

MODELS OF METASTATIC DISEASE

PC3 Prostate Carcinoma

Metastasis to
Via intracardiac injection →

Bone

C26 Colon Carcinoma

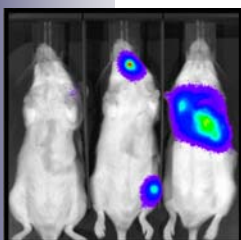
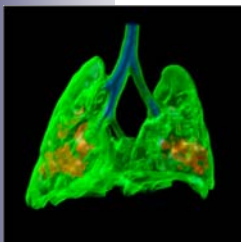
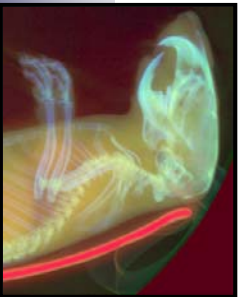
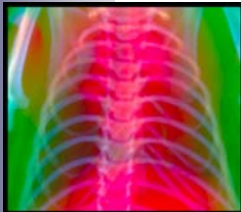
Metastasis to
Via intrasplenic injection →

Liver

B16 Melanoma

Metastasis to
Via tail vein injection →

Lung



- Metastatic disease accounts for a majority of cancer-related mortalities. Genes and proteins involved in metastasis have become potential therapeutic targets to tumor progression.

- MIR has created efficient and reproducible models of metastasis by in vivo serial passage with high take rates.

- MRI, CT and Bioluminescence provides rapid, non-invasive, highly efficient and accurate determination of drug response in a mouse models of metastasis.

- These models have been evaluated for reproducible growth characteristics in vivo and are available for efficacy testing.

MIR

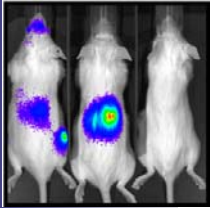
Innovation in Drug
Evaluation

MIR Preclinical Services



Conventional methods of detecting metastasis *in vivo* generally involve serial sacrifice and laborious visual inspection or histopathology of large cohorts. Recent developments in *in vivo* optical imaging (bioluminescence and fluorescence) and micro-PET provide enhanced detection with high sensitivity and increased throughput (optical), but low resolution and limited anatomical context. MRI and Micro-CT is increasingly being used to augment optical and PET imaging by providing high resolution anatomical information

PC3 Prostate Carcinoma Metastasis to Bone



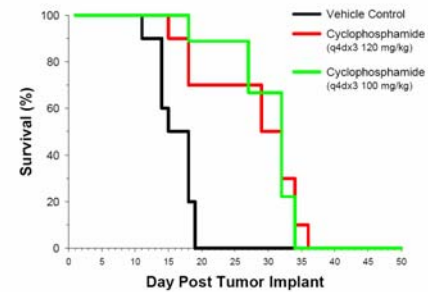
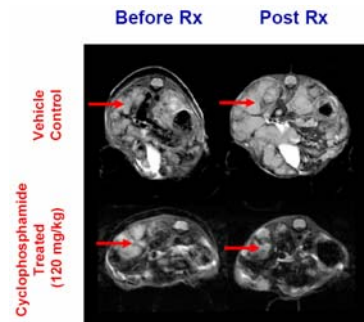
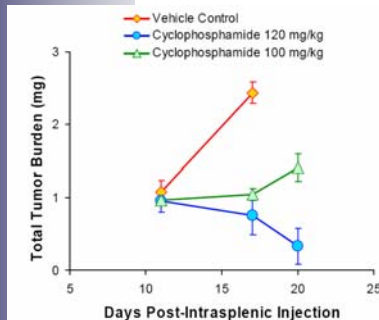
Standard bioluminescence imaging can be used to detect developing metastases. At necropsy, PC3 metastases are evident in the mandible, long bones and spine.



Left are two views of a volume rendering of a large lesion on the proximal tibia (arrowheads). Another smaller lesion is evident on the femur (arrow). CT imaging can be used to assess the extent of bone degradation.

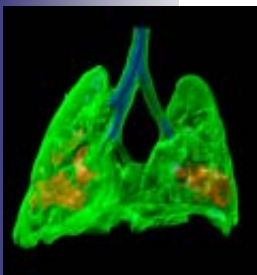
Bioluminescence imaging is able to detect and follow PC3 metastases *in vivo*. Metastases identified by bioluminescence imaging can be characterized as bone lesions by micro-CT *in vivo*. Progression of bone involvement can be followed by serial micro-CT. Bone metastases can be further visualized by 3D volume rendering of the CT data set.

C26 Colorectal Metastasis to Liver

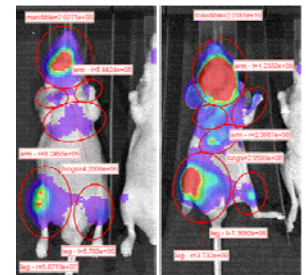


Liver metastases can be monitored by simple, non-gated, T2-weighted MRI. Using MRI, growth of metastases can be readily quantified over time. MRI-determined growth inhibition, as early as day 17 following cyclophosphamide treatment, are correlated with long term survival.

B16 Melanoma to Lungs



Representative data to the left shows a volume rendering of lung micro-CT data from a breathing mouse with lung metastases. Lung tissue is shown in green, major air passages in blue, and metastases nodules in yellow. To the right, in a separate experiment, bioluminescence is used to determine the location of metastases in a different model system. Bioluminescence is a high throughput method of determining tumor burden in an animal and tracking changes in that burden over time. MIR utilizes luciferase expressing B16 melanoma cells to track metastases to the lungs and elsewhere.



Micro-CT is able to detect and delineate B16 lung metastases *in vivo*. Tumor nodule volumes are readily quantified. Despite respiratory motion, nodules as small as 1 mm can be quantified.