IMAGING ENDPOINTS
CONNECTING IMAGING TO THE CURE

TRANSLATIONAL CAPABILITIES

Imaging Endpoints (IE) supports translational studies by assessing the activity of experimental oncology compounds with cutting edge in vivo imaging capabilities and in vivo models. Our value proposition is to design and conduct preclinical imaging trials that both inform and support your product development, and to ensure a critical translation of findings into the clinical trial environment. Through the use of both traditional human cell line-based xenograft models and patient-derived xenograft (PDx) models, IE can assess the activity of experimental compounds using clinically relevant and translatable in vivo imaging methods.

The capabilities and models IE can provide to meet your translational needs are outlined below.

Small Animal Imaging Capabilities - *special focus on translation from preclinical to clinical environment**

- 7T MRI
  - Standard T1W and T2W sequences*
  - Diffusion Weighted Imaging (DWI)*
  - Perfusion Imaging (DCE MRI)*
  - Hypoxia Imaging (BOLD MRI)*
  - pH Imaging (CEST-MRI)*
  - Spectroscopy (single and volume based voxel analysis)*
  - Inflammatory imaging with novel Fe Based MRI contrast agents*
  - Redox Imaging with novel Gd Agents
  - Dixon Weighted Images for Fat assessments*
  - Special focus on Oncology and Neurology with additional novel agents
- MicroCT
  - Anatomic assessments of tumor response*
  - CT perfusion in tumors, tissues and myocardium*
  - Volumetric CT assessments*
  - Bone density and remodeling*
- Ultrasound-Bioluminescence Fusion capabilities
  - Utilization of Lucoferase. eRFP and eGFP tagged cell lines
  - Tumor volume
  - Tumor perfusion
  - Tumor enhancement with novel ultrasound agents
  - Co localization of imaging signal
- microPET/CT – coming soon with high throughput screening for RApid Detection and Assessment of Response (RADAR program)*
- Access to novel PET agents*

In Vivo Techniques

- Traditional s.c. tumor implantation
- Orthotopic tumor implantation – pancreas, renal capsule, and cecum
- Proficient in p.o., i.p., and i.v. dosing routes of administration
- Traditional tumor volume caliper measurements

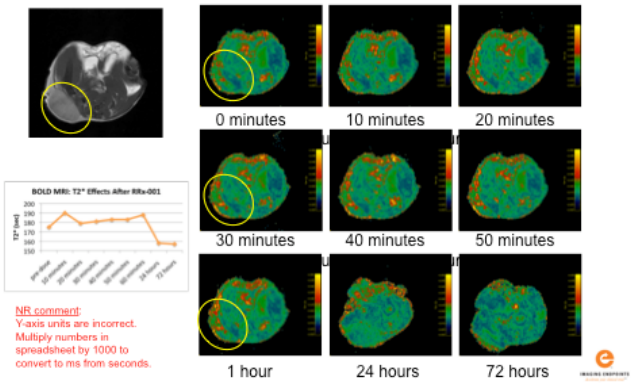
Oncology Models

- Human cell line xenograft models (additional models may be available upon request; * designates in vitro only):
    - Adrenal – H295R, SW13
    - Bladder – 5637*, SCaBER*
    - Brain – D54-MG, D283, DBTRG-05, U251, U87
    - Breast cancer - BT-20*, BT-474, HCC1419*, HCC1569*, HCC-70, MCF7, MCF7/S, MDA-MB-231, MDA-MB-468, MDA-MB-453, MX-1, SUM149PT, ZR-75-1,
    - Burkitt's lymphoma – Ramos
    - Cervical – Caski*, HeLa, SiLa
    - Colon - CaCo-2, COLO-205, DLD-1, HCA-7, HCT 116, HT-29, HT-55, LoVo, Ls 174T, RKO, SW1417*, SW48, SW480, SW620,
    - Endometrial – AN3CA, Hec-1-A, Ishikawa, KLE*, MFE296, RL95-2*, SK-UT-1, SK-UT-1B
    - Epidermis - A-431
    - Fibrosarcoma - HT-1080
    - Gastric – NCI-N87
    - Gastrointestinal Stromal Tumor - GIST48, GIST882
    - Glioblastoma - U-87 MG
    - Head & Neck - Cal-27, FaDu, HN5, SCC-4, SCC-15, Y79
    - Leukemia - CCRF-CEM, HL-60, K562, K562/S, K562/MDR, KG-1, JVM-3, MOLM-13*, OCI-AML3
    - Liver - Hep3B, HEP-G2, PLC/PRF/5*, SK-HEP-1,S NU-398*
    - Lung-NSCLC - A549, H1650, H292, H441, H460, H1437, H1975, H23, H2228 (EML-ALK+), H3122 (EML-AML+), H358, H522*, HCC4006*, HCC827, H720, MV522, NCI-H1299, NCI-H460, NCI-H1975, NCI-H1993, SK-MES-1
    - Lung-SCLC - H1341*, H209, H69, H82*, SHP-77
    - Lymphoma - Daudi, Granta 519, Granta 4, KARPAS-299, CA46, Raji, Ramos, RPMI-8226, U266*, U2932
    - Melanoma – A2058, A375, A431, C8161, DH903, JH1308, KD1592, LOX IMVI, MDA-MB-435, PS1273, SB-CL2, SK-MEL-1, WM1791C
    - Myeloma - 8226/S, 8226/V, 8228/Dox40, ARH-77, ARHD60
    - Neuroblastoma - SK-N-SH
    - Osteosarcoma - Saos-2, U-2 OS
    - Ovarian - A2780, A2780/CP, A2780/ADR, ES-2, IGROV-1, OVCAR-3, OVCAR-8, SK-OV-3, SK-OV-3/CP
    - Pancreatic - AsPC-1, BxPC-3, Capan-1, Capan-2, CFPAC-1, DAN-G*, HPAC, HPAF-II, HS700T*, HS766T*, HUPT3*, KCI-MOHI*, MIA PaCa-2, MUTJ*, Panc 02.03*, Panc 05.04*, Panc 10.05*, Panc 03.27*, Panc 04.03*, Panc 08.13*, PANC-1, PA-TU-8902*, PA-TU-8988S*, PA-TU-8988T*, PSN1*, SU.86.86, SW1990, YAPC*
    - Prostate - 22Rv1, CWR22, DU145, LNCaP, PC-3, PC-3M, VCaP
    - Renal - 786-P*, 786-O, A-498, ACHN, Caki-1, Caki-2*, RXF-393, G-401, SK-NEP-1, SN12CCP
    - Sarcoma- Ewing's - CHP-100, HT-1080, KHOS-NP
    - Uterine Epithelial - RL 95.2

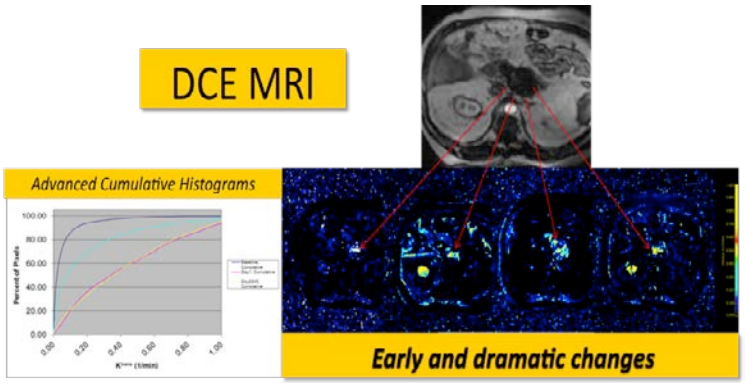
- Patient-derived xenograft (PDx) models (>300 models across tumor types and additional models may be available upon request)
    - Colon - 82
    - Lung - 60
    - Pancreas - 52
    - Melanoma - 25
    - Breast - 23
    - Brain - 23
    - Bladder - 13
    - Endometrial - 5
    - Gastric - 10
    - Head & Neck - 20
    - Hematologic - 4
    - Kidney - 5
    - Liver - 2
    - Ovarian - 22
    - Prostate - 3
    - Sarcomas - 22
    - Other rare tumor types including pediatric tumors – 26
- Syngeneic models
    - Murine Cell Lines: 4T1 (breast), Colon26 (colon), LL/2 (lung), B16 (skin), B16-F10 (skin), Panc.02 (pancreatic)
- Spontaneous tumor models
- Bone metastases models

Example Translational Imaging

Perfusion MRI Mouse Model



Translation to Phase I Clinical Study



The figure on the left shows the location (yellow circle) of a classic xenograft tumor in right hind leg interrogated with perfusion MRI (7T MRI) following tail vein injection of experimental agent. The graph (inset) shows an immediate but significant increase in tumor perfusion at early time points eventually dropping below pretreatment levels. These results, suggesting the vascular disrupting nature of the experimental agent, demonstrated the same behavior in subjects during a Phase I clinical trial (right) using DCE-MRI. Advanced histogram analysis of tumor perfusion showed a leftward shift in the perfusion curves toward increased blood flow (yellow and red curves) compared to baseline (teal curve), followed by a decrease in perfusion at late imaging times (black curve). These results are shown visibly on 1.5 T DCE-MRI images where bright colors are developing in the pancreas tumor (red arrows) within 8 hours of drug delivery. This was developed into a rapid predictor of response/non-response.