



BIOEMTECH

Embracing scientists translate ideas into outcomes



ϕ -eye

A highly sensitive, benchtop, in vivo optical imaging system for preclinical studies

General

BIOEMTECH's vision is to accelerate preclinical research, towards clinical translation for promising drugs, through high quality services and products.

We are a strong research partner who guides, consults, and supports all preclinical research studies of our collaborators.

- As a manufacturing company of novel breakthrough imaging systems (*eyes*), we offer simplicity, speed, and efficiency on a daily workflow, during the first steps of testing novel compounds.
- As a preclinical CRO, we offer a one-stop-shop at our state-of-the-art Laboratories that covers a full chain of preclinical studies, following a Good Laboratory Practice approach in the daily routine.

BIOEMTECH's ultimate goal is to aid scientists innovate, at every step of their research.




BIOEMTECH

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Introduction

BIOEMTECH's ϕ -eye™ is a high-sensitive, low-noise, *in vivo* optical imaging scanner. It enables non-invasive visualization and tracking of fluorescent and bioluminescent probes *in vivo*. ϕ -eye™ is suitable for a wide range of applications, including but not limited to oncology. Cutting-edge technology combined with an intuitive, easy-to-use working environment, transforms ϕ -eye™ into a unique imaging solution.



ϕ -eye™'s footprint of 60 cm × 60 cm x 50 cm and weight of lower than 60 kg, characterizes it as a truly desktop device that can turn any place/space into an imaging lab. It comes with a laptop serving for data processing and acquisition, while standard licenses of the complete software suite **Visual | eyes** are included.

Technology - Specifications

A. General Information

ϕ -eye™ enables non-invasive visualization and tracking of fluorescent and bioluminescent probes in the visible range within a living organism. A large Field-of-View provides high throughput screening in a wide variety of preclinical studies.

Modality	FLI / BLI
Visible range	400 – 800 nm
Fluorescence filter sets	4 (with high expansion capability)
Number of mice	Up to three (3)
Active FOV	17 cm × 17 cm
White light	White light for superior photographic images
Footprint	60 cm × 60 cm x 50 cm
Weight	<60 kg



For fluorescence imaging, filters with different spectral characteristics are provided to cover the visible range between 400 – 800 nm. Excitation and emission filters are integrated on interchangeable cassettes that can be easily alternated by the user. By default, four filter sets are provided. Custom filter sets can be provided upon request.

B. Performance

State-of-the-art technology offers superior sensitivity, resolution and fast frame rates. Novel architecture and high-quality components provide superior fluorescence and bioluminescence images in a benchtop configuration. High quantum efficiency in the visible range enables the efficient screening of newly developed drugs *in vivo*.

Version	Standard	Extended
Detector	sCMOS	qCMOS
Resolution	6.5-micron pixels, 2048 × 2048	4.6-micron pixels, 4096 × 2304
Quantum Efficiency	82% @ 560 nm	90% @ 475 nm
Readout noise (e)	1.5 (rms)	0.27 (rms)
Dark current (e/pixels/s)	0.6	0.016
Dynamic range (Typ.)	33000:1	25900:1
Lens	F/1.8	
	>93% transmittance (VIS-NIR)	
Fluorescence bandpass filters	>93% transmission	
	>OD 6 blocking	

C. Fluorescence imaging in the SWIR window

A state-of-the-art InGaAs sensor is incorporated in ϕ -eye™ SWIR version. Fluorescence imaging in the NIR-II window using ϕ -eye™ allows the screening of newly developed SWIR dyes, which are advantageous for imaging, as tissue components have reduced photon absorption and scattering effects, thus enabling deeper tissue penetration.

General Information

Modality	FLI – NIR II/SWIR window
SWIR range	900 – 1700 nm
Excitation peak wavelength	755 nm
Fluorescence filter sets	2 (with high expansion capability)
Number of mice	Up to three (3)
Active FOV	22 cm × 17.6 cm
Footprint	60 cm × 60 cm × 50 cm
Weight	<60 kg

Performance

Detector	InGaAs sensor
Resolution	15-micron pixels, 640 × 512
Quantum Efficiency	70% @ 900-1700 nm
Readout noise (electrons)	<30
Dark current (e/pixels/s)	<600
Lens	8 mm, F/1.4
Fluorescence bandpass filters	>91% transmission
	>OD 4 blocking

D. Animal handling

To preserve animals' welfare and health, ϕ -eye™ employs standard inputs for gas anaesthesia - fully compatible with third party systems. Anaesthesia then is provided into the mask of the animals, all throughout the imaging study. In addition, the system infers a heated imaging stage, maintaining in such way the temperature of the animal in the desired level.



Anaesthesia	Standard inputs for gas anaesthesia; compatible with third party systems
Heating	Heated stage for optimum body temperature
Light-tight imaging chamber	30cm (L) × 30cm (W) × 30cm (H)

E. Footprint and connectivity

ϕ -eye™'s footprint and standard digital interface connectivity can turn any space into an imaging lab. In addition, ϕ -eye™ is characterized by simple power requirements and anaesthesia connections, allowing real time imaging and quantification inside a clean room, overcoming limitations, and facilitating scientists get great results under challenging conditions.

Outer dimensions	60cm (H) × 60cm (W) × 50cm (L)
Weight	< 60 kg
AC input range	100-240 VAC
PC Connectivity	USB 3.0 and USB 2.0
Outer shielding	Sheet metal and acrylic

F. Visual | eyes Software

The embedded software, **Visual | eyes** is a complete software suite, serving image acquisition, system control and analytical post-processing routines. Among other possibilities, users through Visual | eyes software, can generate imaging studies using custom and/or pre-defined protocols, obtain quantitative information in user's defined Region of Interests and export images to DICOM format.

Fast acquisition	Simplified procedure in a robust environment
Database	Raw data, DICOM storage, Compatibility with third party software
Dual layer imaging	Superimposition with photographic image for superior anatomical mapping
Imaging protocols	Pre-defined and user's defined imaging protocols
Post processing	Integrated ROI manager for detailed post processing image analysis
License	Standalone licenses for Mac OS & Windows

Live imaging console

The Live Imaging Console interface includes the following components:

- Video Windows:** Two side-by-side windows showing a mouse with fluorescent spots. The right window includes a timestamp: "0.1 sec / 09:34:47 am".
- Controls Panel:**
 - Select fiber:** A row of colored circles (green, orange, red, blue) with a "Custom" button and a refresh icon.
 - Exposure time:** A dropdown menu set to "0.1" and a "sec" label.
 - Colormap:** A dropdown menu set to "Royal".
 - Max/Min/Opacity:** Three horizontal sliders for adjusting image parameters.
 - Camera/View Controls:** Three circular icons for camera and view adjustments.
- White Light Panel:** A row of thumbnail images labeled "snap01" through "snap05" and "snap06".
- Study details:**
 - Study ID: 78
 - Animal ID: [blank]
 - Project: [blank]
 - Fluorescent dye: [blank]

Post Processing suite

The Post Processing Suite interface includes the following components:

- ROI Statistics Table:**

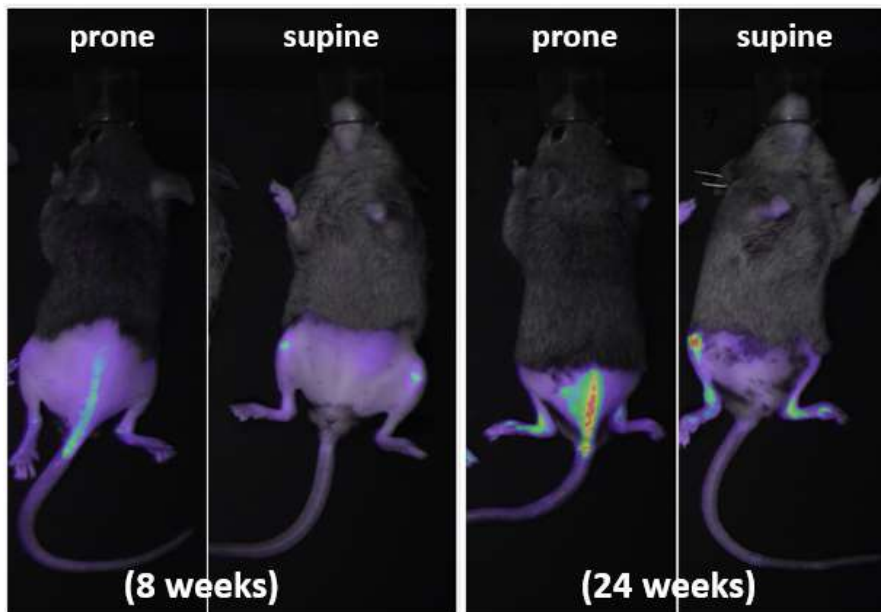
ROI Name	ROI Type	Sum (Ph/s/mm)	Mean (Ph/s/mm)	Max (Ph/s/mm)	Min (Ph/s/mm)	Std.Dev. (Ph/s/mm)
ROI_1	Free	1.48818e+09	1.46708e+07	2.2118e+07	0	4.26038e+10
ROI_2	Free	1.85431e+09	6.37724e+06	8.23992e+06	2.93441e+06	1.02752e+10
ROI_3	Free	6.78832e+09	1.23166e+07	1.60586e+07	6.79403e+06	3.32007e+10
ROI_4	Free	1.83325e+09	6.89339e+06	8.34555e+06	5.12075e+06	1.28387e+10
ROI_5	Free	8.20881e+09	5.03695e+06	4.86889e+06	89127.7	1.64809e+09
- White Light Images:** A row of thumbnail images labeled "snap02_2ms_01:00:32pm" through "snap07_2ms_01:04:46pm".
- Processing Tools:**
 - ROI Selection:** Buttons for "Reset", "EraseROI", "Draw", and "Reset".
 - ROI Manager:** A list of ROI names (ROI_1 to ROI_5) with buttons for "Add ROI", "Delete", "Refresh", "Update position", "Show stats", and "Hide ROI".
 - Reporting:** Buttons for "Export Image As...", "Export data (Excel)", and "Open DICOM Viewer".
- Image Settings:**
 - ColorMap:** A dropdown menu set to "Royal".
 - Opacity:** A horizontal slider.
 - Max/Min:** Two horizontal sliders with numerical values (e.g., 1911.73) and "Auto" buttons.
- Study Information:**
 - Study ID: 89
 - Animal ID: 13
 - Name: Page_evaluation
 - Fluorescent dye: Proxima
 - Reported date-time: 01/17/2013 02:56:34
 - Acq time: 01/17/2013 13:04:37

Indicative Studies

Fluorescence studies

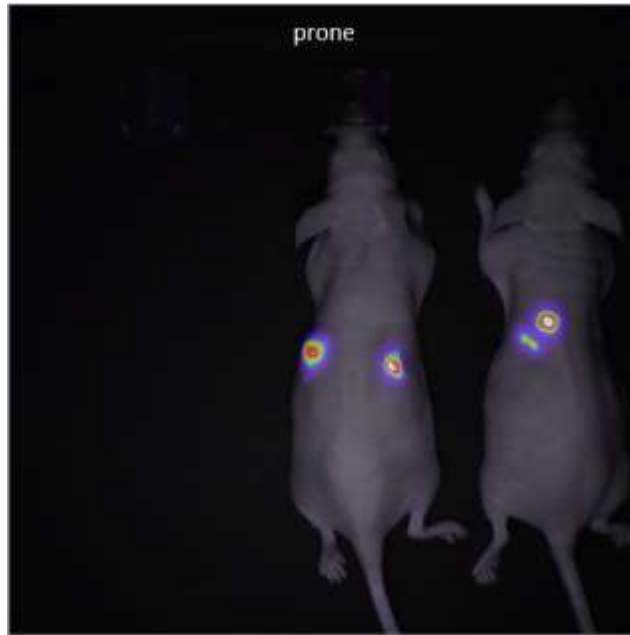
- **Spondyloarthritis model**

Fluorescent dye	OsteoSense [®] 680 EX (PerkinElmer, Waltham, MA)
Mouse model	TgA86 transgenic mouse
Animal depilation	Depilation of fur over hands, legs, and tail with cream, prior to imaging
Administration route	Retro-orbital
Imaging	23 hours post injection



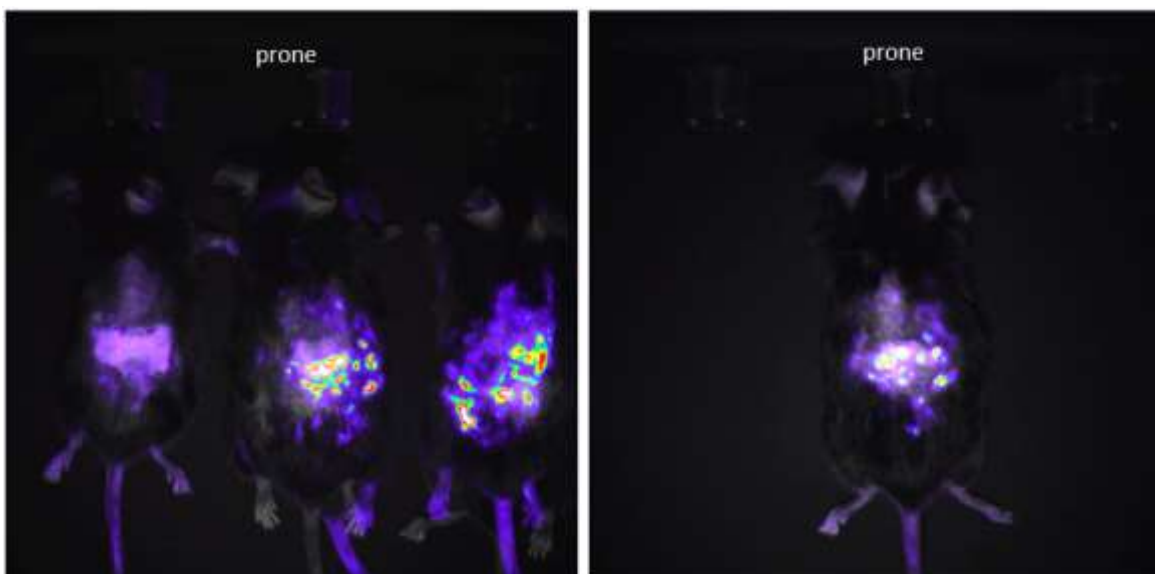
- **Oncology study**

Fluorescent dye	TdTomato
Mouse model	Genetically engineered mouse model (NF1-KO) that spontaneously develop cutaneous neurofibromas
Animal depilation	N/A
Administration route	Intravenous
Imaging	1-5 weeks



○ **Cutaneous Neurofibromas model**

Fluorescent dye	TdTomato
Mouse model	Genetically engineered mouse model (NF1-KO) that spontaneously develop cutaneous neurofibromas
Animal depilation	Depilation of fur over spine with cream, prior to imaging
Administration route	Intravenous
Imaging	1-5 weeks



○ Heart imaging after myocardial infarction

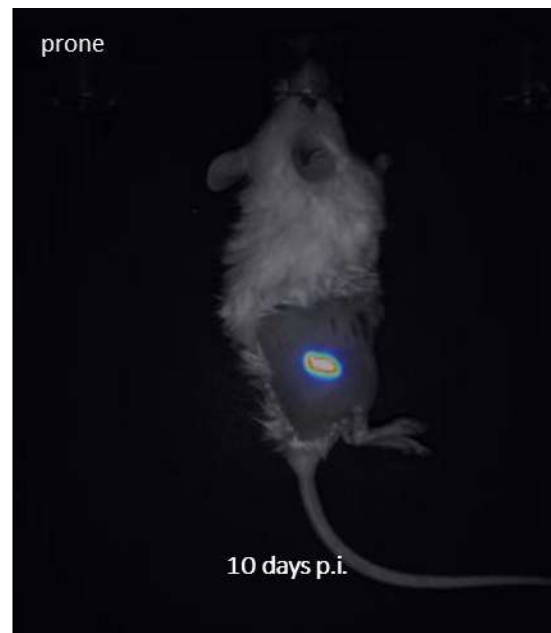
Fluorescent dye	Cy5
Infarction surgery	Thoracotomy and ligation at the level of the left-anterior descending (LAD) coronary artery (CA) approx. 4mm from the left auricle
Animal depilation	Depilation of fur over thorax and abdomen with cream, prior to imaging
Administration route	Intracardiac injection with 20uL (15 uM – Cy5)
Imaging	1 hour post injection



Bioluminescence studies

○ U87MG-Luc2 cells – *in vivo* imaging

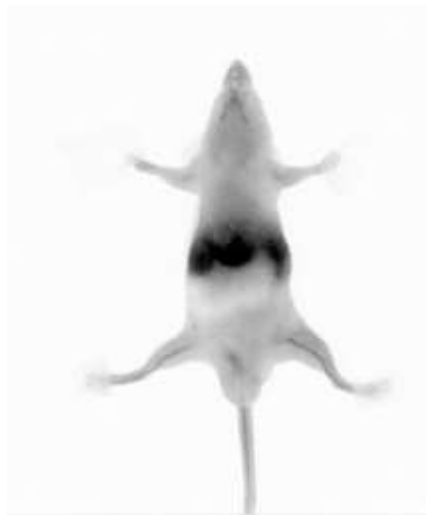
Bioluminescent probe	Luc2
Mouse model	Inoculation of 10^6 U87MG-Luc2 cells to female SCID mice
Animal depilation	Depilation of fur over spine with cream, prior to imaging
Administration route	3mg of D-luciferin in 200ul saline (VivoGlo Luciferin) were administered intraperitoneally (IP)
Imaging	10 days after inoculation / Within the first 30 min p.i. of D-luciferin



Fluorescence in the SWIR window

- **ICG (indocyanine green) *in vivo* imaging**

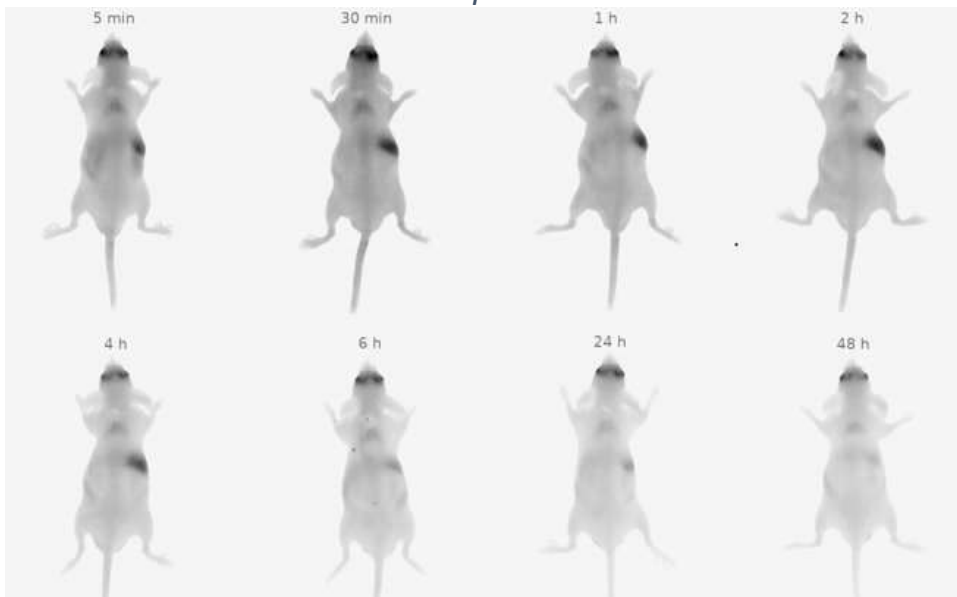
SWIR probe	ICG
Model	SKH-1 hairless albino
Administration route	500uM @ 100uL; Intravenous
Imaging	1 min post-injection
Exposure time	5 ms



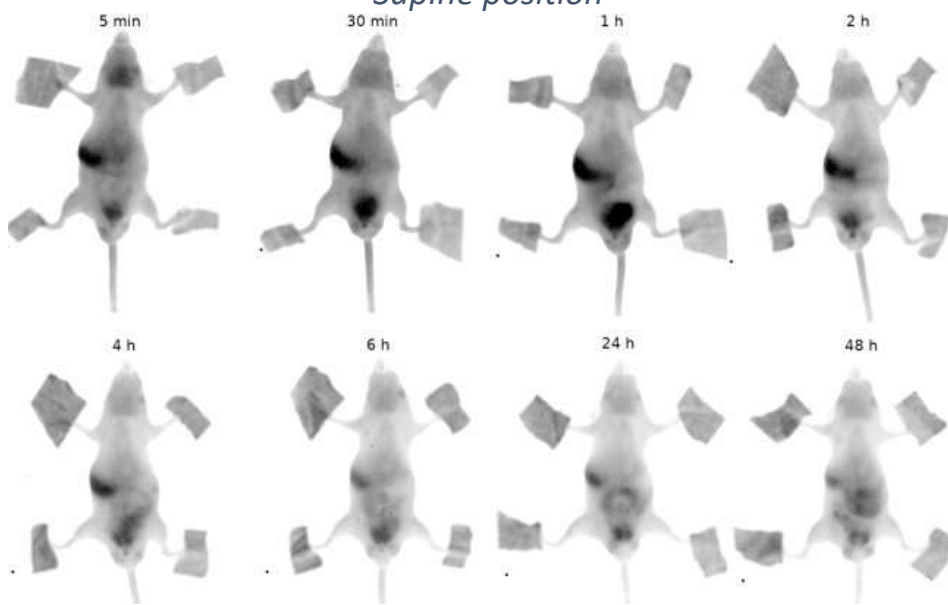
- **IRDye 800CW *in vivo* imaging**

SWIR probe	IRDye 800CW
Model	SKH-1 hairless albino
Administration route	1nM @ 250uL; Intravenous
Imaging	5 min - 48h post-injection
Exposure time	300 ms

Prone position



Supine position






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