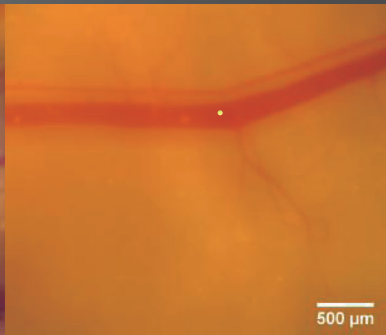
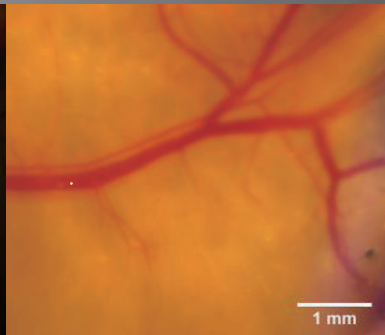
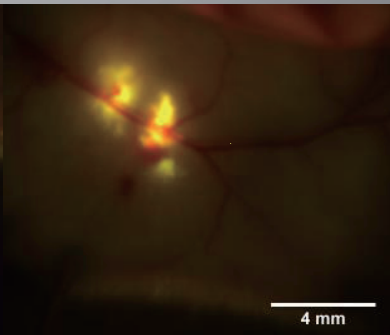
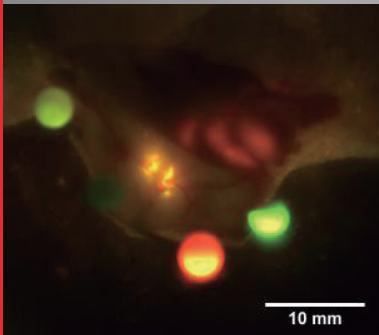


UVP iBOX Explorer²

Closing in on the answers within

Fluorescence Imaging Microscope



Visible to NIR In Vivo Imaging for Macro to Micro Detection of Fluorescent Markers in Small Animals

Capture images with the high sensitivity, cooled CCD camera and optics, ideal for in vivo imaging applications

View whole animal down to single cell via motorized optics

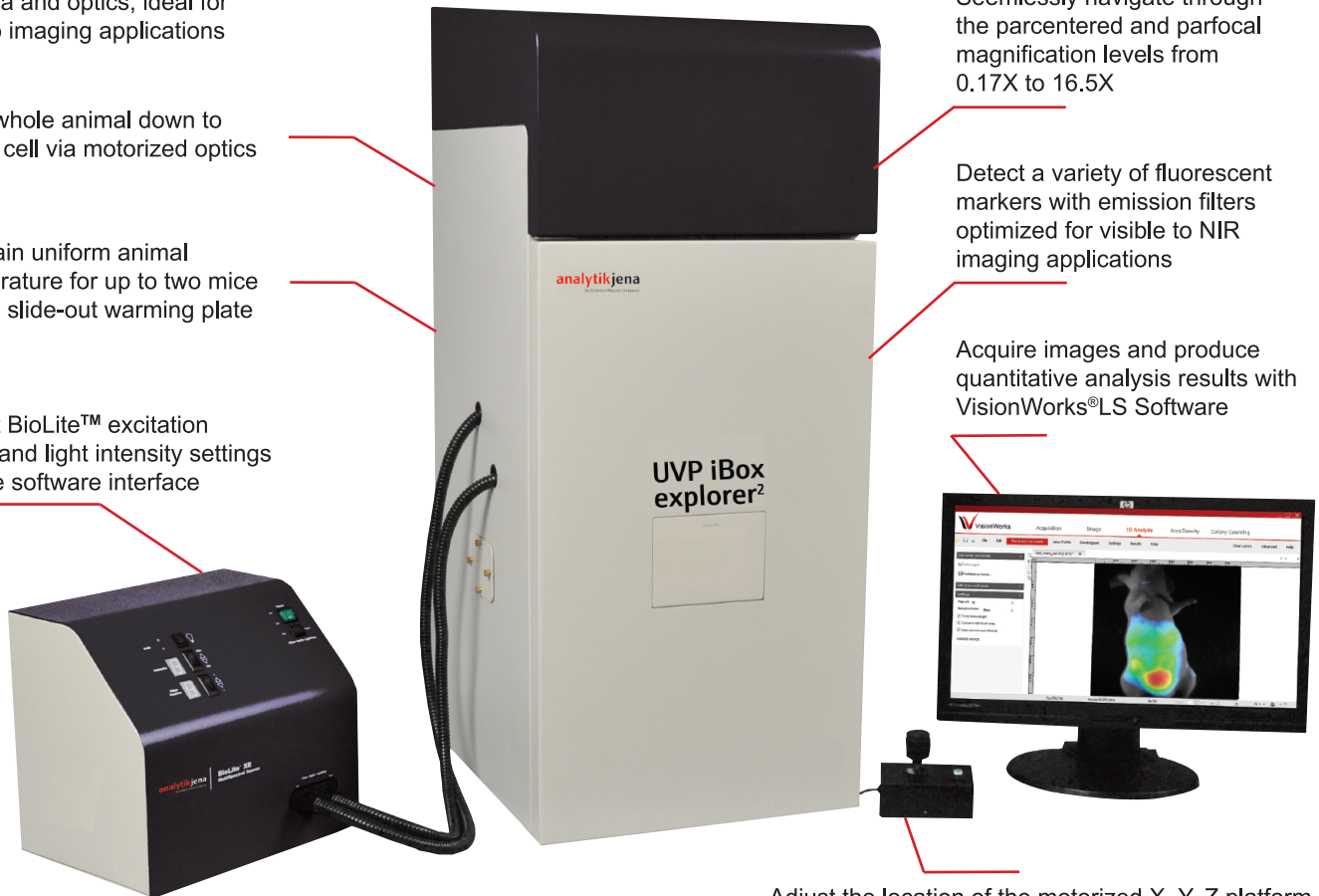
Maintain uniform animal temperature for up to two mice on the slide-out warming plate

Select BioLite™ excitation filters and light intensity settings via the software interface

Seamlessly navigate through the parcentered and parfocal magnification levels from 0.17X to 16.5X

Detect a variety of fluorescent markers with emission filters optimized for visible to NIR imaging applications

Acquire images and produce quantitative analysis results with VisionWorks®LS Software



Adjust the location of the motorized X, Y, Z platform via the external joystick; fine tune and bookmark stage positions using the software interface

BioLite Xe MultiSpectral Light Source

The BioLite is an external light engine for excitation of fluorescent stains. The unit features:

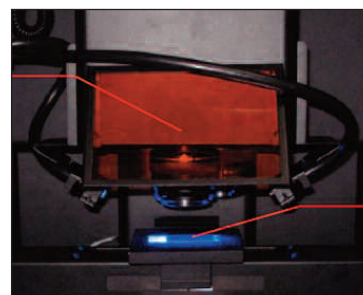
- Xenon light source with uniform and directed lighting via fiber optic light guides to samples inside the darkroom
- Matched excitation/emission green fluorescent protein (GFP) and red fluorescent protein (RFP) filter sets included; custom filter sets available
- Eight excitation filter positions for a variety of filters

Emission filters are placed in the darkroom. The neutral density filter passes emission wavelengths from 400 - 700nm. This filter is used for white light or non-fluorescent imaging. The long pass filter blocks blue light excitation and passes fluorescence.

The BioLite supplies dual excitation light paths:

- Coaxial lighting emits targeted illumination for use with high magnification ranges
- Side lighting emits a broader illumination area for use with the lower magnification ranges

Amber viewing screen



Side lighting onto the sample stage

- Nine discrete magnification levels maximize visualization from whole animal to individual cell, subcutaneously and within the body cavity of living mice
- Parcentered and parfocal optics allow seamless imaging throughout the magnification levels
- High sensitivity cooled CCD camera is ideal for visible to NIR small animal imaging applications
- High intensity xenon light source is optimized for excitation of visible through NIR markers in vivo
- User-defined software templates simplify image acquisition for consistent and reproducible results
- Software analysis capabilities enable area density, tumor size and volume measurements for research studies such as biodistribution, progression and regression

UVP iBOX Explorer² Applications

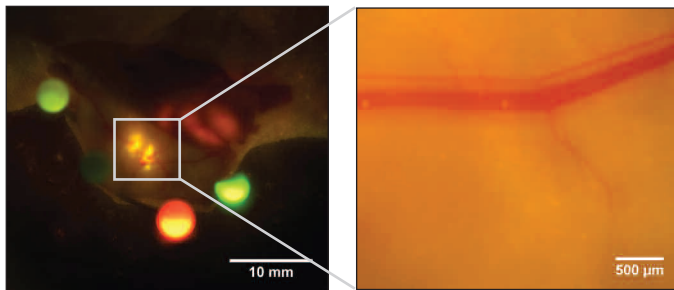
Pre-Clinical Research Applications for the iBox Explorer²

Researchers can visualize in vivo cancer cell migration and tumor progression with the iBox Explorer². The system's upright optics provide an ultra long working distance and high numerical aperture (NA) which is ideal for animal fluorescent imaging studies from the macroscopic (cm) to microscopic (μm) scale.

- Tumor shedding
- Tumor angiogenesis
- Micro/macro metastases
- Tumor/host margins and interactions
- Tumor micro environment
- Primary tumor growth or tumor tracking
- Hematogenous trafficking
- Intralymphatic trafficking
- Biodistribution monitoring

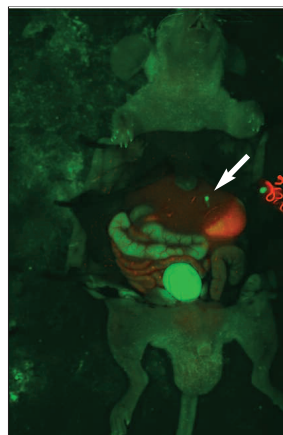
Fluorescent Cancer Cell Detection

Migration of fluorescent cancer cells within vasculature of a mouse. HT-1080 fluorescent cancer cells were injected into the epigastrica cranialis of a mouse. Immediately after injection the fluorescent signature around injection site identifies cells that have escaped into surrounding tissue. A magnified image highlights cancer cells migrating within the bloodstream.



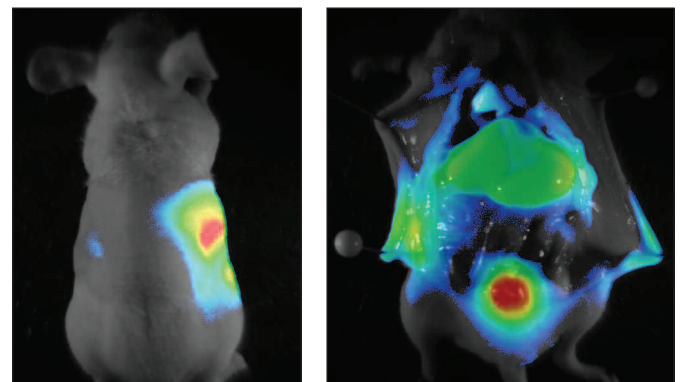
Detection of Multiplex NIR Dyes In Vivo

View of a Qdot conjugated to anti-CD133 monoclonal antibody distribution within a surgically exposed abdomen. The image displays the presence of a GFP expressing tumor lesion within the liver and collection of conjugate in the abdominal organs. The image represents a three color multiplex channels. Application Note FP-173.



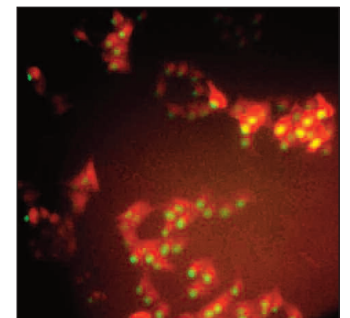
Biodistribution Monitoring

Monitoring biodistribution of DyLight 755, a near infrared (NIR) dye, conjugated to anti CEA monoclonal antibody within the tissues of a nude mouse. Four hours after injection, the dye can be seen accumulating in the liver. Ex vivo analysis shows that the liver has the most intense NIR emission, suggesting the greatest accumulation of dye. Application Note FP-178.



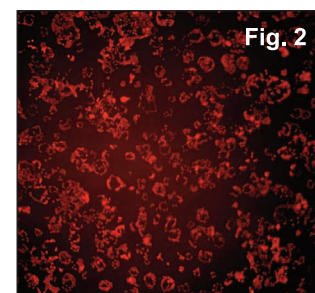
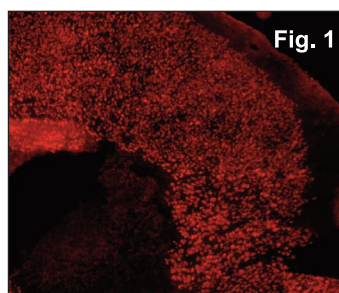
Multiplex Dual Color Imaging

Human osteosarcoma cells at 50% confluence in RPMI media. The multiplexed image is a composite of GFP expressing nuclei and RFP expressing cytoplasm.



Detecting a Mouse Pancreatic Cancer Cell Line

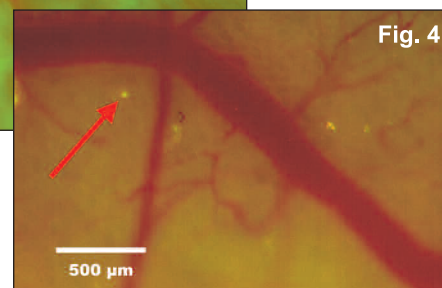
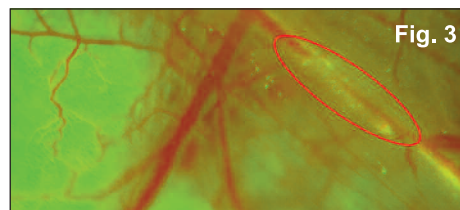
Mouse pancreatic tumor tissue sample imaged at two magnifications: 2.5x and 8.8x. A red fluorescent protein (RFP) filter was used to highlight the RFP-tagged cytoplasm to show the distinct morphologic characteristics of individual cells as well as the tissue microenvironment *ex vivo*. The cell line, XPA1 (Fig 1) shows a histological sample viewed at 2.5x magnification, excited with light funneled through the optical components. At high magnification (8.8x, Fig 2), more distinct detail can be seen, such as cell orientation, areas of high RFP concentration and cytoplasmic morphology. To read more about this research, see Application Note FP-169.



Intravital Imaging of a Mouse Ventral Skin-Flap

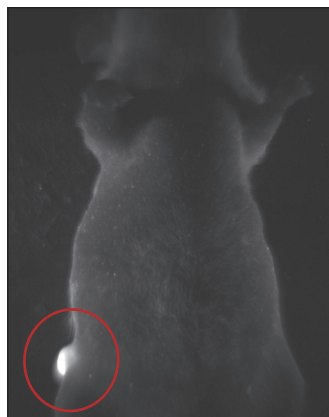
Real-time *in vivo* imaging of HT-1080 cancer cells at several levels of magnification. Figure 3 shows a multiplexed image of a skin flap at 2.5x magnification. The major vessel in the field corresponds to the epigastrica cranialis vein of a nude mouse. Clusters of dual-colored HT-1080 cells can be visualized moving through the vasculature in the right-most aspect of the field.

Figure 4 shows an 8.8x magnification of a skin-flap. Migrated dual-colored HT-1080 cells (bright yellow) within a distal vessel have begun to extravasate. To read more about this research, see Application Note FP-171.



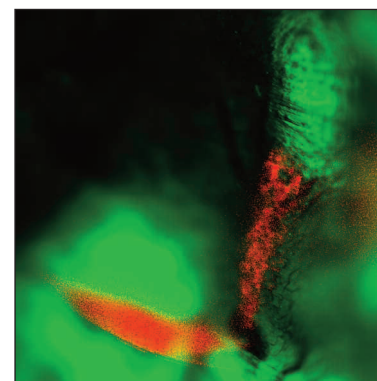
Tumor Targeting of NIR

GFP-expressing tumor bearing CEA surface antigen. Human pancreatic cancer cell line with high levels of CEA surface antigen expressing the GFP reporter gene was implanted into the right flank of a mouse. After four weeks, a NIR dye was injected intravenously, conjugated to an anti-CEA polyclonal antibody. 18 hours after injection, the dye antibody conjugates were co-localized within the tumor.



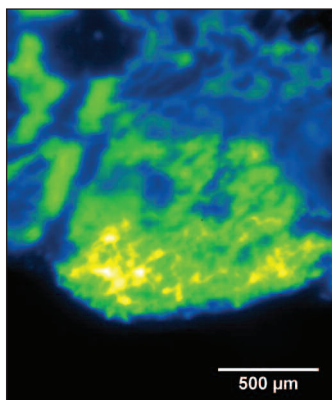
Co-Localization of NIR-tagged Antibody

Subcutaneous tumor implanted in a mouse. Qdot 800-CD133 antibody conjugate was injected into the vasculature of a hepatoma tumor-bearing mouse. High magnification of the tumor vascular shows co-localization of the Qdot conjugate in red within the GFP expressing tumor. Qdot800 signal can be seen within the perivascular region of the tumor vessel.



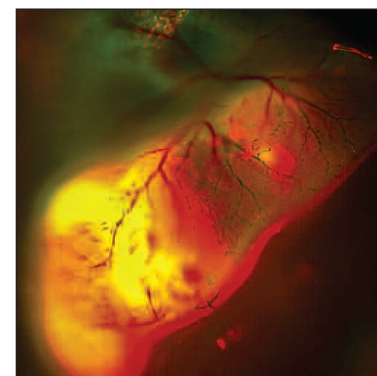
Constitutively Fluorescent CFP Mouse

Labeling of mouse thyroid tissue histology section with Alexa488 conjugated to anti-CEA antibody. Background fluorescent areas appear blue due to co-expression of cyan fluorescent protein (CFP) reporter with an intracellular protein. Areas of high CEA surface antigen expression readily bind to the Alexa488 conjugate and emit green fluorescence.



Tumor Cells in the Colon

Skin flap technique visualizing the MMT (breast cancer cell line) dual color tumor cells in the colon. GFP and RFP filters were used to isolate the green and red fluorescence.



System Name	Camera
iBox Explorer ² 615	OptiChemi 615

Darkroom Specifications:

Emission Filters: Four-position interchangeable tray:
515nm Longpass, GFP, RFP, Neutral Density; Additional filters available

Controls: Automated, software controlled

Stage: Precision motorized X, Y, Z
Travel: X=100mm, Y=100mm, Z=100mm
Resolution: X=10µm, Y= 10µm, Z=1µm
Position/Focus: Controlled by joystick/software

Warming Plate: 37°C, user adjustable

Darkroom Dim.: 17.5"W x 19.5"D x 41"H
(44.5 x 49.5 x 104cm)

Camera Specifications:

Camera: OptiChemi 615

Type: Monochrome

CCD Bit Depth: 16 bit

File Bit Depth: 16 bit

Pixel Resolution: 2184 x 1472

Megapixels: 3.2, extendable to 9.6

Cooling Type: -60°C from ambient, Peltier cooling

Peak QE: 86% (quantum efficiency)

BioLite Xe MultiSpectral Source:

Light Source: 150 watt xenon

Fiber Optic: Coaxial and epi illumination; light heads mounted to the darkroom

Excitation Filters: Eight position wheel includes filters:
GFP and RFP
Additional wavelength filters available

Controls: Via software

Dimensions: 8.75H x 7W x 10D in.
(22.2 x 17.8 x 25.4cm)

VisionWorksLS Software:

Interfaces with: Camera, optics, darkroom, BioLite

Tools: Macros and templates

Analysis: Extensive functions including area density and volume measurements, tumor sizing and compositing tools

Documentation: Create reports and export data

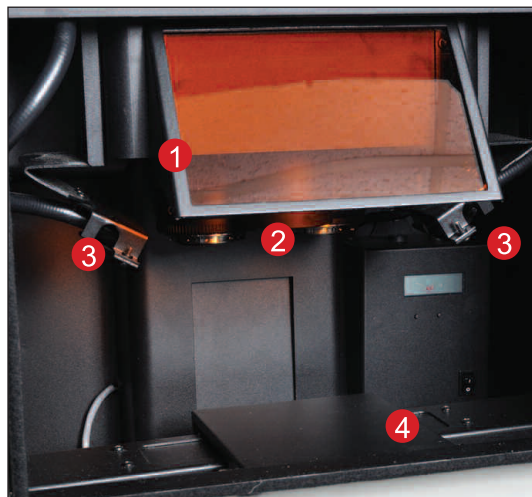
Compliance: Supports 21 CFR Part 11

Compatibility: Win XP (SP2), Win 7, 8, 10

Magnification and Field of View Imaging Area:

Optical Magnification:	0.17x	0.25x	0.5x	1.66x	2.5x	4.5x	7.5x	8.8X	16.5X
FOV Range (mm):	90x90	60x60	30x30	9x9	6x6	3.3x3.3	2x2	1.7x1.7	0.9x0.9

Darkroom Interior:



- 1 Adjustable amber viewing screen
- 2 Optics
- 3 Epi light guides
- 4 Height adjustable stage with warming plate

Excitation/Emission Filter Sets Included:

Filter Type	BioLite Excitation Wavelength	Microscope Emission Wavelength
GFP	455-495nm	503-523nm
RFP	502-547nm	580-630nm
General	--	515 long pass
Neutral Density	--	400-700nm

Additional filter sets are available to cover a wide spectra of fluorescent proteins. For an extensive list of filters, go to UVP.com/pdf/UVPFilterSelectionChart.pdf

BioLite Xe:



- 1 Variable intensity settings indicator
- 2 Position filter indicator
- 3 Access to wheel with 8 filter ports
- 4 Fiber optic cables and light guides connect in the darkroom to supply directed side and coaxial lighting to the animal

iBox Anesthesia System

The iBox Anesthesia system supplies a complete kit for safe anesthetizing of small animals with isoflurane or sevoflurane (gas not included with kit). While imaging is performed with the iBox Explorer, it is important that there is no movement of the animal. The anesthesia system minimizes movement and permits the animal to use less anesthesia, reduces stress and potential side-effects while imaging is performed. The anesthesia allows quick recovery time of the animal.

Several components are combined in the anesthesia system to regulate and administer a combination of oxygen and isoflurane gas to the animal. The initial anesthesia is performed in the induction chamber. The animal is then moved to the warming plate inside the iBox darkroom and connected to a nose cone (two nose cones are included). The plate generates uniform temperature conditions which maintain a safe body temperature of the animal during the imaging process. A low profile breathing device on the plate connects to patented valves. The system's non-rebreathing technology safely prevents backflow of gases into the darkroom.



The iBox Anesthesia System is a portable unit that is designed for maximum efficiency, ease of use and low anesthetic gas consumption.

Cell Lines

Well over 200 cancer cell lines are available that have been engineered to express GFP, RFP, or dual color (nucleus/cytoplasm) for in vivo fluorescent imaging analysis. These cell lines represent a wide range of mainly human cancers such as breast, pancreas, prostate, ovarian, lung, colon, melanoma and many others. In addition, mouse and rat cell lines are also available as well as custom fluorescent cell lines through contract development work.

Tumor Type	Cell Line	GFP	RFP	Dual-Color
Prostate, Human	PC3	X	X	X
Prostate, Human	DU145	X		X
Prostate, Human	LNCap	X	X	

The choice of fluorescent protein used in the cell line will depend in part on the type of mouse being used. Nude mice which express GFP, RFP and CFP as normal background are also available so that the cell line fluorescent color can contrast with that of the normal tissue. For example, a RFP tumor cell line can be tracked with high contrast against a GFP background normal tissue using the GFP mouse.



The chart shows a sampling of over 200 cancer cell lines available.

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