

# Bruker Preclinical Imaging Solution application review

2/3/2015 Jack Yang Bruker PCI





#### Integration for four systems





Albira PET/SPECT/CT



Multimodal Animal Transport System



Icon MRI



FX PRO Multifunction Optical system nodal port System



#### Skyscan microCT

Multimodal Animal Handling System Details Mouse Cassette



•Quick-lock joint connector for anesthesia, warming, respiratory control

3 point ECG, body temperature sensor
Sealed design for safe gas removal

•Nose cone, head fixation by tooth bar

•Feed through for catheters









#### Multi-Modality Optical – MRI Imaging of Subcutaneous Melanoma Tumor Model



- Co-registration of MRI and 2D optical images
- Optical image used to identify tumor





#### Co-register ex vivo fluorescence image with MRI to reveal tumour



#### Image-guided cardiac cell delivery





Image-guided cardiac cell delivery: Sprague-Dawley rats (n = 11) were imaged using highresolution ultrasound, and stably transfected cardiomyoblasts (plasmid-CMV-firefly luciferase) were injected into the anterior cardiac wall under ultrasound guidance (parasternal long-axis view), using a 28-gauge needle. After injection, bioluminescence imaging was performed using a cooled charged-coupled camera. The signal detected was positively correlated with the amount of cells transplanted (R(2) = 0.94, P = 0.03). Optical signal could be followed longitudinally using bioluminescence imaging.

Rodriguez-Porcel & Gambhir et al, 2005

#### In Vivo FX Pro





Camera Performance CCD Monochrome interline CCD Pixel Density **2048 x 2048 pixels** 10X zoom lens Resolution 10 µm/pixel (max.) Imaging Area 2 x 2 cm to 20 x 20 cm 16-bit single capture Light Source **400W** Xenon Ex filter **410-760nm** Em filter **535-830nm** 

# Bruker Optical Unique advantage



- The Xtreme provides a powerful multimodal solution for preclinical molecular imaging (Luminescence, Fluorescence, X-ray radiography, radioisotope)
- High resolution & sensitivity 4 MP CCD detector, 400W Xenon light, high quality x-ray source, unique phosphor screen for isotope imaging.
- Whole range spectral with multiple excitation filter allows for the simple removal of autofluorescence and imaging of multiple molecular pathways simultaneously.
- MARS allows for the 360 degree visualization of your subject, while maintaining accurate co-registration and improving S/N in your experiments.











- Lentivirus was used to transduce cells with proteins
- HIF1a and constitutively active HIF1a improve bone repair
- X-ray gives analysis faster than high resolution CT

Innovation with Integrity

Zou et al. STEM CELLS 2011;29:1380-1390

Imaging Vascularization in Heart Failure Models BRUKER

## Sham 3 weeks 8 weeks 8 weeks MMP9-/-



• Heart failure induced with aortic banding

 Hearts were injected with contrast and imaged in vivo and ex vivo

Areas of contrast were selected and quantified

Givvimani et al. Archives of Physiology and Biochemistry. 2010



#### X-ray Imaging of Tumor Size

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Day 16 post-injection



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#### X-ray Imaging of Mouse Paw





Mouse trebecular structure

Details of each mouse bone in paw

## Geometric Magnification







#### **BMD** measurement



#### **ROI Tool for Bone Density Analysis**

User can select and define multiple Regions of Interest with just a few clicks.

#### **Cylindrical Modeling**

Bone Density Software automatically converts a planar X-ray image into a density image.



#### Automatic Energy Calibration

Calibration uses standard Aluminum filters and includes attenuation of air, supporting substrates and the screen.

#### **Highly Detailed Bone Density Reports**

The report is generated in seconds and contains:

- Bone and marrow column densities (units of cm<sup>-1</sup>)
- Inner and outer radius of long bone (units of cm)
- Bone asymmetry (displacement of center of marrow from the center of the bone, cm)
- Tissue depth (cm)
- Mean X-ray energy (according to the filter used, Kev)
- Bone and marrow surface density (g/cm<sup>2</sup>)
- Bone volume density (g/cm<sup>3</sup>)
- Estimate of mathematical fitting quality (Chi-Squared).

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Barry Barbary Density Index "47a	1.000041	-	



# Luminescence





### Orthotopic Lung Cancer



- A549 Cells transduced with luciferase
- Cells were surgically implanted in the lungs
- Cell growth was monitored for 65 days
- Images were co-registered with X-ray for easy localization to lungs

Day 7 Day 14 Day 21 Day 28 Day 35 Day 41 Day 49



Day 55 Day 61 Day 64

Α



Madero-Visbal et al. Surg Oncology (2010) 1-7

# Stem Cells in Heart





5 x10<sup>5</sup> Luminescent Stem Cells were injected into the heart

Innovation with Integrity courtesy of Prof. M. Leevy, Notre Dame, USA

## **Prostate Imaging**





Innovation with Integrit, Images Courtesty of Prof. Bob Handa, Arizona State Univ.

# **Multispectral Fluorescence**





Multiple Excitation Filters

### Cells in Bone Marrow



# 10<sup>6</sup> DiR and GFP positive leukemic cells after intratibial injection ...



Innovation with Demot Images from Cancer Research UK, London, F. Lassailly & D. Bonnet

#### Signal Co-registers with RFP Tumors





PNAS. 2010 107 (4) 708-9. 1284-88

#### Traumatic Brain Injury Model





- Treatment at 24 hr post TBI challenge:
- →Test rat: 3 mg/kg PSVue 794 IV
- $\rightarrow$ Neg. control rat: saline IV

Images courtesy of Dr. Nae Dun, Temple University

### In Vivo Targeting of Plaques



191

128

**Negative Control** 

 $A\beta$  Positive



Ran, C., et al. Design, Synthesis, Testing, of Difluoroboron-Derivatized Curcumins as Near-Infrared Probes for In Vivo Detection of Amyloid-b Deposits. JACS. (2009),





#### Bone Regrowth





2 nmol Osteosense (PE), 2 s, f/2.5, no binning

### H. polygyrus Larvae Injected into Stomach



• The solution of NIR labeled *H. polygyrus* larvae were injected into the stomach of a mouse

 Mice were imaged using NIRF and X-ray

 Mice were imaged immediately post injection and at 1 hr post injection

• Larvae migrated to the GI



## Tracking and Delivery of siRNA Nanoparticles



- Nanoparticles injected iv
- Targeted nanoparticles selectively accumulate at the tumor site
- Both tumors of similar size receive similar doses of nanoparticle



Medarova et al. Nature Medicine. 2009. 372-7.

# Radioisotopic







# Radiolabeled Compounds Incorporating: <sup>18</sup>F, <sup>111</sup>In, <sup>99m</sup>Tc, <sup>125</sup>I, <sup>64</sup>Cu, <sup>32</sup>P

# ex. FDG, Octreotate

Co-registration of Radioisotopic Signal with Thyroid



<sup>125</sup>I Probe 50uCi



X-ray Image

#### Multi-modal X-ray and Radioisotope in Guinea Pig

Innovation with Integrity Images courtesy of Pfizer Research Labs

### Rapid Evaluation of SPECT Tracers



• PSMA + LNCap tumor xenograft model established

 Binding evaluated by DUPA-FITC ex vivo

• In Vivo evaluation conducted via DUPA-99mTc

 Specificity confirmed by chemical and biological negative controls

• Follow up with 3D SPECT imaging



Kularatne et al. Molecular Pharmaceutics. 2009. 6 (3): 708-9.

# Multimodal Animal Rotation (MARS) 360度全景造影套件





### MARS: Optimizing S/N In Vivo





#### S.P. Orton, et. al. 2011, MIDD Conference poster

#### MARS with Multispectral Unmixing



- Barium sulfate X-ray contrast agent and X-SIGHT 761 Nanospheres
- IV injection of Visipaque<sup>™</sup> (iodixanol) (320 mgI/ml) & X-SIGHT 670 Large Stokes Shift (LSS) Dye, TFP ester
- MS acquisition at each angle
- Co-registration of fluorescent signals and multiple modalities in one image



X-SIGHT 761 Nanospheres X-SIGHT 670 LSS Dye

Visipaque is a trademark of GE Healthcare.

#### Multiple application





#### Multiple tumor





#### GI tract





#### Kidney & bladder





# Xtreme Co-registration with CT





Xtreme MARS image and Albira CT image co-registration

# Thanks