PRODUCT NOTE

Multi-species optical imaging with integrated x-ray.

Key features

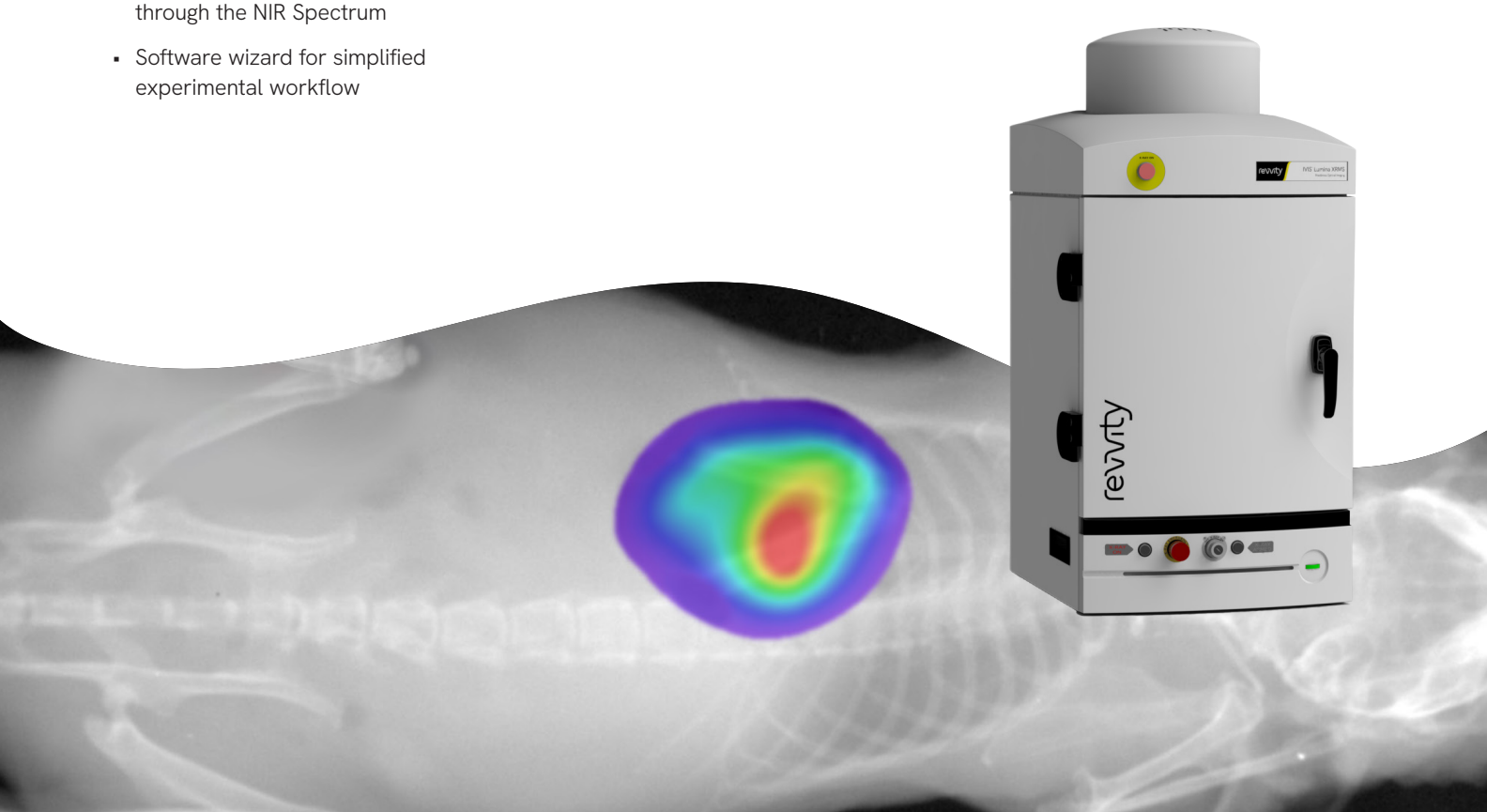
- 2D optical imaging with integrated planar X-ray
- Imaging capacity of up to 3 mice
- Multi-species imaging including mice and rats
- High sensitivity bioluminescence with imaging down to a single cell
- Spectral unmixing for enhanced signal separation and improved fluorescence sensitivity
- Full fluorescence tunability through the NIR Spectrum
- Software wizard for simplified experimental workflow

The IVIS® Lumina XRMS from Revvity integrates the best in class *in vivo* bioluminescence and fluorescence imaging with 2D X-ray capability. The IVIS Lumina XRMS offers the flexibility to image small as well as large animals with precise optical and X-ray overlay, giving anatomical context to the optical signal. The system includes state of the art spectral unmixing for sensitive multispectral imaging to monitor multiple biological events in the same animal.

Leading innovator in bioluminescence, multispectral fluorescence and integrated X-ray technologies

The IVIS Lumina Series III platform brings together years of leading optical imaging technologies into one easy to use and highly sensitive bench top system. The IVIS Lumina XRMS offers leading 2D bioluminescence and enhanced fluorescence imaging with integrated planar X-ray giving anatomical context to optical imaging studies.

IVIS Lumina XRMS



The system is equipped with up to 26 tunable filters to image fluorescent sources that emit from green to near-infrared. All IVIS Lumina Series III systems come with a novel illumination technology that effectively increases fluorescent transmission deep into the near infrared range with full transmission through 900 nm. Moreover, the IVIS Lumina XRMS incorporates Revvity's proprietary Compute Pure Spectrum (CPS) algorithm for spectral library generation software tools to ensure accurate autofluorescence removal, unmixing and fluorophore quantitation.

Standard on all IVIS instruments, absolute calibration affords consistent and reproducible results so that researchers can compare data from one instrument with data from any another IVIS instrument around the world.

Flexibility for imaging both small and large animals

The IVIS Lumina XRMS offers the flexibility to image mice, rats and other animals up to 500-600 g in weight with an accurate optical overlay on X-ray image. The X-ray scintillator can easily be moved to effectively image mice and rats with ease and is the only instrument that can overlay an optical signal to the X-ray image at all Fields of View (FOV's), as shown in Figures 1 and 2.

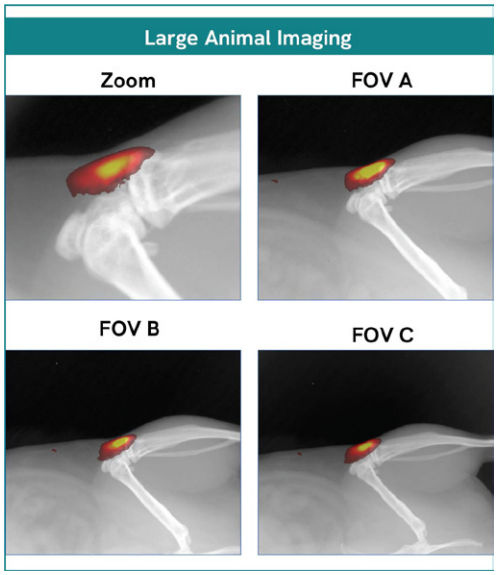


Figure 1: Optical overlay of IVISense™ Folate Receptor fluorescent probe signal on X-ray image at multiple FOV's in a 560 gram rat. Optional accessory ZFOV lens is needed for zoom image.

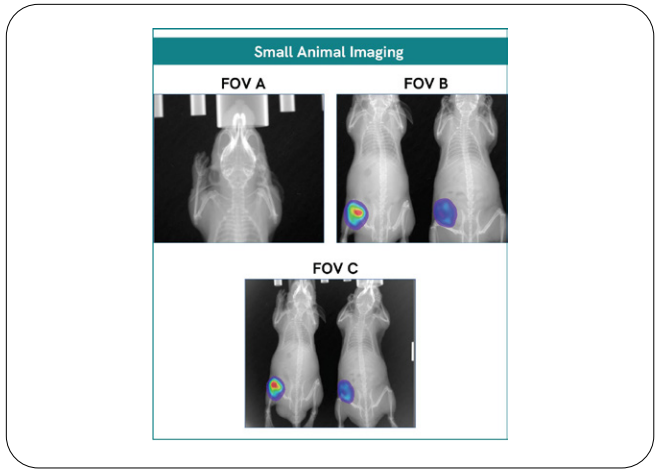


Figure 2: Optical overlay of bioluminescence signal on X-ray image at multiple FOV's in mice. Optional accessory ZFOV lensis needed for zoom image.

Applications in multimodal imaging

Precise optical and X-ray overlay brings your optical signal into anatomical context. Key applications in oncology, infectious diseases, implant biology or any model that requires anatomical context, the IVIS Lumina XRMS offers complete and rich calibrated datasets for longitudinal studies with supporting analysis software.

Oncology

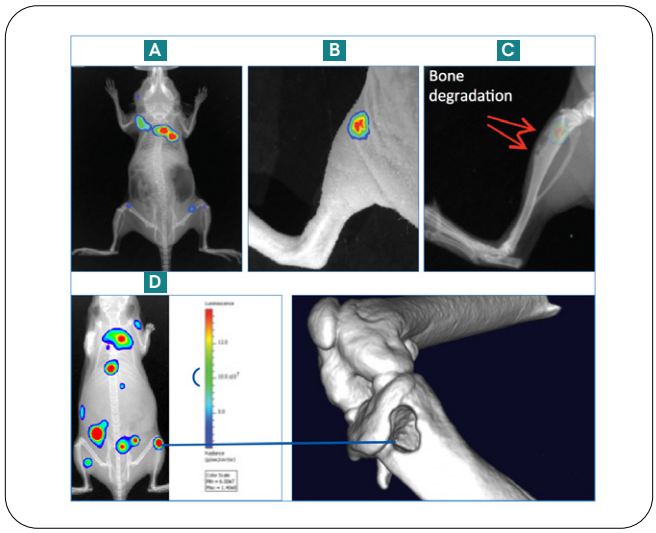


Figure 3: A) Mouse injected with 5 x 10^5 IVISbrite™ 4T1 Red F-luc bioluminescent tumor cells. Bioluminescence image was taken of cells colonized in the various parts of body. B) Two dimensional overlaid photographic and bioluminescent image. C) Two dimensional overlaid X-ray and bioluminescent image. Red arrows highlight areas osteolysis. D) MicroCT image (Quantum microCT system) confirming bone degradation in the right tibia.

Infectious disease

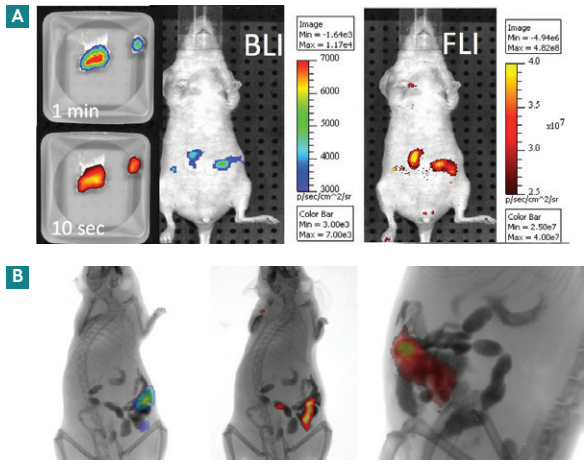


Figure 4: GI tract infection model was established by feeding contaminated peanut butter, which contained bioluminescence and fluorescence dually labeled IVISbrite™ Salmonella typhimunium Xen33 bioluminescent bacterial strain. Bioluminescence and fluorescence (Ex605/Em660 nm) images were taken at 3 hours. A) At 5 hours, trimodality imaging was performed and the overlaid images were shown B) The GI tract was highlighted due to the presence of barium sulfate (150 mg) in the peanut butter.

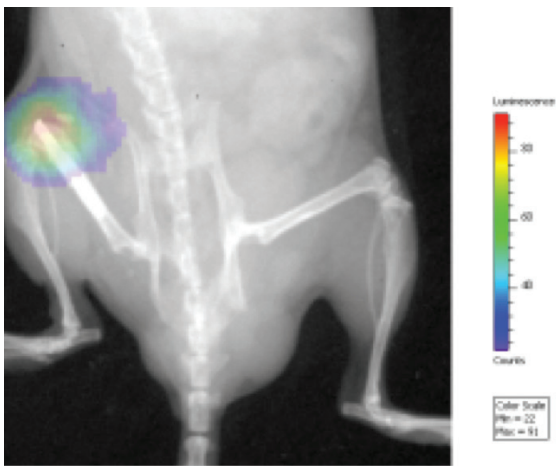


Figure 5: Chronic post-arthroplasty infection. Monitoring bacterial burden, inflammation and bone damage longitudinally using optical and X-ray imaging in an orthopedic implant infection model.

Inflammation

Figure 6: Detection of rheumatoid arthritis with fluorescent probe

Living Image software

Living Image® software brings IVIS technology to life by facilitating an intuitive workflow for *in vivo* optical, X-ray image acquisition, analysis and data organization. The software's design creates an intuitive, seamless workflow for researchers of all skill levels. Features include: wizard based guidance for advanced imaging protocols, spectral unmixing tools, expanded fluorescent agent database and a simplified tool palette.

Multispectral imaging with advanced spectral unmixing algorithms

With 2D fluorescence imaging, the presence of multiple spectrally overlapping fluorophores in the subject can present challenges for interpreting imaging results. With the Living Image spectral unmixing tool you can easily identify, separate, isolate, visualize and quantify multiplexed fluorescent signals.

Living Image software is designed to simplify advanced and complex biological models by intuitively guiding the user through experiential setup and analysis. The imaging wizard with a probe library helps design imaging settings and select the right filter pair for fluorescence studies.

Advanced spectral-unmixing algorithms and a broad range of high spectral resolution filter sets minimize autofluorescence and provides the opportunity to image a wide variety of targeted and activatable fluorescent probes and reporters.

IVIS Lumina XRMS - Standard excitation and emission filter sets

Excitation filter ranges (nm)	Emission filter ranges (nm)
410-430	500-540
430-450	550-590
450-470	600-640
470-490	650-690
490-510	690-730
510-530	770-810
530-550	825-865
550-570	
570-590	
590-610	
610-630	
630-650	
650-670	
670-690	
690-710	
710-730	
730-750	
750-770	
770-790	

Common dyes / Agents / Reporters
IVISense™ targeted, vascular, & activatable probes
IVISense dyes
IVISense self-quenching dyes
IVISense cell labeling dyes
AlexaFluor® 600-750
Cy5-Cy7.5
DsRed, Doxorubicin**
mCherry**
tdTomato**
GFP*
FITC*
ICG

* Best used with *in vitro*, *ex vivo* and surface imaging techniques

** Enhanced quantification with Spectral Unmixing

Inside the IVIS Lumina XRMS

CCD camera

- The IVIS Lumina XRMS CCD camera is 13 x 13 mm square, with 1024 x 1024 pixels 13 micron in width, yields higher imaging resolution
- Back-thinned, back-illuminated grade 1 CCD provides high quantum efficiency over the entire visible to near-infrared spectrum
- 16-bit digitizer delivers broad dynamic range
- The CCD is thermoelectrically (Peltier) cooled to -90 ˚C ensuring low dark current and low noise

Imaging chamber

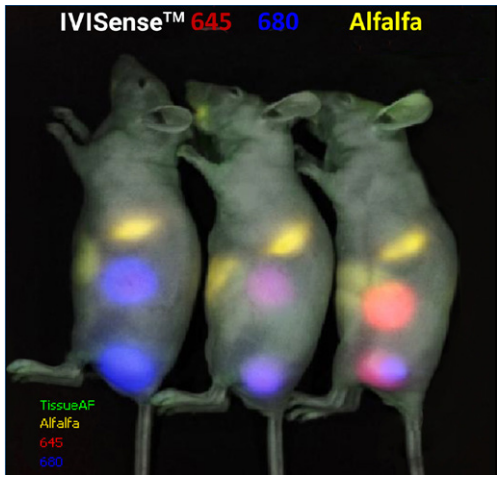
- Back-thinned, back-illuminated grade 1 CCD provides high quantum efficiency over the entire visible to near-infrared spectrum
- Light-tight imaging chamber
- 8-position emission filter wheels – 7 filters
- 20-position excitation filter wheels – 19 filters
- LED lamps for photographic images
- Heated stage to maintain optimum body temperature
- Motor controlled stage, filter wheels, lens position, and f-stop

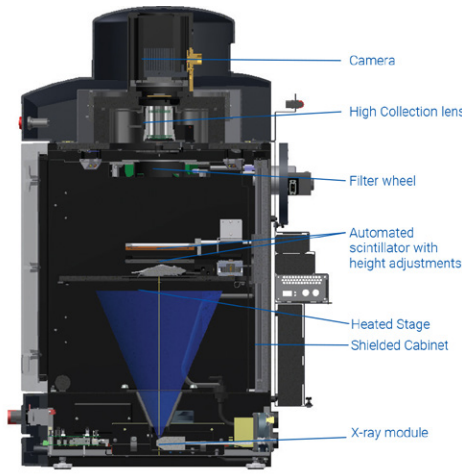
X-Ray module

- Large and small animal X-ray
- The high sensitivity camera allows fast X-ray image acquisition times of 1-10 seconds reducing radiation exposure
- Fully shielded cabinet
- Exceeds standards set by the U.S. FDA Center for Devices and Radiological Health (21 CFR 1020.40)
- Automated image integration to overlay with bioluminescence, fluorescence, and photographic.

Optional accessories

- Optical zoom lens attachment for close up and high resolution X-ray images
- Gas anesthesia ports and 3 position manifold within imaging chamber allows anesthesia to be maintained during imaging sessions
- Optional syringe injection system controlled by Living Image Software enabling the user to acquire real-time functional responses to compounds





Nu/nu mice received local injections of different ratios of IVISense™ 645 NHS and IVISense 680 NHS fluorescent dyes in two sites per mouse to provide full titrations from 0-100 pmols of fluorescence per spot. Tissue autofluorescence (green), chow autofluorescence (yellow), IVISense 645 (red), and IVISense 680 (blue) fluorescent dyes were separated by guided spectral unmixing (SPUM). This dataset yielded pure spectra for each component allowing the independent quantification of each of the individual fluorescence signals respectively and a composite image of all four components was generated.

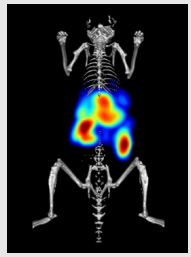
The IVIS Lumina Series III platform offers a selection of instruments tailored to your *in vivo* imaging needs

Features	IVIS Lumina LT	IVIS Lumina	IVIS Lumina XRMS
Capacity	▪ Up to 5 mice	▪ Up to 5 mice	▪ Up to 3 mice
Bioluminescence	✓	✓	✓
Fluorescence	✓	✓	✓
Enhanced Fluorescence		✓	✓
Radioisotopic Cerenkov Imaging	✓	✓	✓
Proprietary Spectral Unmixing Algorithm		✓	✓
Integrated X-Ray			✓
Absolute Calibration to NIST® Standards	✓	✓	✓

IVIS Lumina XRMS imaging system

Imaging system components:	Specifications
Camera Sensor	Back-thinned, back-illuminated, cooled Grade 1 CCD, frame transfer
CCD Size	13 x 13 mm
CCD Operating Temperature	-90 °C
Imaging Pixels	1024 x 1024
Quantum Efficiency	>85% at 500-700 nm, >30% at 400-900 nm
Pixel Size	13 microns
Optical Field of View (FOV) cm	5 x 5, 7.5 x 7.5, 10 x 10, 12.5 x 12.5 (Optional zoom 2.4 x 2.4)
X-Ray Field of View (FOV) cm	5 x 5, 7.5 x 7.5, 10 x 10 (Optional zoom 2.4 x 2.4)
Lens	f/.95 – f/16, 50 mm
Minimum Image Pixel Resolution	50 microns
Minimum Read Noise (e-)	Better than 5
Dark Current (Typical)	<3 x 10-4 e-/pixel/s
Illumination Source	Extended NIR Range 150W Tungsten EKE
Excitation Fluorescence Filters	19 hard-coated narrow band pass
Emission Fluorescence Filters	7
Radiation Shielded Cabinet	Exceeds standards set by the U.S. FDA Center for Devices and Radiological Health (21 CFR 1020.40)
Radiation Leakage	<0.1 mR/hr
Automated Aluminum Filter	0.4 mm
Plate Voltage Range	10-40 kV
Tube Current Range	1-100 uA
Anode Material	Tungsten
Typical X-Ray Image Acquisition Time	10 s
Average Mouse Dosage	1-3 mGy
X-Ray Tube Window	0.127 mm beryllium
Animal Height (cm)	0-5.3 (average mouse is 2 cm, average rat is 4.5 cm)
Scintillator	Automated Csl plate placement during X-Ray acquisition
Imaging System Space Requirement	48 x 71 x 104 cm (W x D x H)
Imaging Chamber Interior Dimension	43 x 38 x 43 cm (W x D x H)
Power Requirements	6A at 120V
Stage Temperature	20-40 °C
Computer (Minimum specifications)	Dell Precision 5820, Intel Xeon Quad Core 3.6 GHz; 32 GB RAM; Nvidia Quadro P620 2 GB; 500 GB system HD, 2TB data HD; 8x DVD+/-RW Drive; 24″ widescreen LED Monitor; 24″ Dell Monitor, Win 10 Enterprise
Living Image Software	Included with IVIS purchase

In Vivo Imaging Solutions

OPTICAL			MICRO-CT	ULTRASOUND	REAGENTS
					

IVIS® Lumina Series III
▪ 2D optical imaging
▪ Imaging up to 5 mice
▪ Optional integrated x-ray
	IVIS® Lumina 5 Series
	▪ 2D optical imaging
	▪ Imaging of up to 10 mice using optional manifold
	▪ Optional integrated high-resolution x-ray
	▪ Optional Smart accessories to streamline imaging workflow
	▪ MVI-2 for automated 360 degree imaging
		IVIS® Spectrum 2 Series
		▪ 2D & 3D optical imaging
		▪ Imaging of up to 10 mice using optional manifold
		▪ Fully automated, one-click co-registration with IVIS SpectrumCT
		▪ Seamlessly co-register 3D optical and hi-res, microCT data
		▪ Two powerful modes of fluorescence excitation—epi- and trans-illumination
			Quantum GX3
			▪ High spatial resolution
			▪ Low dose microCT for longitudinal imaging
			▪ Step and continuous imaging modes
			▪ Cardiac and respiratory gating
				Vega®
				▪ Automated, hands-free
				▪ High-throughput 3 mice imaging
				▪ Scan times in < 1 minute
				▪ Whole body field of view
				▪ Multiple 3D imaging modes
				  ▪ Elastography (tissue stiffness)
				  ▪ B-mode (soft tissue imaging)
				  ▪ 4D B-mode/ M-mode (cardiac imaging)
				  ▪ Acoustic angiography (microvessel networks)
					IVISbrite™
					▪ Bioluminescent substrates, cells, and lentiviral particles
					IVISense™
					▪ Fluorescent probes, labels, and dyes
					VesselVue®
					▪ Microbubble contrast agent for vascular ultrasound imaging

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