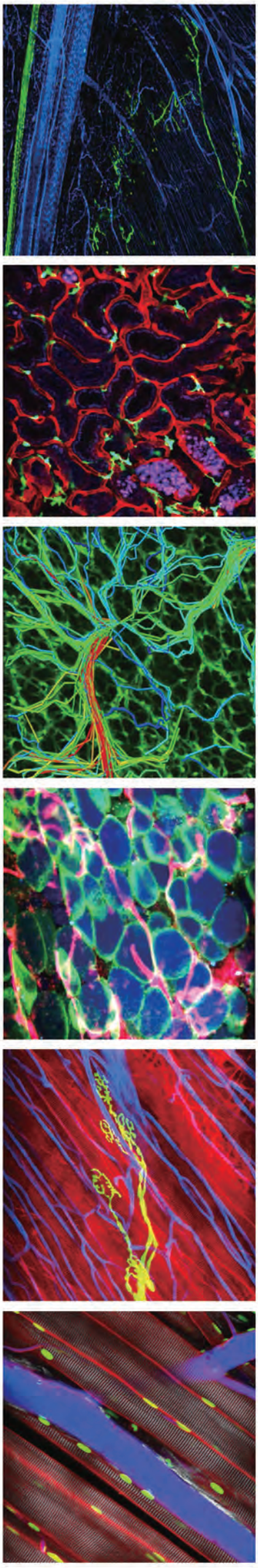


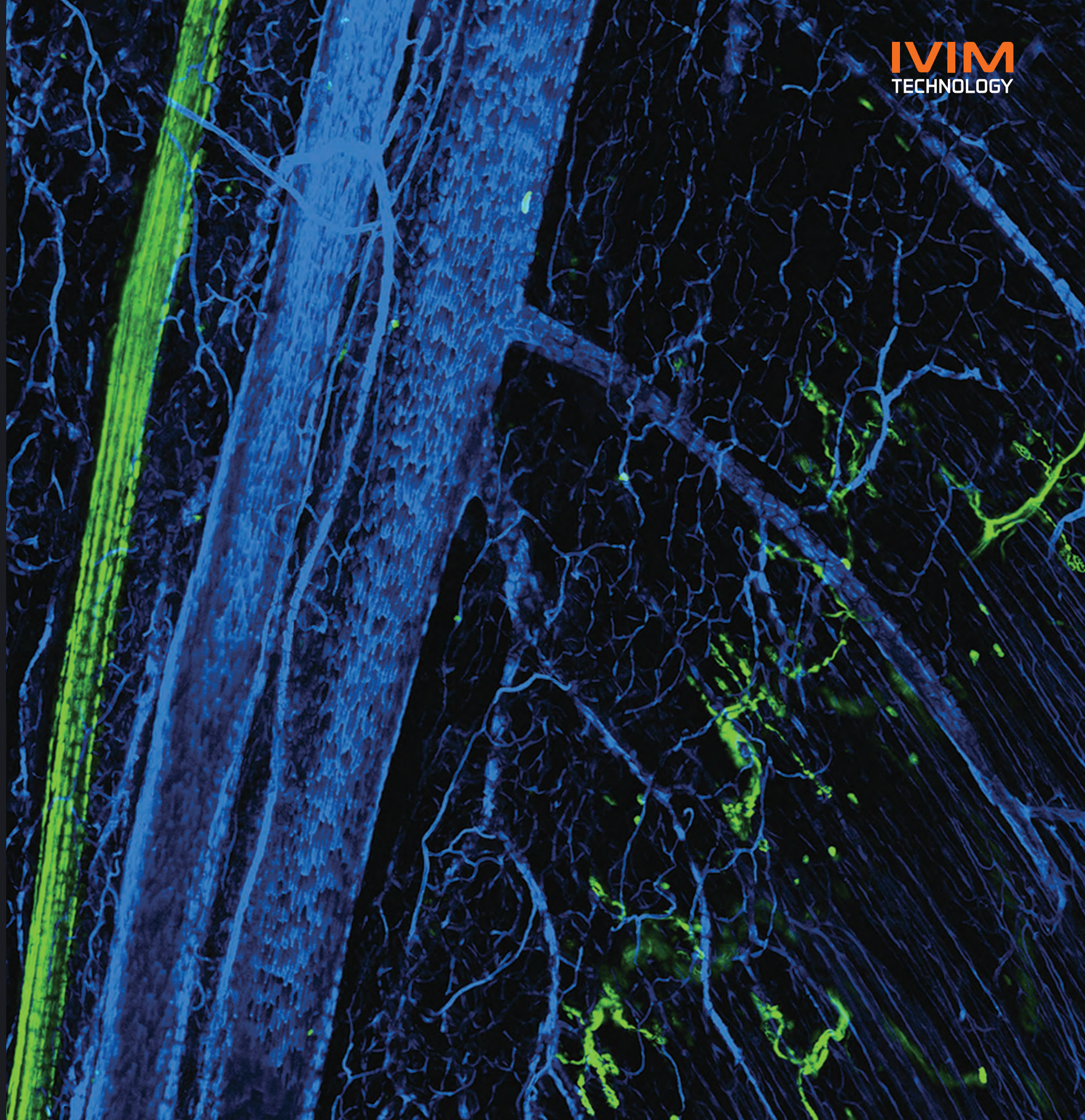
The New All-in-One IVM Series

All-purpose *In vivo* Intravital Microscopy

Service provider for intravital microscope and preclinical in vivo imaging

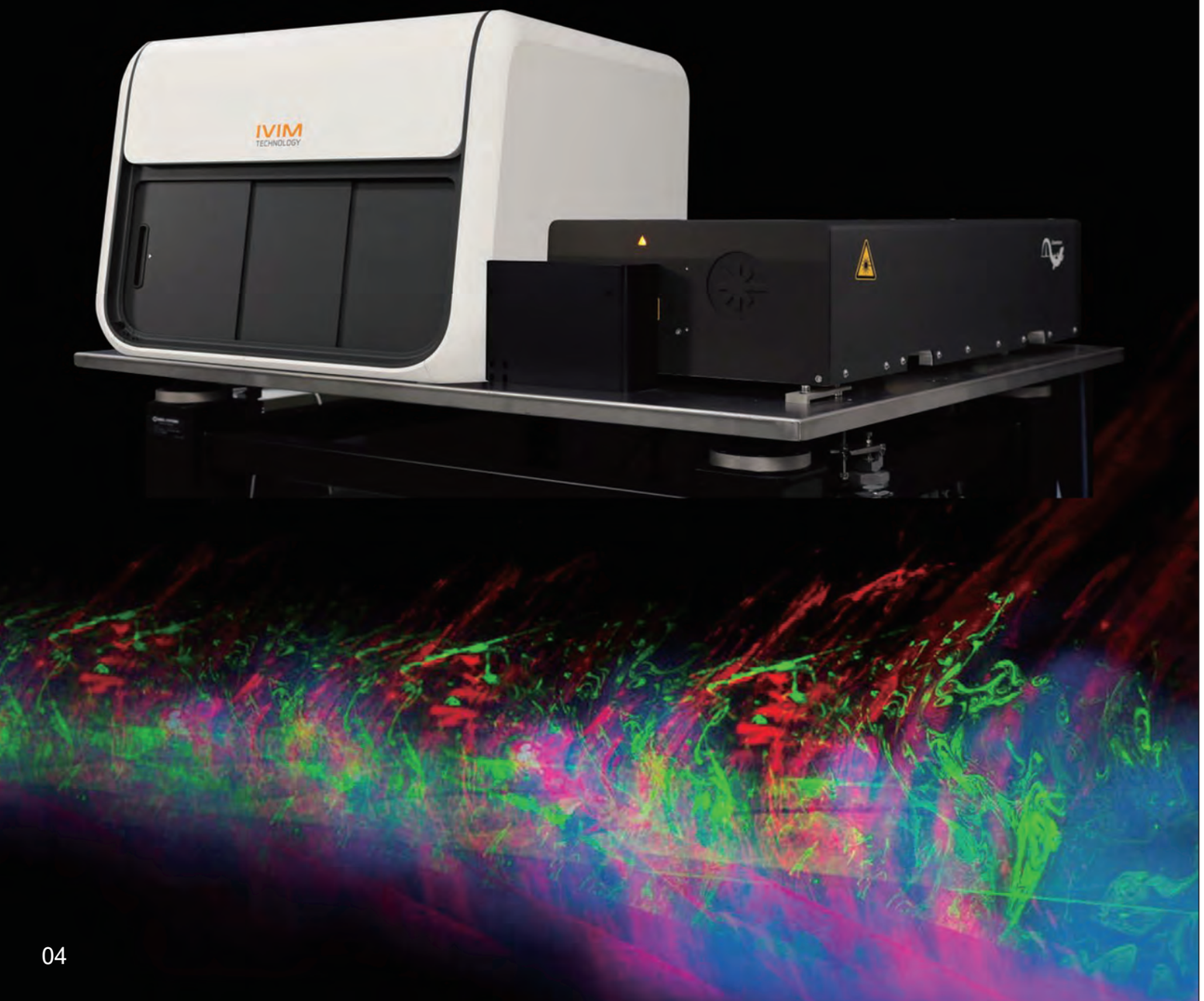
IVIM
TECHNOLOGY

Contents



IVIM TECHNOLOGY

REAL-TIME HIGH RESOLUTION *IN VIVO* IMAGING



Solution and Service Provider for Intravital Microscope and *In Vivo* Imaging

About IVIM Technology

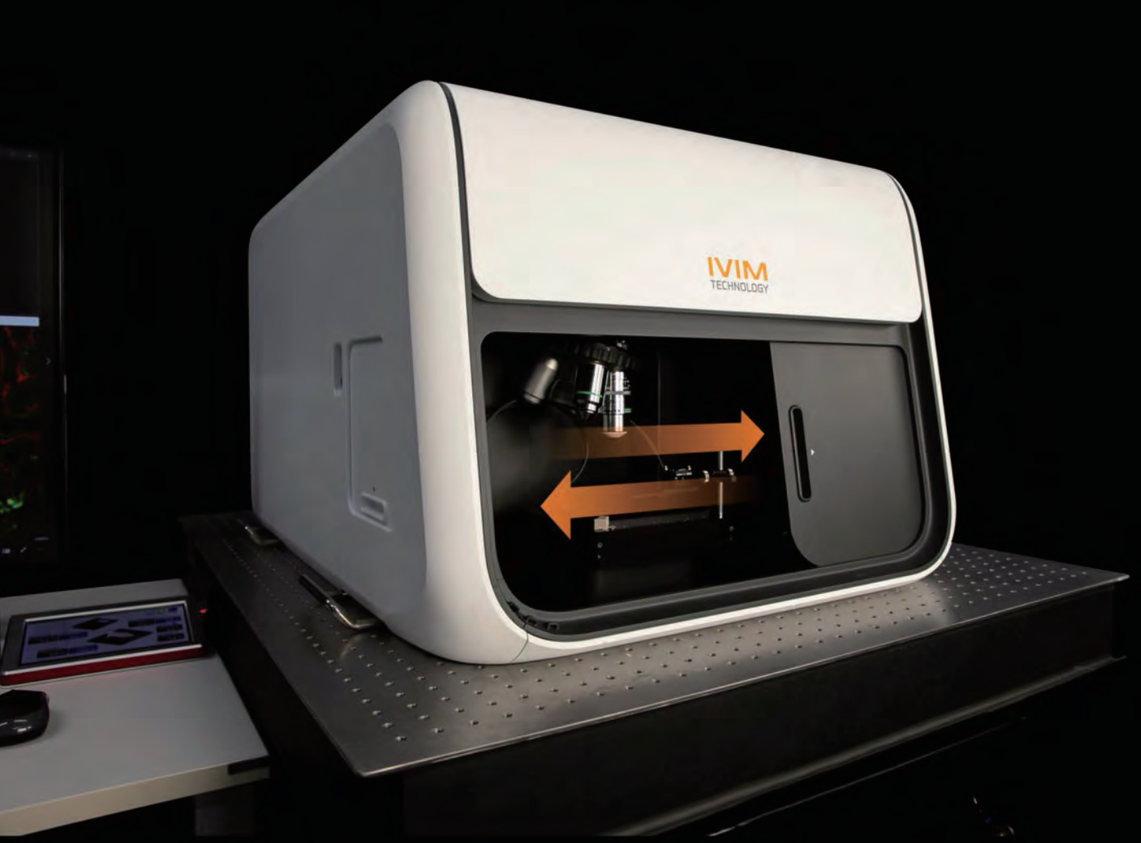
IVIM Technology was established in 2017 based on the highest technology of intravital microscopy developed in KAIST, South Korea. In 2018, we released our first confocal and two-photon microscopes to take *in vivo* images of a living animal. By the following year, we had developed the smart version with a 920nm fs laser, the most affordable and compact intravital two-photon microscope in the world. The same year, we owned our animal facilities and built an R&D center in Daejeon. In the last two years, we have expanded our global team, business partners, and reference sites, intending to be the number one global provider of intravital microscopy.

IVIM Technology has become world-renowned in a short time for its rapidly increasing global team and activities, innovation momentum and superior customer service. Inspired by its diligent expert staff, IVIM Technology started to offer CRO services on preclinical *in vivo* imaging this year. It will also provide training services to its customers beginning in 2023.

IVIM Technology is all around the world.

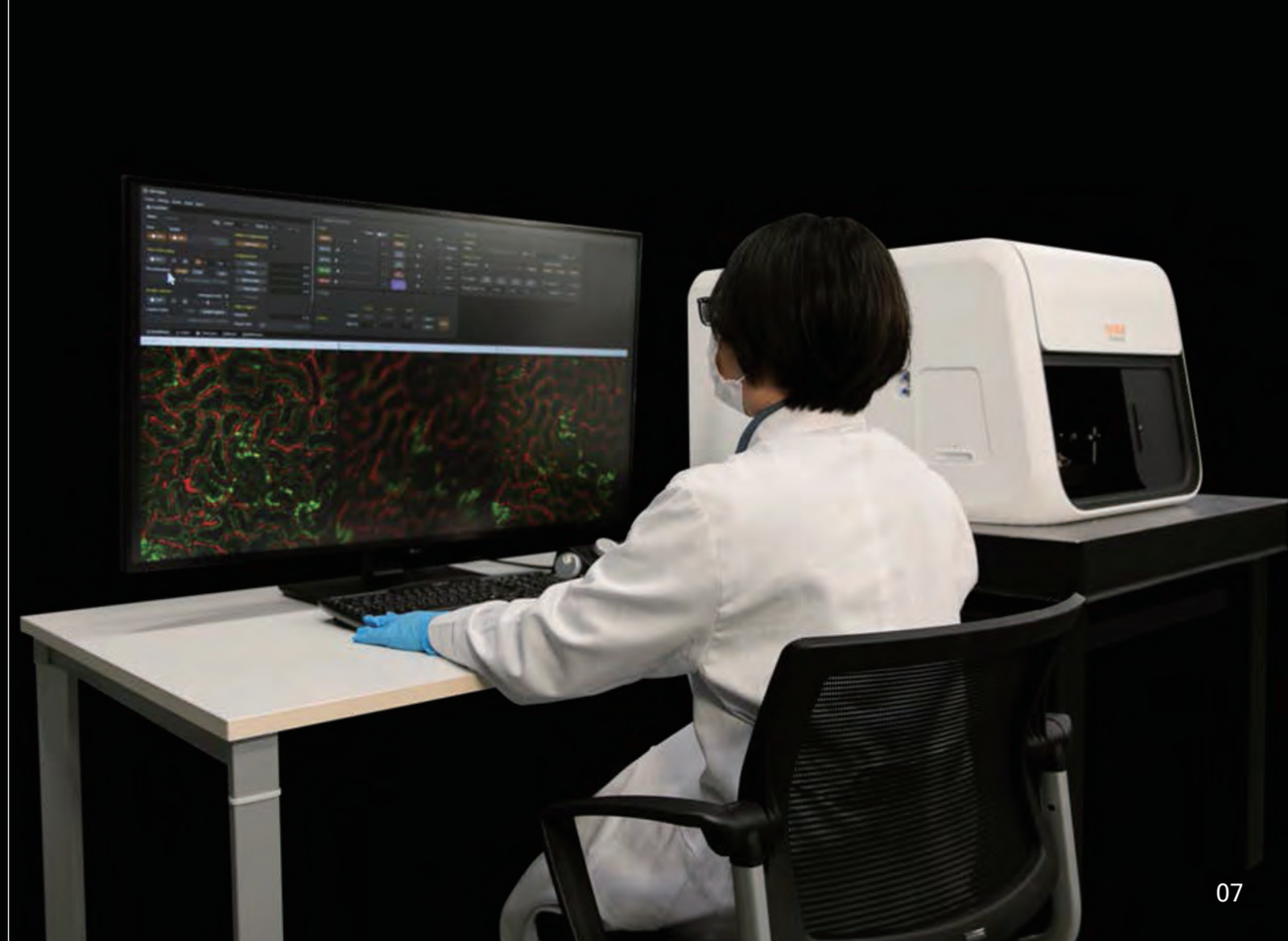
IVIM
TECHNOLOGY

- Multi-color Simultaneous Imaging
  (4 channels, 4 different colors)
- Fully Integrated *In vivo* Maintenance Unit / Animal Stage
  (Monitoring & Homeostatic Regulation of Animal Vitality)
- Ultra High-Speed Imaging (max. 100 fps - 512x512 pixels)
- 4D Animal Motion Compensation (XYZ & Time)
- Cost - Effective



One-stop solution provider for intravital *in vivo* imaging

- **Optimized system** for *in vivo* cellular to subcellular level intravital imaging of a live animal model
- **All-in-One packaging** for easy installation, cost and space saving, and high usability
- **Hands-free** maintenance of laser systems for minimal long-term operation cost



IVIM TECHNOLOGY

The New All-in-One IVM Series Product Line
One-device, unlimited solutions

IVM-C3 (Confocal v. 3)
Tractable, Fast and Gentle

IVM-C3 is a highly integrated for *in vivo* imaging with an enormously increased detection efficiency, optical resolution, and contrast of the image compared to conventional fluorescence microscopy. Equipped with a 4-wavelength laser and four high-sensitivity confocal detectors, IVM-C3 allows multi-dimensional views of living cells and tissues in 3D or 4D up to four different colors.

IVM-MS3 (Two-Photon Smart v. 3)
Compact, Cost-saving, Hands-free

IVM-MS3 is the smart version of IVM-M3, an All-in-One Two-Photon Intravital Microscopy optimized for *in vivo* imaging. It integrates a compact, high-stability and maintenance-free fs-pulse laser unit into a single box. IVM-MS3 is perfectly capable of imaging deep tissues within a wavelength fixed at 920nm, which makes it an excellent resource for researchers with a specific target but limited resources and budget.

IVM-M3 (Two-Photon v. 3)
Deep Tissue Imaging, High-resolution, Tunable Laser

IVM-M3 has the flexibility feature of the traditional converted microscope and the high-resolution imaging ability of second-harmonic generation microscopy. It is equipped with a fully-automated tunable fs-pulse NIR laser system. IVM-M3 is optimal for deep tissue imaging using less-scattering NIR wavelength. Full control functionality of the fs-laser system is integrated with the two-photon imaging software for user convenience with various automation algorithms.

IVM-CMS3 (Confocal and Two-Photon Smart v. 3)
Cost-Effective, Straightforward, Dual-mode

IVM-CMS3 is the world's most compact and affordable dual-mode intravital confocal and two-photon microscope, providing versatile functionality in a single box. Having the Confocal laser units of IVM-C3 and the compact Two-Photon laser unit of IVM-MS3 with a one-switch mode changing feature, IVM-CMS3 provides comfortable multi-purpose use for intravital functional imaging and saves from unnecessary space and high costs.

IVM-CM3 (Confocal and Two-Photon v. 3)
High Contrast and Resolution, Dual-mode and Tunable

IVM-CM3 can focus on the desired wavelength with its tunable Two-Photon laser unit for wavelengths as low as 690 nm, higher up to 1050 nm, or in between. IVM-CM3 combines the advantages of both Confocal and Two-Photon microscopy providing endless possibilities for three-dimensional imaging of living cells near the skin or deep into the tumor in small animals.

IVM-Customized
Explicit, Practical, and Versatile

The IVM-Customized provides the researcher with a specific design and high level of ease of use. Apparatus such as GRIN Lens Endo-Microscopy System, Retina Imaging System, Rotatable Objective Lens System can be easily adjusted for your research. Also, since it is a free space system, the sizes of the microscope can be optimized according to the animal that you are working with.

Why intravital *in vivo* imaging is needed?

According to data from regulatory authorities, the acceptance rate of new drug candidates has been stuck at around 10 percent worldwide for the last few decades. Determining the validation, tracking, and mode of action (MOA) of new drug candidates at the preclinical development stage *in vivo* is vital for the effectiveness and finally the permission to use of the new drug.

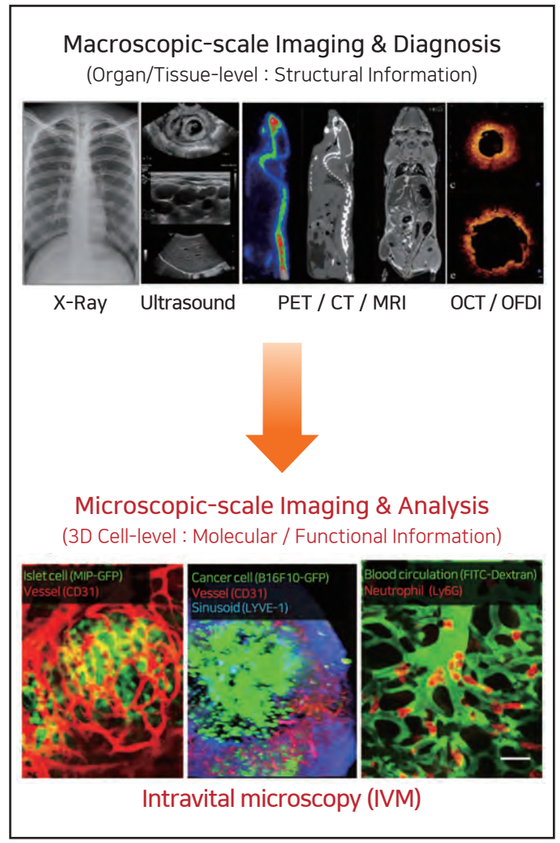
IVIM Technology continuously optimizes its products with its engineers and the know-how gained in the field with its application specialists. IVIM Technology provides reliable results in validating the ADME, drug delivery/efficacy and MOA studies at the early stages of new drug development process.

What is Intravital Microscopy (IVM)?

IVM is an optical imaging technique designed to observe living animals in vivo in cellular and subcellular levels at very high resolutions through window preparations in the tissue region of interest for once or periodically.

IVM is a key solution that can explore the complex dynamic behavior of numerous cells inside living organisms.

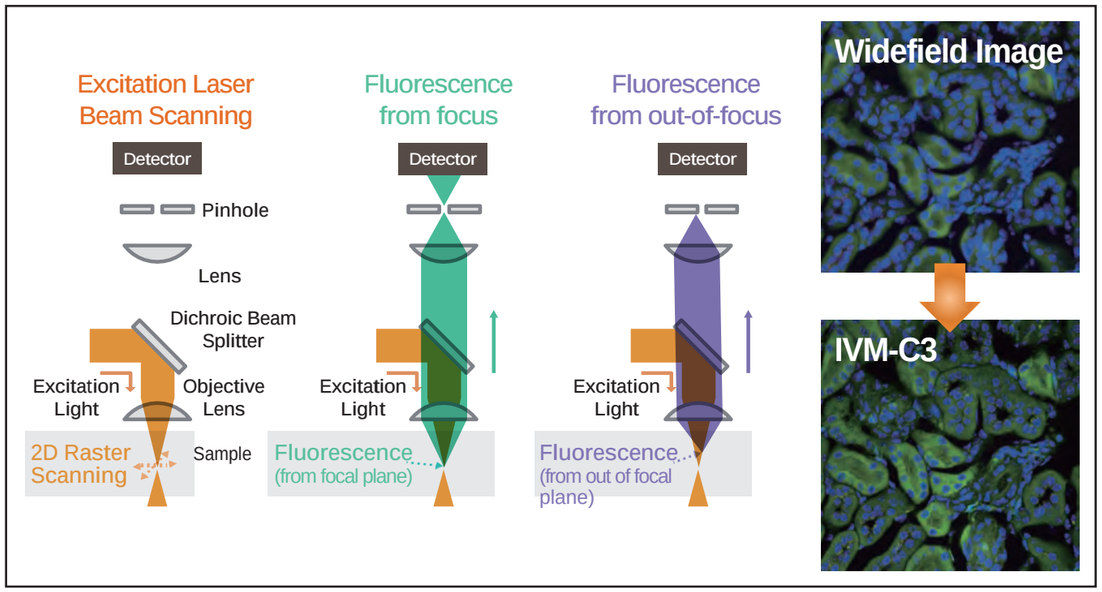
IVM continues to grow as a next-generation key technology to explain the unknown pathophysiology of various diseases and discover new treatments. It is differentiated from macro-scale structural images at the organ or tissue level that can be obtained from conventional X-ray, ultrasound imaging, MRI, PET, and CT.



IVM is capable of real-time 3D imaging of single cell-level *in vivo* cell dynamics and interactions of cell to cell or proteins and drug molecules in living organisms. It can directly provide information on the *in vivo* development process or progress of various diseases. As such, the biggest advantage of this technology is that it is possible to directly observe and analyze real-time cell-level dynamics of cell movement in a real-life in vivo environment.

What is Confocal Microscopy?
(IVM-C3, CM3, CMS3)

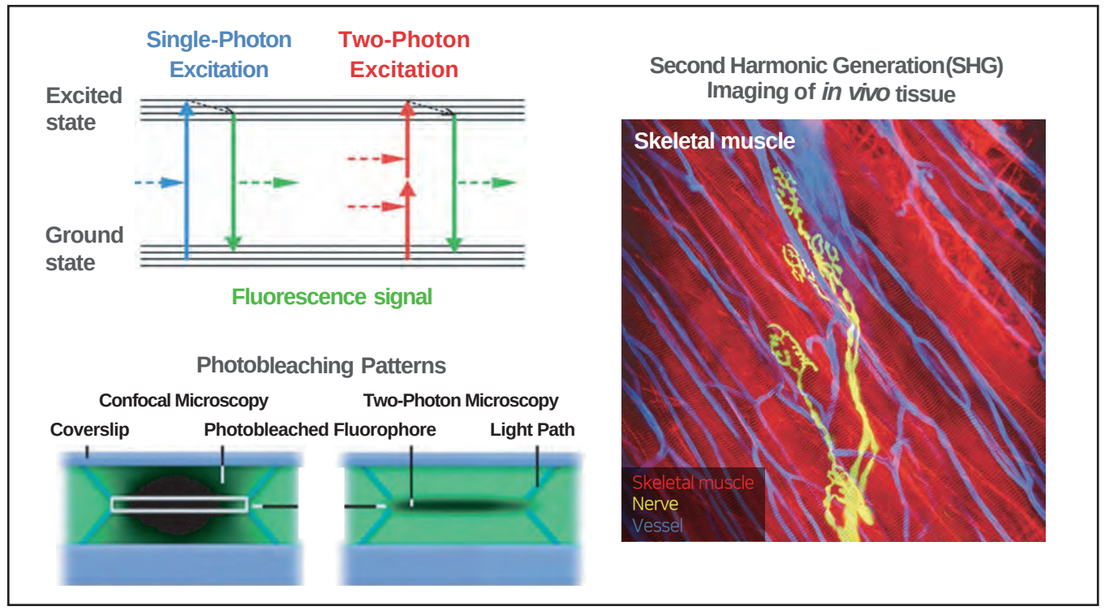
Intravital Confocal Microscopy offers *in vivo* imaging in four dimensions (XYZ and time), layer-by-layer. In principle, it utilizes white or laser light and pinhole and enables the light to be focused at one point and deflected the reflected, scattered light from a second confocal aperture.



The size, orientation and surface of structures can affect light scattering due to different refractive indices for each system. For example, rough surfaces scatter the beam widely and vice versa. Multiple layers can be visualized by slicing a tissue at various focal planes.

What is Two-Photon Microscopy?
(IVM-M3, CM3, MS3, CMS3)

In a two-photon microscope, two or three photons of the higher wavelength do the work of one: When they strike the fluorophore simultaneously (typically within a few femtoseconds), they are absorbed, resulting in fluorophore excitation and light emission. Two-photon microscopy is used for live cell imaging for deeper and ticker tissues compared to the confocal with its second harmonic generation ability which provides very high axial and lateral resolution comparable to confocal microscopy without having to use pinholes.



Confocal Microscopy

- Single-photon excitation
- Point scanning + Pinhole
- Optical sectioning : Fluorescence signal from out-of-focus is blocked
- Imaging Depth : 100-200 μm
- Continuous-wave solid-state laser with flexible choice of wavelength at the range from ultraviolet (UV) and visible (VIS) to near-infrared (NIR)
- Descanned confocal detector
- Easy & efficient, multi-color 3D intravital imaging

Two-Photon Microscopy

- Two-photon excitation
- Point scanning + No Pinhole
- Optical sectioning : Fluorescence signal is intrinsically generated only at the focus
- Imaging Depth : 250-1000 μm
- Femto-second pulsed laser tunable at near-infrared (NIR) wavelength range
- Non-descanned detector (NDD)
- Deeper-tissue 3D intravital imaging

Expertise in intravital *in vivo* imaging

IVIM Technology provides dynamic 3D imaging of various cellular-level dynamics such as cell trafficking, cell-cell interaction and cell-microenvironment interaction inside the living body *in vivo*, as well as the ADME studies such as direct imaging analysis of the drug delivery to target tissue and cell, drug efficacy and mode of action (MOA) in microscopic cellular-level in various preclinical model providing a new insight in the processes of human disease development.

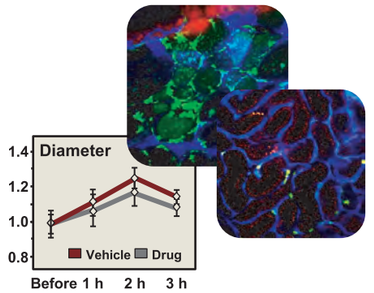
+ Thymus, Lymphatics, Microcirculation ··· etc.

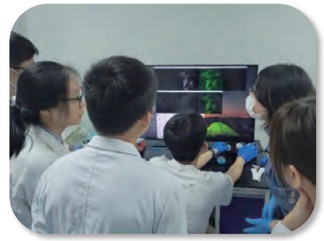
IVIM Technology is the worlds first company providing All-in-One intravital microscope in a small box with the best intravital imaging performance. All-in-One single box package enables easy installation, operation and maintenance. It has co-optimized software and hardware for superb *in vivo* imaging performance with ultrafast imaging speed up to 100 fps.

Together with automatic, hassle-free motion compensation function and various accessories such as live animal maintenance system and imaging windows for wide-range of applications, users can easily get the high-quality *in vivo* data without any limitation in live imaging of various organs.

Why IVIM Technology Research Service?

IVIM Technology Offers a One-Stop Total Solution for Intravital Imaging





Consulting
Intravital Imaging Experiment

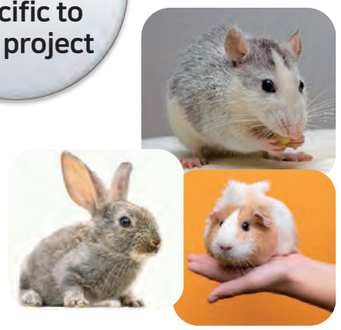
Internal Evaluation
Validation & Optimization

Utilization of Animal Models
Specific to your project

***In vivo* Imaging**
Using target compound

Image Processing & Analysis
Final Report

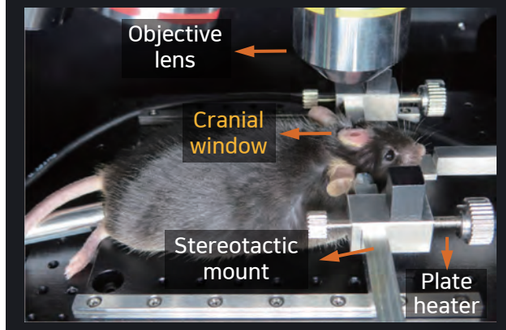
IVIM TECHNOLOGY IN VIVO IMAGING MICROSCOPY

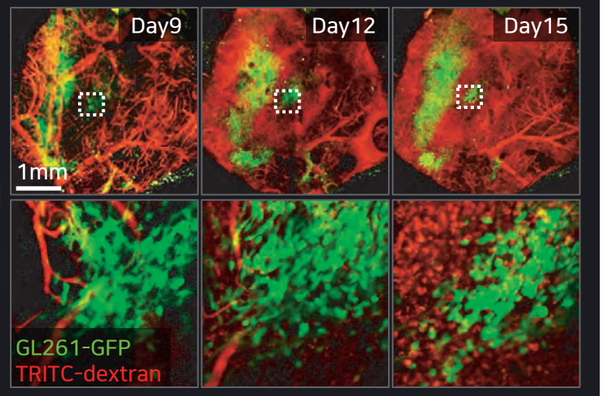


Key Applications: Case Study 1

Longitudinal Brain Tumor Imaging

Intravital Imaging of Brain





Cranial Imaging Window

- Longitudinal intravital imaging of orthotopic glioma, GL261

| **Objective** |

Intravital Brain imaging technique utilizing a Cranial window can be applied to brain tumor imaging research.

| **Result** |

We've implanted the glioma cells to the brain and monitor the tumor development in the same brain imaging area in the same mouse model over 15 days.
IVIM Technology`s intravital microscope imaged the number of Glioma cells increased with the round cell morphology over the days of tumor growth.

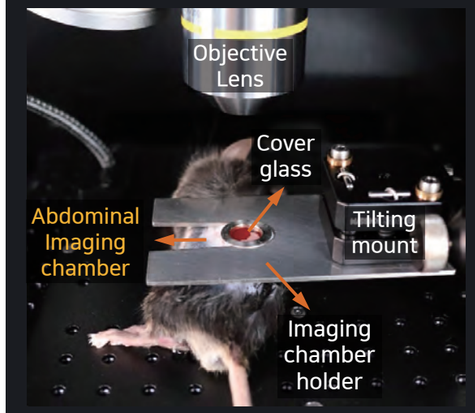
IVIM TECHNOLOGY

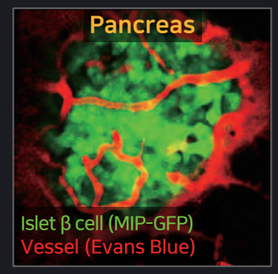
Key Applications: Case Study 2

Longitudinal Abdominal Organ Imaging

Intravital Imaging of Abdominal Organs

- Monitoring of cellular behavior in pancreas and spleen





MIP-GFP mouse
- endogenously expresses GFP in pancreatic beta-cells under the control of mouse insulin 1 promotor.

CX3CR1-GFP mouse
- endogenously expresses GFP in monocytes, macrophage, brain microglia and DCs under control of endogenous Cx3cr1 locus.

| **Objective** |

For abdominal organs, we utilized abdominal imaging window for longitudinal *in vivo* monitoring of internal organs such as pancreas, spleen, and kidney.

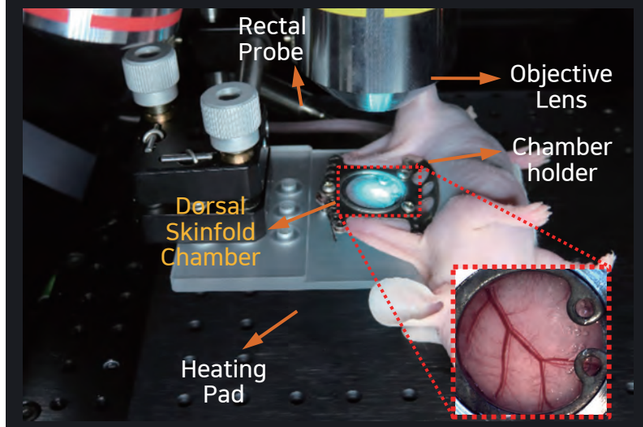
| **Result** |

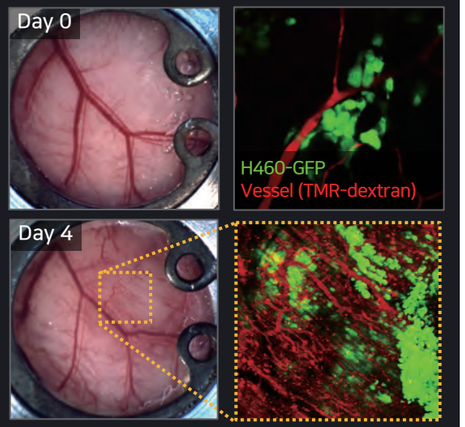
We could visualize real-time cellular dynamics of endogenous monocytes and dendritic cell in spleen, And visualize pancreatic islet b cell using MIP-GFP Tg mouse. The cell dynamics and the development were monitored in long-term basis by utilizing abdominal imaging window.

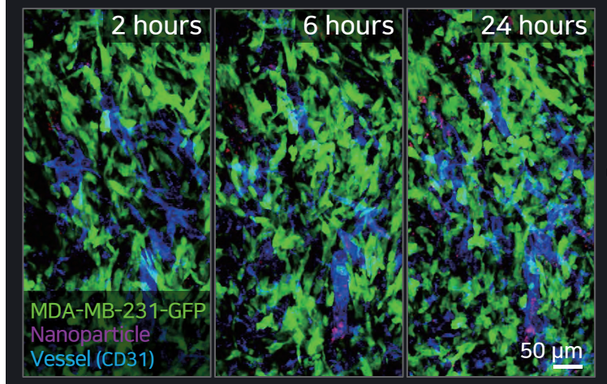
Key Applications: Case Study 3

Longitudinal Cancer Xenograft Imaging

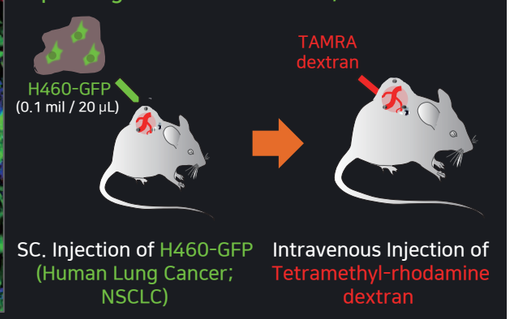
Intravital Imaging of Lung and Breast







- Monitoring of nanoparticle delivery to triple-negative breast cancer, MDA-MB-231



| Objective |

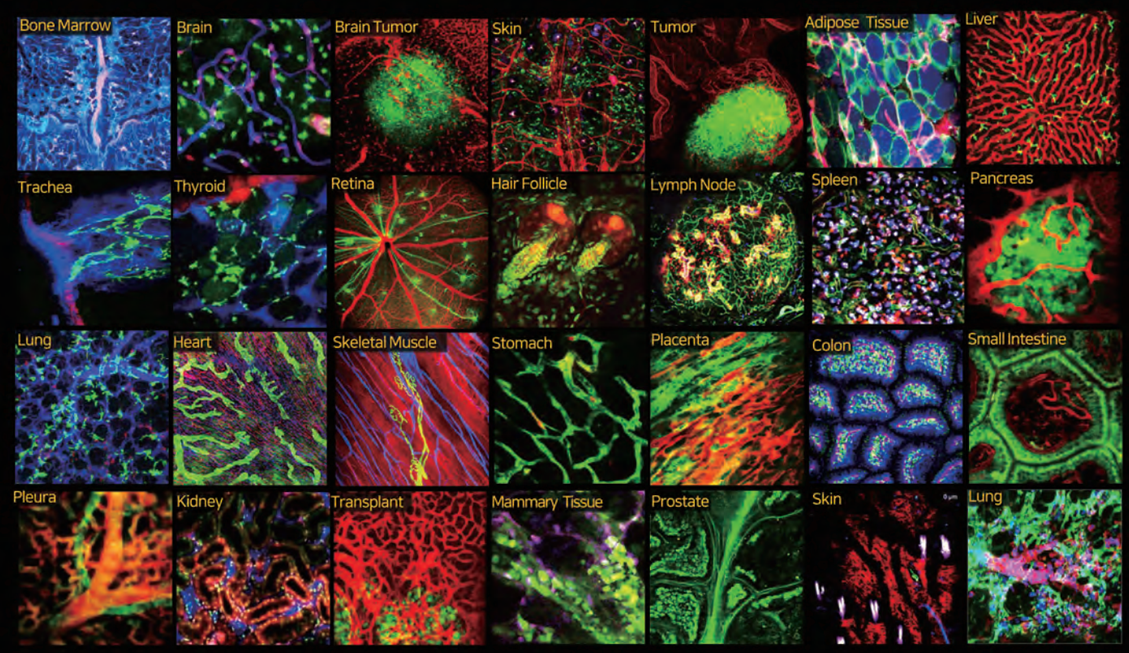
In vivo monitoring and analysis of the drug efficacy in tumor including quantitative analysis of angiogenesis, vessel dilation and measuring real-time blood flow in one single mouse model over time.

| Result |

IVIM Technology implanted the tumor cells and monitored the development of tumor on site and investigated drug delivery and distribution to the target breast cancer in a long-term manner.

IVIM
TECHNOLOGY

QUALITY CAN BE IMAGED...



www.ivimtech.com

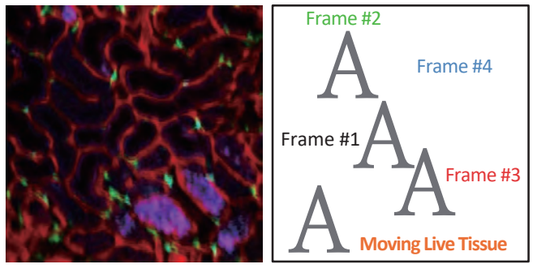
IVIM Technology Makes The Difference

Ultrafast Rotating Polygonal Mirror Scanner

- Ultra-high speed (up to 100 fps, 512x512 pixels)
- Improved image quality without wasting excessive photons
- Uniform excitation illumination over entire imaging field of view (FOV)
- No reduced fluorescence signal and signal-to-noise ratio (SNR) at center area of FOV
- No excessive photobleaching at edge area of FOV
- Uniform high signal-to-noise ratio over entire FOV

4D Integrated Motion Artifact Compensation

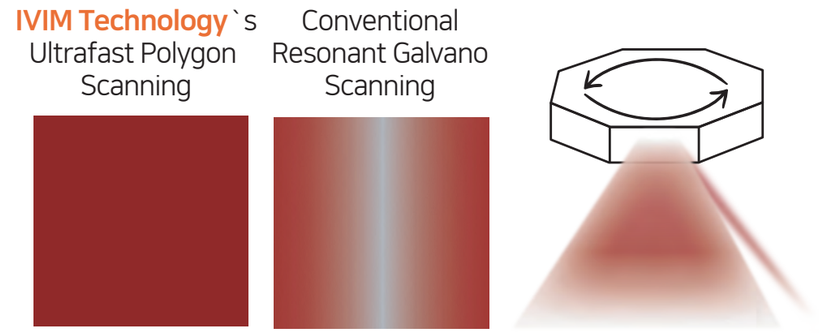
- Automatic hassle-free and high-precision motion compensation
- Immediate acquisition of motion-compensated imaging results by GPU-assisted parallel computing of algorithm processing



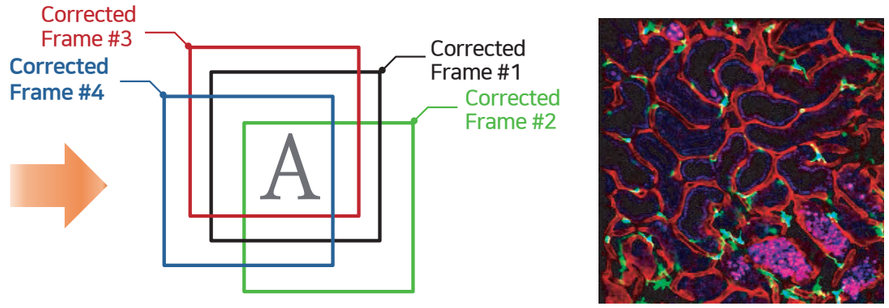
- Upgraded imaging algorithms that enable animal motion compensation

Customized System

- IVM-Customized system provides the researcher with the most appropriate free space intravital microscopy.
- According to the needs of the research and the researcher, the apparatuses such as the objective lens rotation system (for brain imaging, etc), retina imaging objective and GRIN Lens Endo-Microscope can be easily installed.



Ultrafast Uniform Laser-beam Scanning



Ergonomic Design, Reduced Space

- Ergonomic design integrated all the essential features necessary for hands-free imaging in high speed and resolution.
- Upgraded apparatuses for heating, anesthesia, window chamber observation, and longtime inspection to keep the physiological conditions of the animal stable in the best possible way
- Minimum space requirements

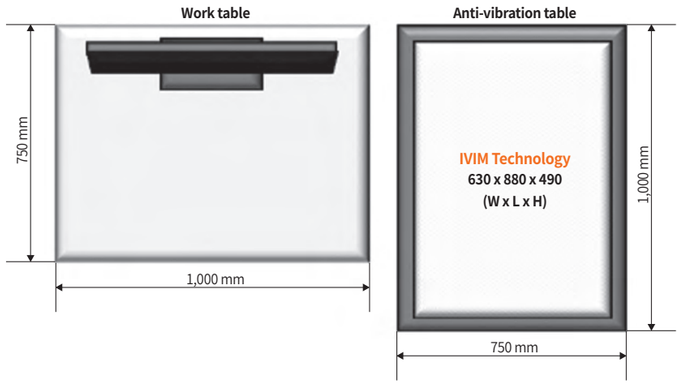
Consulting and Research Service

- Only company offers both the intravital microscopy equipment and intravital imaging research service
- On-site free demo service and consulting
- Imaging experiments on IVIM Technology`s facility without the need to buy the device

SPECIFICATIONS

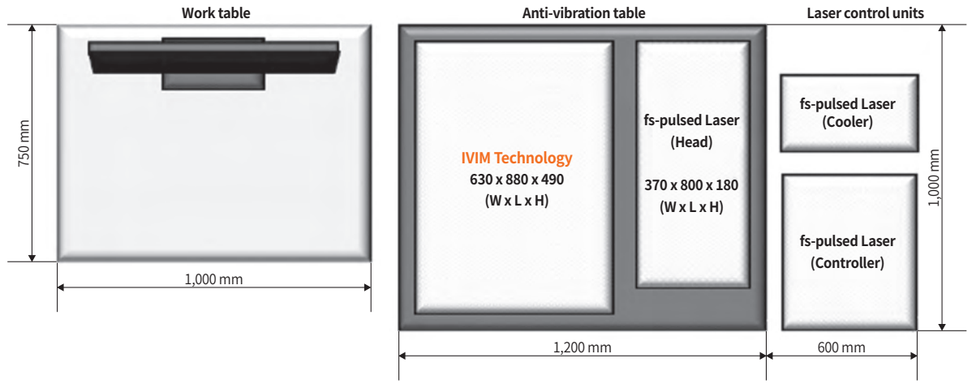
Laser	**Confocal Laser Unit**	• 405 nm (20mW), 488 nm (20mW), 561 nm (20mW), 640 nm (20mW)
	Tunable Two-Photon Laser Unit	• Ti : Sapphirelaser • Wavelength: 690-1050 nm, Pulse width < 75 fs, Rep. rate: 80 MHz • Avg. power > 2.5 W, Dispersion compensation: 0 to - 49,000 fs^2
	Compact Two-Photon Laser Unit	• Air cooled fs-fiber laser system with bulit-in power control • Wavelength: 920 nm, Pulse width < 150 fs, Rep. rate: 80 MHz • Avg. power > 0.8 W, Dispersion compensation: 0 to - 22,000 fs^2
Fluorescence Detector	**Confocal Detector**	• Wavelength: 185 - 900 nm (DAPI, CFP, GFP, YFP, RFP, Cy5, Cy5.5, etc.) • 4 Ultra-broadband high SNR PMTs (UV to Near IR, Ultra High Sensitivity, Low Dark Current) • 25-2,000 µm variable pinhole
	Two-Photon Detector	• Wavelength: 185 - 760 nm (DAPI, CFP, GFP, YFP, RFP, Cy5, Cy5.5, etc.) • 4 High quantum efficiency PMTs (UV to Near IR, Ultra High Sensitivity, Low Dark Current)
	Variable Emission Filter (Optional)	• 2 or 6 emission filters can be mounted on each of four detectors
Scan Head	**Scanner**	• Polygonal mirror (Fast axis scanning, Max. 66 kHz) • Galvano scanner (Slow axis scanning, Max. 200 µs /step)
Imaging Head	**Objectives**	• Max. 5 objectives are mountable on S/W controlled motorized turret (1X – 100X) • Compatible for commercial objectives
Image	**FOV**	• 100 x 100 $µm^2$ - 10 x 10 mm^2
	Pixel Resolution	• Max. 2,048 x 2,048 pixels
	Imaging Speed	• Standard : 30 fps @ 512 x 512 pixels • (Optional) High Speed: 60 fps @ 512 x 512 pixels • (Optional) Ultra High Speed: 100 fps @ 512 x 512 pixels
Animal / Sample Stage	**3D Stage**	• Travel Range : 50,000 x 50,000 x 75,000 µm (XYZ) • Micromanipulation (Max. 0.2 µm resolution) • 3-axis independent control with Jog Dial & IVM Engine software
	Specimen Holder	• Flexible-design universal *in vivo / ex vivo / in vitro* specimen holder can be mounted • (Optional) Homeothermic warming system, Holders for window chamber

IVM-C3/ MS3/ CMS3 Size Information



Animal Motion Compensation	**4D *In vivo* Imaging Motion Compensation**	• XY motion compensation : Averaged image acquisition with motion artifact compensation • Z motion compensation : Image-based sample Z position adjustment for long-term intravital microscopic imaging & sample tracking (Feedback-loop automatic stage control) • T motion compensation : Image-based image XY position adjustment for long-term intravital microscopic imaging & sample tracking (Feedback-loop automatic stage control) • Combination of above three compensation for 4D in vivo motion compensation • Controllable by IVM Engine software
Additional *In vivo* Modules	**Live Animal Maintainance Unit**	• Body Temp. Monitoring & Feedback Heater Control, including tablet PC • 4CH Rectal Probe, Body Plate Heater, Thermometer Sensor & Cover Glass Heater
	***In vivo* Imaging Chamber**	• Standard Dorsal Skinfold Chamber SET • Lung Imaging Chamber SET • Cranial Window SET • Abdominal Imaging Window SET • Pancreas Imaging Window SET • Mammary Imaging Window SET • Heart Imaging Window SET
	Inhalation Anesthesia System	• Whole Rodent Animal Inhalation Anesthesia System • Anesthesia Mask and Connections
Engine & Studio Software	**Image Display**	• Independent 4 single channel display (RGBA channel) • Overlay channel display (Selection among RGBA channel)
	***In vivo* Imaging Mode**	• Mosaic imaging (XY), Z-stack imaging (Z), Time-lapse imaging (T) • Time-lapse imaging at Multi-position (T- M), • Time-lapse & Z-stack imaging (TZ), • Time-lapse & Z-stack imaging at Multi-position (TZ- M)

IVM-M3/ CM3 Size Information



Recent Publications

Intravital Imaging of Various Organs in Human Disease Animal Model

Lung
- I. Park, et. al., *European Respiratory Journal,* 53:1800736 (2019)
- I. Park, et. al., *Biomedical Optics Express,* 9(5):2383-2393 (2018)

Liver
- J. Moon, et. al., *Med Laser,* 10(1):1-6 (2021)
- J. Moon, et. al., *Biomed. Optics Express,* 11(9):5132-5146 (2020)
- B. Oh, et. al., *Diabetes,* 67(3):473-485 (2018)
- Y. Hwang, et. al., *Biomed. Optics Express,* 8(10):4706-4716 (2017)

Lymph Node
- S. Jeong, et. al., *J Control Release,* 335(10):86-102 (2021)

Spleen
- H. Choi, et. al., *Science Advances,* 6(15):eaa6980 (2020)

Eye / Retina
- J. Jeon, et. al., Trans. Vis. Sci. Tech., 10(4):31 (2021)
- H. Kim, et. al., Trans. Vis. Sci. Tech., 9(6):20 (2020)
- J. Kim, et. al. *Science Advances,* 5(2):eaau6732 (2019)
- S. Ogura, et. al., *JCI Insight,* 2(3):e90905 (2017)

Skin
- K. Kim, et. al. *Adv. Funct. Mater.* 31:2103413 (2021)
- H. Kwak, et al. Vaccine, 37(36):5191-5202 (2019)
- J. Ahn, et. al. *Biomedical Optics Express,* 9(8):3974-3982 (2018)
- J.Y. Kim, et. al., *ACS Nano,* 12(7):6904-6916 (2018)
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Brain
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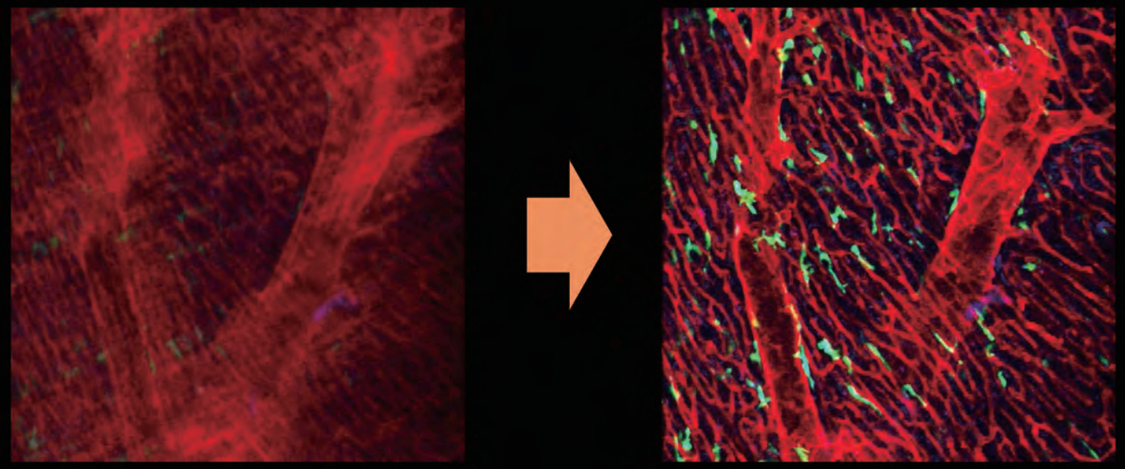

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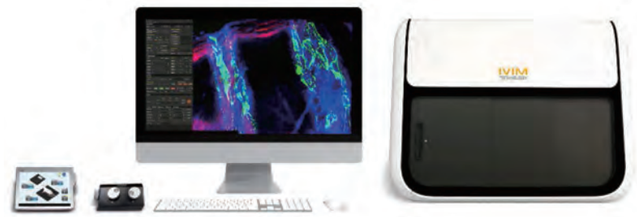

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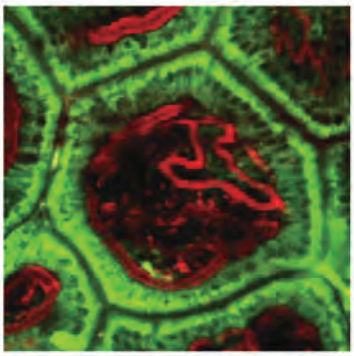

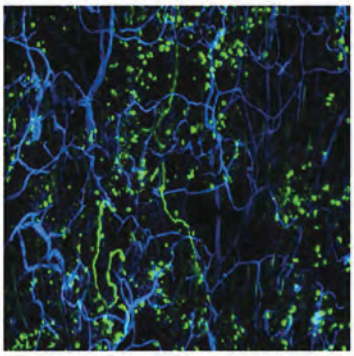

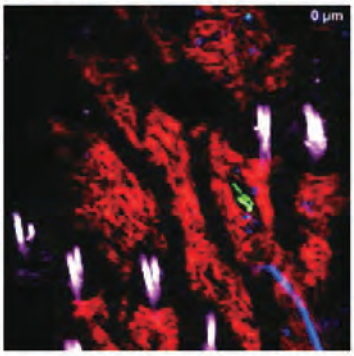

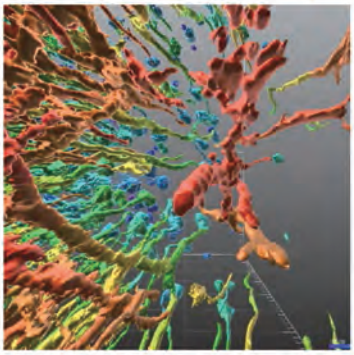

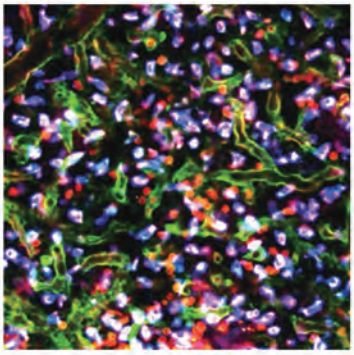

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