-dextran is a non-specific, small molecular tracer for vascular imaging. The tumor bearing mouse was imaged alongside a negative control mouse. Due to the long circulating kinetics of antibodies, the mouse was first injected with Pmab-IRDye 800, followed by Cy5-dextran 48 hours later. Negative and tumor bearing mice were imaged on the IVIS Lumina III temporally for 10 minutes. Dual expression can be quantified in a single tumor.



USEFUL LINKS

↗ UAB SAIF
Homepage for the Small Animal Imaging Facility core.

↗ PRE-CLINICAL IMAGING CALENDAR
Check for any available time slots for imaging modalities.

↗ TRAINING FORMS
Download training material for submission prior to scheduling imaging.

↗ PERKIN ELMER RESOURCES
Educational material related to the IVIS Lumina III.

↗ DEPARTMENT OF RADIOLOGY
Homepage for UAB's Department of Radiology.

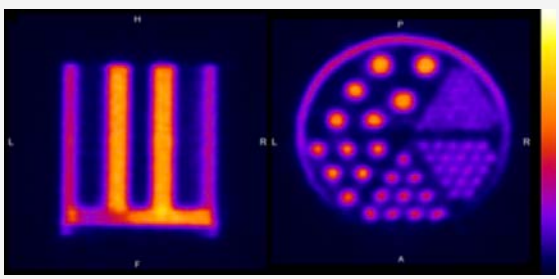
↗ O'NEAL COMPREHENSIVE CANCER CENTER
Homepage for O'Neal Comprehensive Cancer Center at UAB.

↗ O'BRIEN CENTER
Homepage for O'Brien Center for Acute Kidney Injury Research.

↗ UAB CYCLOTRON FACILITY
Homepage for UAB's Cyclotron Facility.

DID YOU KNOW?

The Small Animal Imaging Facility regularly performs quality control measures to confirm instrument reliability, uniformity, and functionality. These QC checks are usually done on a monthly basis or follow instrument maintenance.



An example of an F-18 Derenzo phantom, which can be used to determine resolution on the PET scanner.

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IMAGING FACILITIES

WTI Imaging Suite
WTI 630D

MRI 9.4T Imaging Suite
LHL B15, 934-0265

Volker Hall Imaging Suite
VH B21A, 975-6466

SAIF MODALITY PRICING

*Labor charges are $40 per hour (for each personnel), when assisted during imaging.

Prices effective 11/1/2018.

*Training is available on some modalities, free of charge.

MODALITY	COST	INSTRUMENT
Bioluminescence	$7/mouse OR $55/hour (re-agent dependent)	IVIS Lumina III
Fluorescence	$55/hour	Custom Leica microscope with Nuance CRI spectral camera
		IVIS Lumina III
Ultrasound	$75/hour	Vevo 660
MRI	$125/hour	Bruker 9.4T
SPECT/CT	$100/hour + dosing	XSPECT system
PET/CT	$200/hour + dosing	Sofie GNEXT PET/CT
Gamma Camera	$20/hour + dosing	Picker Camera with Numa computer
Specialty Fluorescent Imaging	$100/hour	Li-Cor Pearl Impulse
		Luna/SPY Systems
		FMT 4000
Staff Image Analysis	$40/hour	

*NON-CANCELLATION POLICY:

If user is not present at scheduled appointment time without prior notification of cancellation, user will be charged an hourly-use fee for that instrument.

IMAGE SUBMISSIONS

Submit images that you would like featured in the newsletter to jordynlawrence@uabmc.edu. Please include PI's name, modality, brief experiment summary, and species.

PUBLICATION REFERENCE

Please acknowledge support of SAIF services in grants and publications by citing the O'Neal Cancer Center Grant P30CA013148.

For data obtained with the IVIS Lumina III systems, please cite S10 instrumentation grant 1S10OD021697.

Please acknowledge DK079337 and the UAB-UCSD O'Brien Center support for all preclinical imaging of the kidney and related biological processes.