

3D optical and microCT data – The power of multimodality imaging.



Key benefits

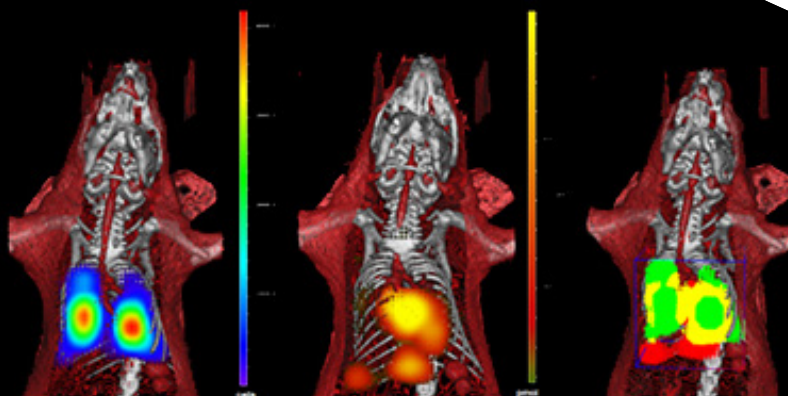
- Easily obtain molecular, functional, and anatomical data from a single subject
- Seamlessly co-register 3D optical and microCT data with just one click

Introduction

The IVIS® Spectrum 2 *in vivo* imaging system provides highly sensitive 2D and 3D molecular imaging using bioluminescence and fluorescence reporter genes and/or probes; advanced 2D fluorescence functionality includes transillumination and spectral unmixing capabilities.

The Quantum GX3 microCT imaging system supports *in vivo* anatomical, physiological, functional and metabolic imaging via fast, low dose gated scans in a wide variety of animal models. Subvolume reconstructions allow users to redo the reconstruction of static images at higher resolution without the need to rescan the subject.

The rationale behind the combination of the IVIS Spectrum 2 optical imaging system and Quantum GX3 microCT scanners lies in the ability to combine 3D anatomical, functional and molecular imaging modalities via automatic coregistration of datasets. Coregistration enables accurate anatomical localization of the optical signal and depth-corrected quantification of signal intensity. In addition, each system can be used alone as either a single high-throughput IVIS optical imaging system or a high-resolution microCT scanner.



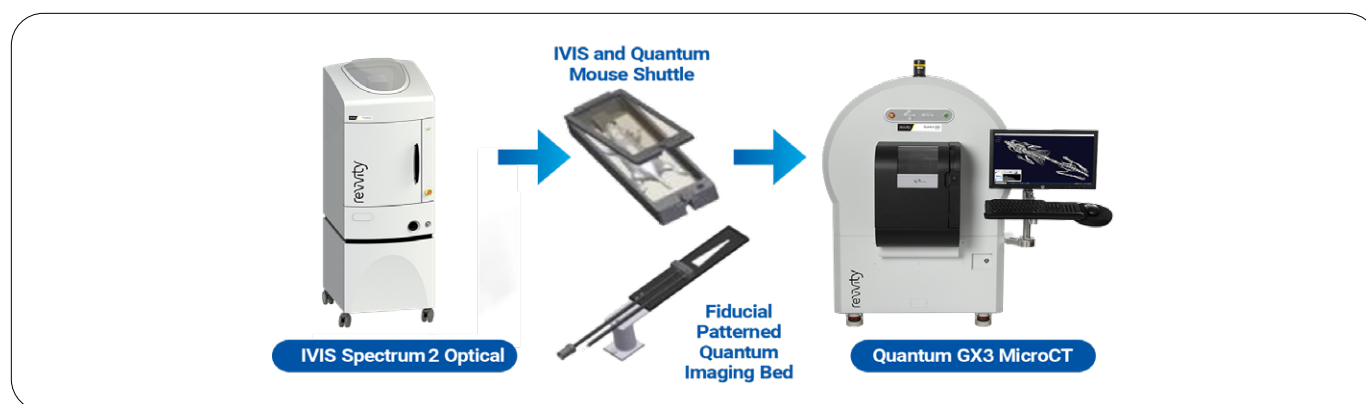


Figure 1: Schematic illustration of a multimodality kit to combine 3D optical and microCT data.

Table 1: Key Advantages of combining 3D optical and MicroCT imaging.

3D Optical only	MicroCT only	3D Optical + MicroCT
Non-invasive imaging technology that affords researchers the ability to longitudinally assess biological processes, disease progression and therapeutic efficacy in the same animal, thus reducing the number of animals needed while generating more robust data.	The Quantum GX3 microCT system provides high-resolution (2.3 um) microCT scanning of specimens and live animals up to 5 kg in weight. Multiple fields of view (18, 36, 72, and 86 mm) allow for multispecies imaging, including mouse, rat, ferret, guinea pig, rabbit, and others. With a 163 mm bore diameter and a scannable length of 385 mm, the Quantum GX3 can image animals as large as rabbits (<5 kg).	Co-registration enables researchers to harness the capabilities of each imaging modality to elucidate molecular and functional information from optical readouts and anatomical context from microCT data, which allows for more comprehensive investigation of animal models.
Broadly applicable imaging technique that has been used to explore disease models including, but not limited to, oncology, infectious diseases, neurobiology, vasculature, diabetes, gene therapy, tissue engineering, inflammation and immunology.	The Quantum GX3 has a highly sensitive, high-resolution CMOS flat panel X-ray detector, which allows for faster scan times with fewer X-rays compared to most other CT systems. Preclinical microCT is often excluded from use in longitudinal studies due to high radiation doses which could impact the biology of the animal. The CMOS X-ray flat panel detector enables fast scan times allowing for high signal-to-noise ratios and repeated CT scans of animals with low X-ray exposure.	Co-registration of 3D optical sources with microCT provides anatomical context and allows for pinpoint localization of optical signal at depth, a powerful feature for virtually every end-user application.
Provides molecular and functional insights into preclinical disease models.	The Quantum GX3 microCT system features an advanced subvolume reconstruction workflow, creating high-resolution images from original <i>in vivo</i> or <i>ex vivo</i> CT scans.. This functionality improves overall experimental workflows, enabling high-resolution images to be generated without the need to rescan animals, reducing time and X-ray exposure to the animal.	Multimodal imaging with optical and microCT gives users the ability to image multiple readouts in the same animal in order to answer more complex biological questions with fewer animals.
3D tomographic algorithms correct for tissue absorption and scattering of light and enable the most accurate location and quantification of optical sources at depth, and calibration curves translate radiance units into pmol of dye or cell number.	The Quantum GX3 utilizes proprietary image-based algorithms (instead of external monitoring) to reliably synchronize and, retrospectively, gate the microCT data to produce motion-free images; with a fast scan time and low radiation dose (4 min, 131 mGy at 70 kV). This workflow is ideal for <i>in vivo</i> cardiac and respiratory applications, while maintaining the Quantum GX3's advantageous high-throughput scanning capabilities.	Lung or cardiac gated CT scans can be combined with 3D optical images to more accurately identify optical signal and measure functional organ readouts.
3D reconstructions can elucidate pinpoint localization of colocalized probes at depth.	The Quantum GX3 microCT control panel was designed with the ease of use for the end user in mind. Thanks to constant innovation and factoring in customer feedback, every iteration of the software is engineered to ensure researcher success in CT imaging studies.	The multimodality mouse imaging shuttle has built-in fiducial markers to seamlessly co-register microCT with 3D optical data acquired on Revvity's IVIS Spectrum optical imaging system with one-click automated co-registration.

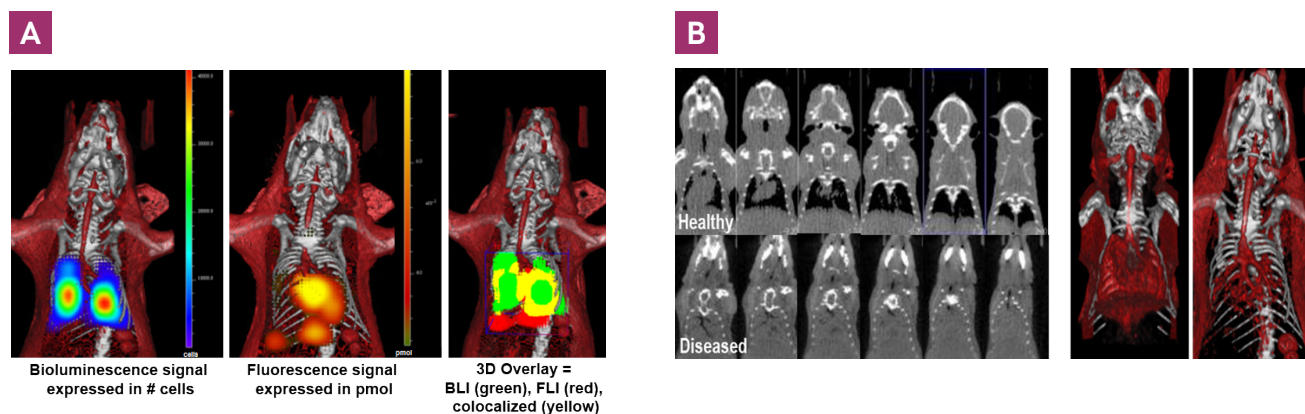


Figure 2: Study using microCT with (A) and without (B) coregistered 3D optical imaging.

A. Mice were injected with 1 million IVISbrite™ 4T1-rLuc tumor cells directly into lungs 2 weeks prior and IVISense™ Integrin Receptor 750 fluorescent probe 24 h prior to imaging on the IVIS system. 3D bioluminescence imaging (BLI) data demonstrates significant tumor burden in the lung, while 3D fluorescence imaging (FLI) detected an IVISense Integrin Receptor 750 in the lung cavity, specifically in areas of heavy tumor burden as indicated by colocalized signal. This data suggests $\alpha v \beta 3$ Integrin upregulation in tumor cells, indicating growth, viability and angiogenesis.

B. Mice were then imaged using image-based retrospective lung gated imaging on the Quantum microCT, and results demonstrate that diseased lungs showed a decrease in normal healthy lung tissue.

Collectively, these results highlight the benefits of multimodality imaging: here, 3D optical imaging provides molecular and functional data, such as the precise number of cells in the diseased lungs and upregulation of certain biological events. Adding longitudinal microCT imaging shows the associated reduction in normal healthy lung tissue in the diseased animal.

Why combine 3D optical with 3D microCT?

This study demonstrates how harnessing the power of two standalone imaging modalities can provide a better understanding of disease biology. In this case, 3D optical readouts (BLI and FLI) allow researchers to gain molecular and functional information from disease models, and co-registration of 3D optical reconstructions with microCT data adds anatomical context to answer more complex biological questions.

About Revvity *In Vivo* imaging

Whatever approach you choose, having a supplier that has the resources and expertise to partner with you on your *in vivo* imaging can help you avoid potential pitfalls, and get the quality results you need, faster. Revvity offers a range of imaging technologies to address the breadth of applications that require a non-invasive, sensitive and/or high-resolution imaging approach.

revvity