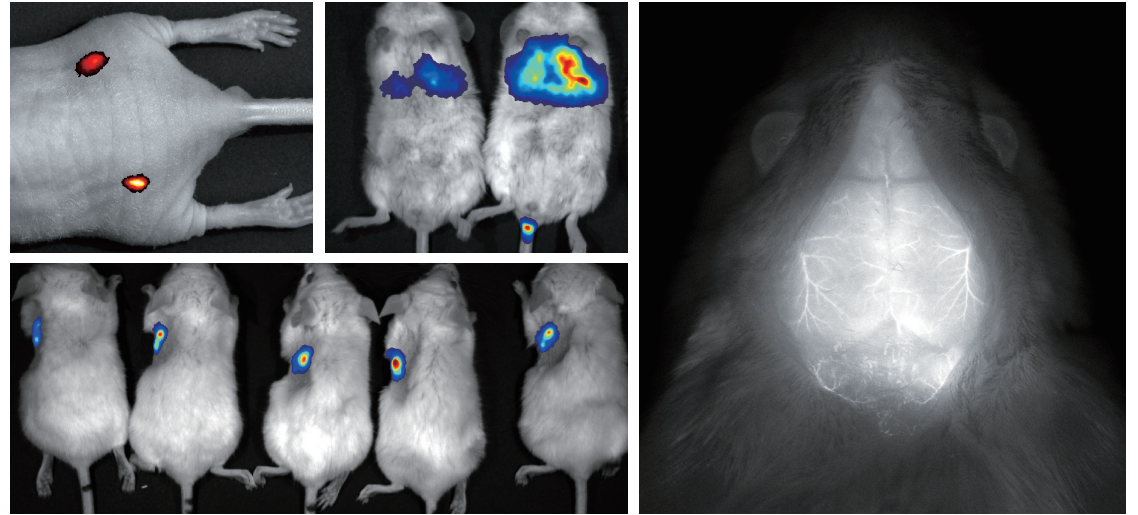


VISQUE

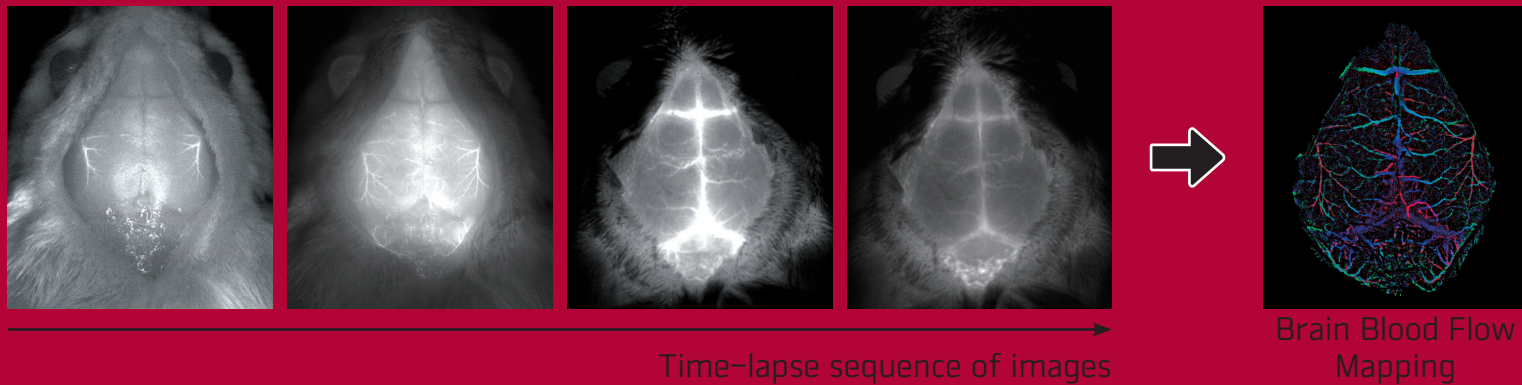


VISQUE™ InVivo Elite
Preclinical Optical Imaging System



For high resolution imaging to support not only in simple ROI analysis but also Kinetics analysis, VISQUE™ InVivo Elite provides all the necessary features.

[Kinetics Analysis with Real-time Fluorescent Images]





Fluorescent/Bioluminescent Imaging



Convenient Image Analysis



Reasonable Price

Vieworks Co., Ltd is ranked number one and four worldwide in ultra-high resolution camera and X-ray detector markets respectively. This milestone ensures that the company has the advanced technologies, plus a strong financial structure.

VISQUE™ InVivo Elite is a noninvasive *in vivo* imaging system for preclinical phase which is based on a combination of Vieworks' high performance industrial camera and medical imaging solution.

The **InVivo Elite** allows researchers to perform ***in vivo* optical imaging in a wide range of research applications** including **cancer, angiogenesis, liver function, neuroscience, inflammation research, stem cell biology, pharmacokinetics, cardiovascular, lymphoid organs**, etc.

CleVue™ designed exclusively for the InVivo Elite provides not only a various tools that help you to analyze fluorescent and bioluminescent images but also Vieworks' patented algorithms that are useful in real time imaging and kinetics. These high-level capabilities achieved from long term studies in cooperation with researchers allow you to generate images and statistics for your research papers with ease.



VISQUE™ InVivo Elite Best performance and ease of use are our top priority



- Stable TEC cooled camera
- Light-tight imaging chamber
- Motor controlled full HD zoom lens
- Simultaneous anesthesia of up to 5 mice
- Motor controlled filter wheel
- High quality hard coated emission filters
- High quality hard coated excitation filters
- High performance LED lighting
- Easy to use LCD touch screen
- Gas anesthesia ports

High Sensitivity Cooled Camera (Peltier Cooling)



The InVivo Elite is based on a combination of thermoelectric cooling technology and radiating structure (patent applied for) to compensate disadvantages of existing ultra-cooled cameras.

Disadvantages of existing ultra-cooled cameras

- ① Cooling systems with gas refrigerant
→Very failure prone
- ② Turn on the systems all the time and replace gas refrigerant periodically→High cost of maintenance

InVivo Elite's Cooled Camera Features

- ✓ Imaging solution ensuring low dark noise
- ✓ Operating temperature range from 10 to 27°C
- ✓ Ready to use immediately after power up
→No need to wait for the camera to cool down
- ✓ Fluorescence and bioluminescence imaging from visible to near infrared wavelengths (green to near infrared region)
- ✓ Optimized design (patent applied for) for real time fluorescence imaging
- ✓ Up to 24 frames per second in real time

Light-tight Imaging Chamber

The imaging chamber of the InVivo Elite is light-tight, so that no light penetrates from the outside. It provides the best bioluminescence imaging for low luminescent signals for which long exposure time is essential.

Full HD Lens – Motorized Control

Motor controlled full HD zoom lens

- ✓ Zoom with 9 steps ($\times 1 \sim \times 6$)
- ✓ Iris with 10 steps (f/1.8 ~ Close)
- ✓ Focus with 21 steps (0 cm ~ 10 cm)

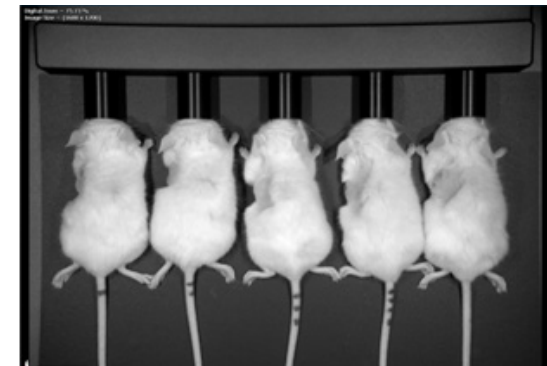
You can acquire high resolution images with its minimum image pixel resolution 33 μm at $\times 6$ zoom. Furthermore, you can check the interior of the imaging chamber in real time with the Preview feature. This allows you to check the position of the subject or adjust the zoom and focus of the lens correctly before acquiring an image.

Precise Iris Control

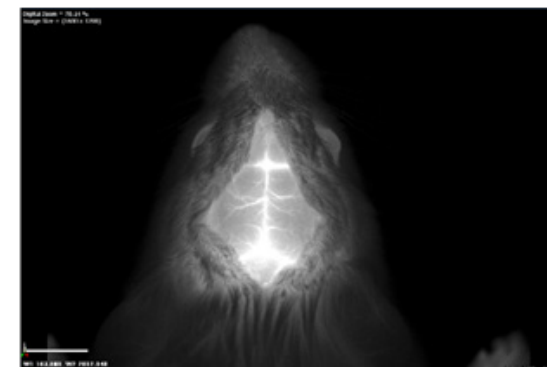
You can control a motorized iris from the maximum iris f/1.8 (the widest opening) to the minimum iris (closed completely) with ten steps. By default, the iris is set to f/1.8 and f/2.5 for typical bioluminescence and fluorescence imaging respectively. When you try to image strong signals, you can use a larger iris value (narrower iris) than the default to close the iris. The narrower iris produces a longer depth of field allowing clearer focus and preventing saturation of strong signals.

Field Of View

You can simply control an adjustable field of view (FOV) from 5 cm \times 4 cm to 28 cm \times 21 cm with a dedicated software. Setting the field of view to 28 cm \times 21 cm allows imaging of more than five mice at the same time. The 5 cm \times 4 cm field of view setting is suitable for imaging magnified specific organs or tissues.



Imaging of 5 mice at the same time at $\times 1.5$ zoom
(FOV: 21 cm \times 16 cm)



In vivo imaging of blood vessels in mouse brain
at $\times 6$ zoom

Automated Emission Filter Wheel

Fluorescence imaging is the visualization of signal intensities emitted by a fluorescent dye after irradiating light at a specific wavelength (applicable to the dye) and then exciting the dye.

To image positions and intensities of fluorescent signals accurately, only the signals emitted by the fluorescent dye must be imaged. The use of high quality filters is therefore essential to acquire an accurate fluorescent image without autofluorescence or reflection.

Equipped with emission filters produced using advanced hard-coating technique

- ✔ Minimize autofluorescence and reflection, block to a level of OD 7
- ✔ Motorized filter wheel → mount a multiple filters at the same time
- ✔ Convenient control with a dedicated software
- ✔ Accommodate up to ten emission filters

* By default, one filter for imaging the shape of subjects and four filters for imaging green, red, far-red and infrared fluorescence are provided.

With four default emission filters, you can image most fluorescent dyes used in laboratories. You can mount five more customized filters as desired.

The following table shows representative fluorescent dyes detectable with the InVivo Elite.

<Typical detectable fluorescent dyes, four groups>

InVivo Elite Acquisition Mode	I (GFP)	II (PE)	III (Cy5.5)	IV (ICG)
Typical detectable fluorescent dyes	GFP EGFP Alexa448 FITC QD 525	RFP DsRed PE Alexa 568 TRITC QD 585 QD 605 QD 62	Cy5.5 PKE680 Alexa 680 Alexa 700 QD 705	ICG QD 800

* You can verify whether you can image with other fluorescent dyes that are not listed in the table above by following the procedures below.

1. Check the emission and excitation wavelength ranges of the fluorescent dye to image.
2. Compare the wavelength ranges with the emission and excitation wavelength ranges listed in the Technical Specifications. You can set the InVivo Elite's emission filter and irradiation light manually to change the detectable wavelength range as desired.

LED (Irradiation Light Source)

The InVivo Elite uses LEDs as an irradiation light source for fluorescence imaging. LEDs provide lower power consumption and more stable operation than lasers. With multiple 2-watt high power LEDs, the InVivo Elite produces greater light output than those of conventional laser-based light sources.

Typically LEDs emit light at one specific wavelength, however they also emit other light at shorter or longer wavelengths than the one. The InVivo Elite is designed to pass the LED light through the excitation filter and then irradiate the fluorescent dyes. This enables only the light at a specific wavelength required to excite the fluorescent dye to be irradiated accurately.

The combination of four default excitation filters, four main irradiation light (I, II, III and IV) and one auxiliary light covers a various wavelength fluorescent dyes.

Refer to the Technical Specifications for more detailed information about the excitation filters.

With its advanced hard-coated emission filters, undesired light emitted by the LEDs is blocked to a level of OD 7. This contributes to high quality fluorescence imaging without autofluorescence.

Due to optical properties, longer wavelengths penetrate the biological tissue deeper than shorter wavelengths. Therefore, it is recommended that you use a long wavelength fluorescent dye for deep-tissue fluorescence imaging. Especially if you use near infrared fluorescent dyes requiring wavelengths longer than 760 nanometers, you can image up to about 4 to 7 millimeters deep into tissue.

LCD Touch Screen

The LCD touch screen panel located on the front of the InVivo Elite allows you to control the external light, stage temperature, lens zoom, imaging setting values conveniently or monitor its status at a glance.



LCD Touch Screen

Special Design for Real Time Imaging

When you try to acquire real time images of molecular movement, you need to begin the image acquisition immediately after injecting a probe or dye into the blood or lymphatic vessel of the animal subject to acquire accurate images. It is especially important for the fast moving molecules that an injection of a probe or dye is immediately followed by the image acquisition.

The InVivo Elite's special design including double-layer doors allows you to begin the image acquisition immediately after providing stimulation or injecting a probe or dye into the animal subject. In general, double-layer doors should be closed to prevent the outside light from penetrating while acquiring fluorescent or bioluminescent images. When you try to acquire near infrared fluorescent images, however, the outside light may not affect the imaging because the natural light or white light almost does not contain near infrared wavelengths. Therefore, you can start the near infrared fluorescence imaging using only the inner door by following the procedures in the right figure.

As described above, the InVivo Elite's unique design (patent applied for) including inner door, sliding stage, Preview feature (monitoring the interior of the imaging chamber in real time) and foot switch allows you to start the image acquisition while handling the subject with both hands.

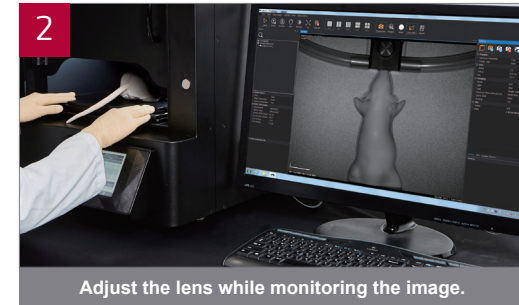
The world's only in vivo imaging system with a unique design offers not only convenient real time imaging methods but also precise experimental environments. For examples of how to acquire and analyze real time images, watch the videos on the **Vieworks website** (www.vieworks.com).

Real time fluorescence imaging with the InVivo Elite



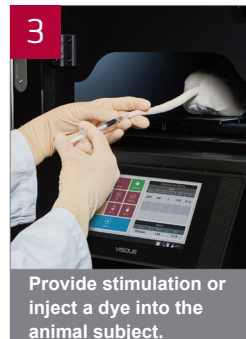
Place the animal subject in position on the stage.

① Pull out the sliding stage and place the subject on the stage through the open part of the inner door while the inner door is closed.

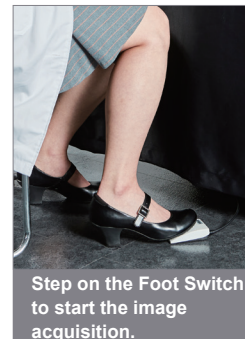


Adjust the lens while monitoring the image.

② Adjust the position of the subject or lens focus using the Preview feature.

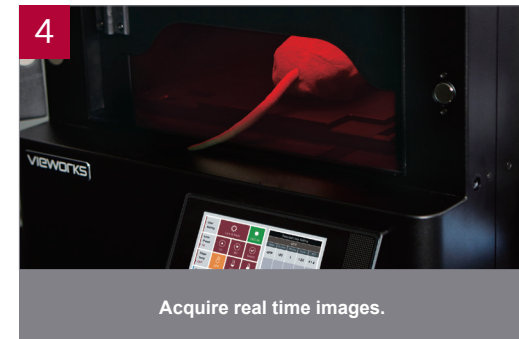


Provide stimulation or inject a dye into the animal subject.



Step on the Foot Switch to start the image acquisition.

③ Provide stimulation or inject a dye into the subject through the open part and at the same time start the image acquisition using the foot switch.

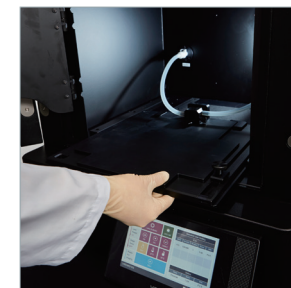


Acquire real time images.

④ The light for fluorescence imaging is turned on when the image acquisition begins.



- Double-layer doors for real time imaging (patent applied for)
- Real time near infrared fluorescence imaging with only an inner door closed



- Temperature controlled stage included
- Sliding stage (patent applied for) to maintain and manipulate animal subjects conveniently

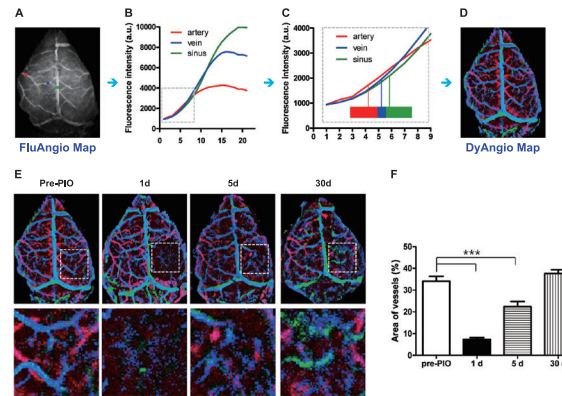
Research in pharmacokinetics and cardiovascular system using real time images

To perform *in vivo* studies, such as pharmacokinetics, cardiovascular, lymphatic system by measuring molecular events *in vivo*, you must acquire real time images and then verify changes in position, velocity and quantity of the targeted molecules.

With the InVivo Elite, you can acquire up to 24 frames per second in real time. Furthermore, the CleVue software designed exclusively for the InVivo Elite provides the color map and graph capabilities to verify changes in position, velocity and quantity of the targeted molecules at a glance. The CleVue includes ten types of algorithms which allow for velocity measurements and quantifications of the targeted molecules.

Not only the Mean Transit Time (MTT) and Blood Flow Index (BFI) algorithms typically used in MRI for analyzing Cerebral Blood Flow (CBF) but also the exclusive algorithms (Trising, Imax, Fluangio, Dyangio, etc.) achieved in cooperation with researchers in Korea Advanced Institute of Science and Technology (KAIST) and Kyung Hee University are included.

Several studies and researches performed with these exclusive algorithms are already have been cited in high-impact SCI journals. This ensures that those algorithms provided by the CleVue are very applicable to *in vivo* optical imaging (refer to figure 1 to figure 5).



Blood flow visualization of the infarct area using color-coded pial vasculature image showing the time-course of recovery after PIO
J Neurosci Methods. 2015, 248, 46 [IF 2.0]

Figure 1 Study in cerebral blood flow restoration process after a photothrombotic ischemic operation

To analyze cerebral blood flow, injected near infrared fluorescent dye, ICG, into the tail vein of the mouse and then acquired real time fluorescent images. Generated the blood flow map (D, DyAngio Map) indicating each blood vessel's blood flow velocity by analyzing the vasculature map (A, FluAngio Map) and comparing changes (B and C) in fluorescent signals of the arteries, veins and venae cavae. With this blood flow map, quantitatively analyzed (E and F) the blood flow recovery of an infarct region over time after a photothrombotic ischemic operation (PIO).

Researchers from Kyung Hee University and Vieworks Co., Ltd. collaborated on the development of the FluAngio Map and DyAngio Map algorithms. The CleVue enables equivalent analysis as described in this paper.

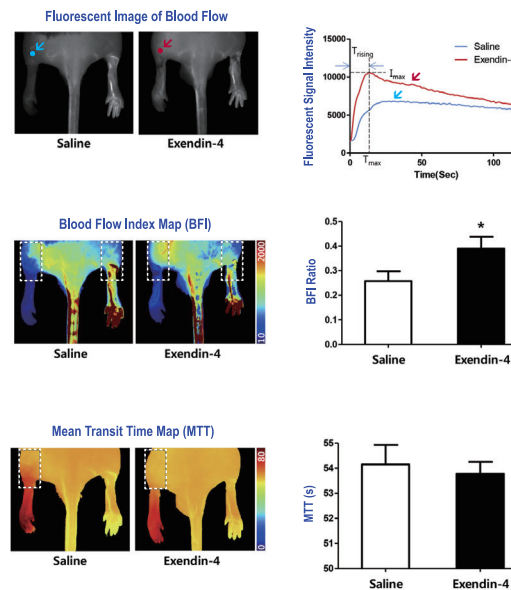
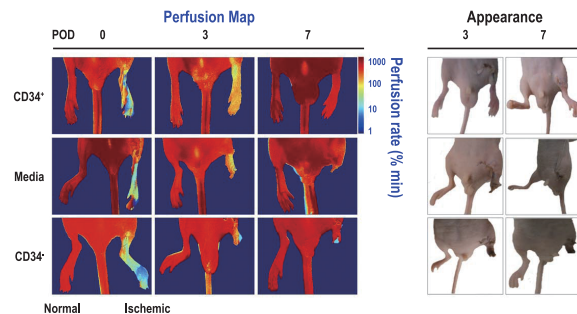


Figure 2 Study in proangiogenic effects of Exendin-4 on ischemic hind limbs

Ischemic hind limbs were induced by hind limb ischemia surgery. Following surgical induction, Exendin-4 injected into the ischemic hind limbs of the experimental groups while Saline injected into the control group. Injected near infrared fluorescent dye, ICG, into the tail vein and then acquired real time fluorescent images on the third day after surgery. Quantified the blood flow rate (changes in fluorescent signals) with the graph at the red and blue point on the real time fluorescent image (first figure and graph). Generated the maps (second/third figures) for verifying the blood flow rates at a glance and graphs (second/third graphs) for the quantitative comparison by calculating Blood Flow Index (BFI), an algorithm used for analyzing blood flow rates in real time fluorescent images, and Mean Transit Time (MTT).

The real time fluorescent images, BFI and MTT maps and graphs included in this paper are generated by the CleVue.

Exendin-4 protects hindlimb ischemic injury by inducing angiogenesis.
Biochem Biophys Res Commun. 2015, 465 (4) 758 [IF 2.3]

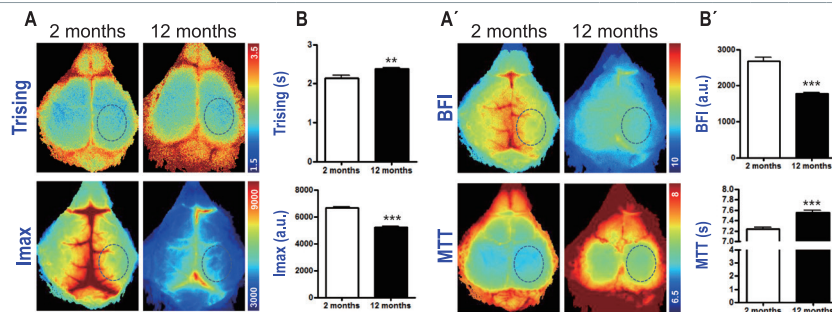


Perfusion recovery analysis after CD34+ stem cell treatment into the ischemic limb
Blood 2010, 116 (25) 5762 [IF 10.4]

Figure 3 Study in therapeutic effects of pluripotent stem cells on ischemic hind limbs

Ischemic hind limbs were induced by hind limb ischemia surgery. Following surgical induction (POD 0), compared the perfusion maps to confirm that the perfusion rates of each group are equivalent. Injected near infrared fluorescent dye, ICG, into the tail vein, acquired real time fluorescent images, and then generated the perfusion maps by using these images. After comparison, progenitor cells (CD34+) injected into the ischemic hind limbs of the experimental groups while media or CD34- injected into the control group. The perfusion maps quantitatively indicated that the experimental group showed improved perfusion rates compared to the control group on the third and seventh day after surgery (left figure). The animal photographs (right figure) of the control group showed tissue necrosis due to delayed recovery of the perfusion rate.

The perfusion maps included in this paper are generated by the CleVue's algorithm.

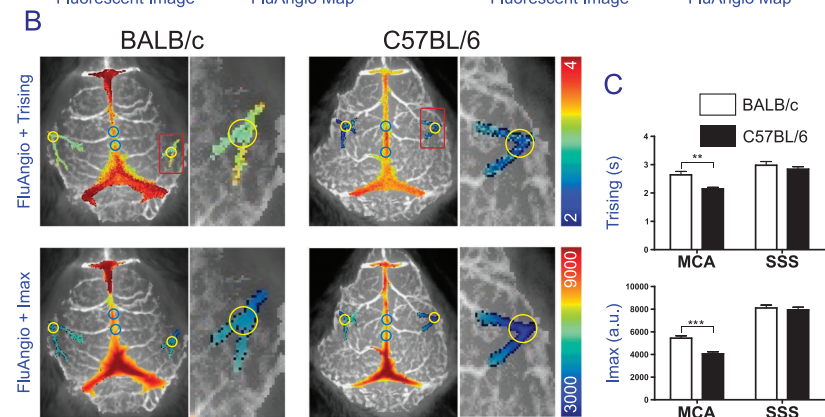
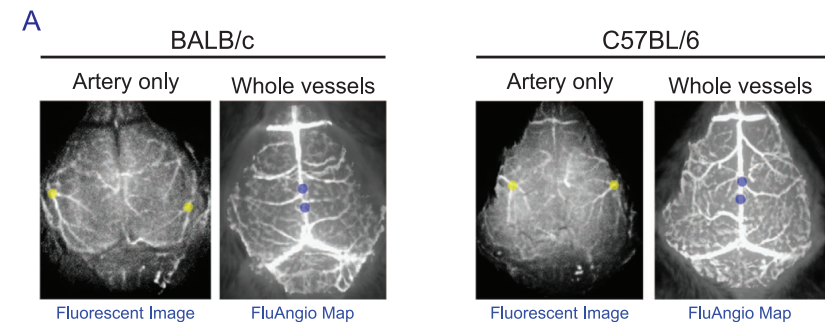


Age-related changes in pial arterial structure and blood flow in mice
Neurobiol Aging 2016, 37, 161 [IF 5.1]

Figure 4 Study in age-related changes of blood flow

Injected near infrared fluorescent dye, ICG, into the tail vein of mice to compare cerebral blood flow of 2-month-old and 12-month-old mouse and then acquired real time fluorescent images. Analyzed the blood flow with the velocity and quantity parameters respectively and then generated maps (A and A') to verify changes at a glance. The Trising map indicates the velocity of the blood flow, the Imax map indicates the amount of the blood, and the BFI and MTT maps indicate the blood flow affected by the interaction between the velocity and quantity. To analyze these maps quantitatively, generated the graphs (B and B').

The real time fluorescent images, Trising, Imax, BFI, MTT Map and graphs included in this paper for quantitatively analyzing cerebral blood flow are generated by the CleVue.



Mouse Brain blood perfusion analysis in the specific ROIs, super sagittal sinus (SSS) and middle cerebral arteries (MCA)

J Cereb Blood Flow Metab. 2015, 35 (6) 912 [IF 5.4]

Figure 5 Study in differences in cerebral vasculature and blood flow depending on strains of experimental mice

Studied on differences between BALB/c and C57B/6 mice's cerebral vasculature and blood flow to determine what causes the revascularization differences among strains of experimental mice. Injected near infrared fluorescent dye, ICG, into the tail vein of each mouse and then acquired real time fluorescent images. Compared and analyzed the images (A, Artery) which show the artery blood flow well among the real time fluorescent images and the cerebral vasculature maps (B, FluAngio Map). Analyzed the velocity (B, FluAngio + Trising Map) and amount of the blood in the regions of interest, middle cerebral artery (MCA) and superior sagittal sinus (SSS), and then generated the maps (B) for verifying them at a glance and the graphs (C) for the quantitative comparison.

Researchers from Kyung Hee University and Vieworks Co., Ltd. collaborated on the overlay of the FluAngio Map and Trising or Imax Map included in this paper. The CleVue enables equivalent analysis as described in this paper.

Technical Specifications

Appearance

Dimension (W × D × H)	56 cm × 56 cm × 90 cm
Weight	> 100 kg
Display	7" color LCD touch screen
Operating Temperature	10 ~ 28°C

Cooling Camera

Sensor	4/3" CCD
Cooling	-10°C (T = -20°C)
Resolution (H × V)	1,600 × 1,200
Frame Rate	up to 24 fps
Min. Image Pixel Resolution	33 μm (at ×6 zoom)
Binning	1 × 1 / 2 × 2 / 4 × 4
Detection Spectral Range	500 ~ 850 nm
Min. Exposure Time	1 ms
Max. Exposure Time	50 min
Imaging Type	Single-Frame / Time-lapse (Real Time Imaging) / Accumulation

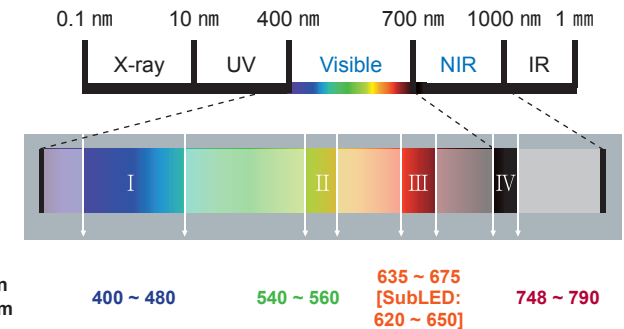
Full HD Lens

Control	Motorized Zoom, Iris, Focus Control
Focus	0 ~ 10 cm, 21 steps, 0.5 cm increment
Iris	Max. f/1.8, 10 steps
Zoom (Field of View, H × V)	28 × 21 cm (×1) ~ 5 × 4 cm (×6), 9 steps

Excitation Light and Excitation Filters

Source	LED
Excitation Wavelength Range	440 - 490 nm (blue) 500 - 545 nm (green) 640 - 680 nm (far-red) 760 - 780 nm (NIR) 620 - 650 nm (red → No excitation filter)
White Light	epi white LED
Excitation Filters	8 (4 types × 2)
Excitation Filter Positions	8

LED Irradiation Spectrum (unit: nm)



Irradiation Light Transmittance of Biological Tissue

Low High

- It is recommended that you use an irradiation light with a high transmittance of biological tissue for accurate in vivo fluorescence imaging.
- You can use the auxiliary LED emitting light at wavelengths of 620 - 650 nm depending on the excitation properties of fluorescent dyes in group III (The filter wheel and light settings are selected in the CleVue software).
- Refer to the Technical Specifications for a detailed list of fluorescent dyes for each group.

Imaging Stage & Anesthesia

Imaging Stage Type	<ul style="list-style-type: none"> • Stage for imaging up to 5 mice at the same time (default) • Stage with teeth holder for 1 mouse or 1 rat (optional)
Stage Heating Module	Yes
Stage Temperature Range	Off / 25°C / 36°C
Gas Anesthesia adapter	Yes

Special Design for Time-lapse Imaging

Double-layer Door	<ul style="list-style-type: none"> • Big outer door functions as a light tight imaging chamber for bioluminescence and visible fluorescence imaging. • Light inner door includes an open part for time-lapse imaging.
Sliding Stage and Open Part	Allows you to easily place the animal subject in position, provide stimulation or inject a dye into it and then start real time imaging immediately.
Teeth Holder on the Stage	Hold the animal subject (mouse or rat) firmly for real time imaging (an optional one mouse stage or one rat stage is available).
Foot Switch	Allows you to start real time imaging while handling the animal subject with both hands.

Software, CleVue

Exclusive File Format	*.CIF (CleVue Image File) Saves all information of an image such as a raw image, analyzed image, ROI information, acquisition information, comments et al.
Supported Image File Format	TIFF / Bitmap / JPEG / PNG
Image Merging	Merges images of multi-fluorescent dyes.
Removal of Autofluorescence	Removes autofluorescence or reflection from fluorescent images.
Report Mode	Displays an analyzed image with color scale bar, analyzed data, acquisition info, comments et al.
Kinetics Analysis	<ul style="list-style-type: none"> • Includes 10 kinds of algorithms, i.e. MTT, BFI, and patented other algorithms to analyze Kinetics. • Dynamics graph • Maps Kinetics values on an image.

Emission Filters

Filter Selection	Automated Control
Emission Filters	4
Emission Filter Positions	10
Wavelength Range of Emission Filters	500 - 550 575 - 640 690 - 740 810 - 860

InVivo Elite Acquisition Mode	I (GFP) II (PE) III (Cy5.5) IV (ICG)
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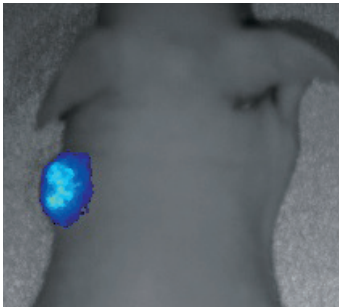


Representative Detectable Dyes	<p>GFP / EGFP / Alexa448 / FITC / QD 525 (Ex: 390 - 490 nm, Em: 500 - 550 nm)</p> <p>RFP/ DsRed / PE/Alexa 568 / TRITC / QD585 / QD605 / QD625 (Ex: 530 - 570 nm, Em: 575 - 640 nm)</p> <p>Cy5.5 / PKE680 / Alexa 680 / Alexa 700 / QD 705 (Ex #1: 620 - 650 / **Ex #2: 630 - 680 nm, Em: 690 - 740 nm)</p> <p>ICG / QD 800 (Ex: 740 - 790 nm, Em: 810 - 860 nm)</p>
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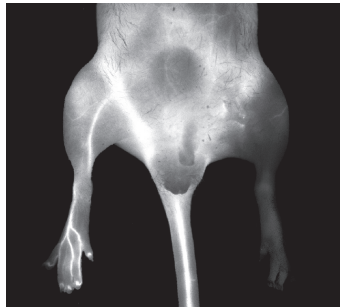
* User defined combinations of excitations and emissions are available. These enables you to detect other fluorescent dyes that are not listed in the table above.

Applications

Photograph	<ul style="list-style-type: none"> Fluorescent Imaging Bioluminescent Imaging Real-time Imaging Structural Imaging
Research Applications	<ul style="list-style-type: none"> Cancer, Angiogenesis, Liver function, Neurology, Inflammation Disease, Stem Cells, Cardiovascular and Lymphoid Organs and Pharmacokinetics



• Bioluminescent Image



• Fluorescent Image



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