



# BIOEMTECH

*Embracing scientists translate ideas into outcomes*



$\phi$ -eye

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

Technical Specifications

## 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

Lefkippos Attica Technology Park-N.C.S.R Demokritos, Greece

[info@bioemtech.com](mailto:info@bioemtech.com) • [www.bioemtech.com](http://www.bioemtech.com)

## Introduction

BIOEMTECH's  $\phi$ -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*.  $\phi$ -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  $\phi$ -eye™ into a unique imaging solution.



$\phi$ -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

$\phi$ -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.

<b>Modality</b>	FLI / BLI
<b>Visible range</b>	400 – 800 nm
<b>Fluorescence filter sets</b>	4 (with high expansion capability)
<b>Number of mice</b>	Up to three (3)
<b>Active FOV</b>	17 cm × 17 cm
<b>White light</b>	White light for superior photographic images
<b>Footprint</b>	60 cm × 60 cm x 50 cm
<b>Weight</b>	<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  $\phi$ -eye™ SWIR version. Fluorescence imaging in the NIR-II window using  $\phi$ -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

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

### D. Animal handling

To preserve animals' welfare and health,  $\phi$ -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.



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

## E. Footprint and connectivity

$\phi$ -eye™'s footprint and standard digital interface connectivity can turn any space into an imaging lab. In addition,  $\phi$ -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.

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

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

## Live imaging console

The Live Imaging console interface includes the following components:

- Live Imaging:** Two side-by-side video windows showing a mouse with fluorescent spots. The right window includes a timestamp: "0.1 sec / 09:34:47 am".
- Controls:**
  - 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.
  - Buttons:** Play, Stop, and Camera icons.
- White Light:** A row of thumbnail images labeled "snap01" through "snap05" and "snap06".
- Study details:**
  - Study ID: 78
  - Animal ID: [blank]
  - Fluorescent dye: [blank]
  - Study Name: [blank]
  - Project: [blank]

## Post Processing suite

The Post Processing suite interface includes the following components:

- ROI Statistics:** A table showing statistical data for five Regions of Interest (ROIs) across two mice.

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	1.48815e+09	1.46708e+07	2.2118e+07	0	4.26033e+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	1.23195e+07	1.60586e+07	6.79469e+06	3.32007e+10
ROI_4	Free	1.83325e+09	6.89339e+06	8.34555e+06	5.12075e+06	1.28367e+10
ROI_5	Free	8.20881e+09	5.03695e+06	4.86689e+06	89127.7	1.64809e+09

- White light images:** A row of thumbnail images showing the mice under white light.
- Processing Tools:**
  - ROI Selection:** Buttons for "Best", "Erase ROI", "Draw", and "Reset".
  - Image Settings:** ColorMap (Royal), Opacity, Max (1911.73), and Min (0.00) sliders.
  - ROI Manager:** A list of ROIs (ROI\_1 to ROI\_5) with buttons for "Add ROI", "Remove", "Update position", "Show stats", and "Hide ROI".
  - Reporting:** Buttons for "Export Image As...", "Export data (Excel)", and "Open DICOM Viewer".
  - Study info:**
    - 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

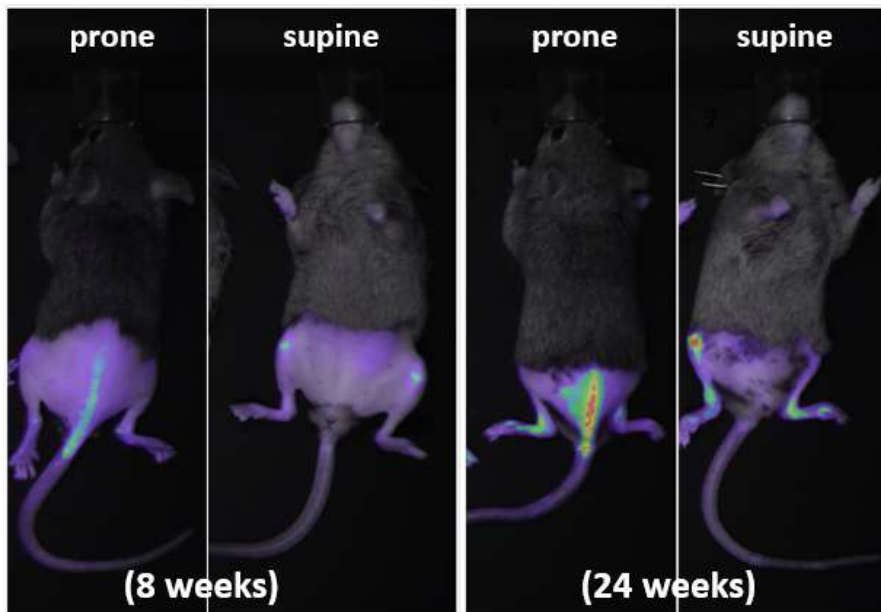


# Indicative Studies

## Fluorescence studies

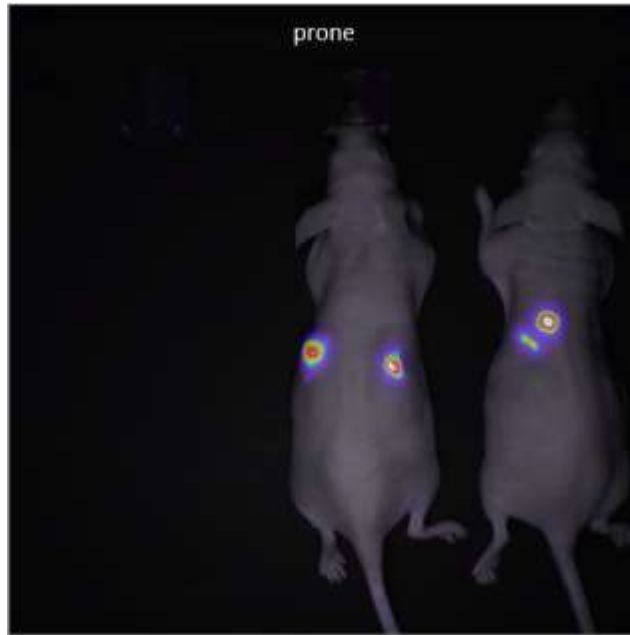
- **Spondyloarthritis model**

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



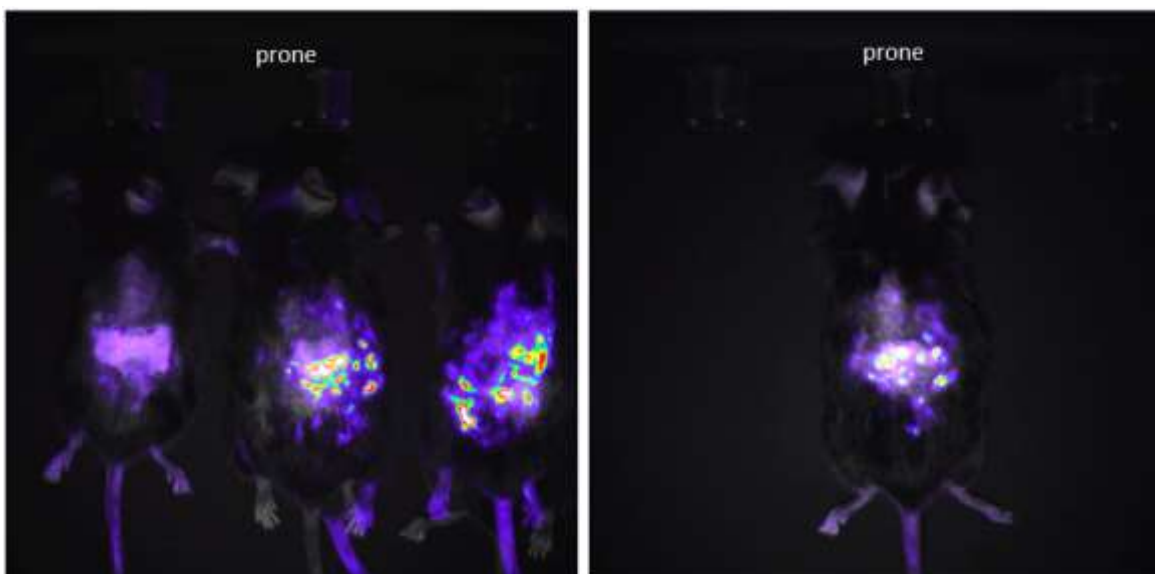
- **Oncology study**

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



○ **Cutaneous Neurofibromas model**

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



○ Heart imaging after myocardial infarction

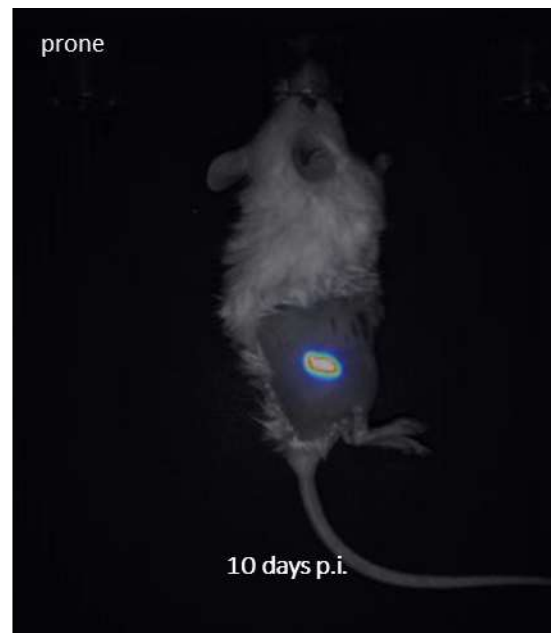
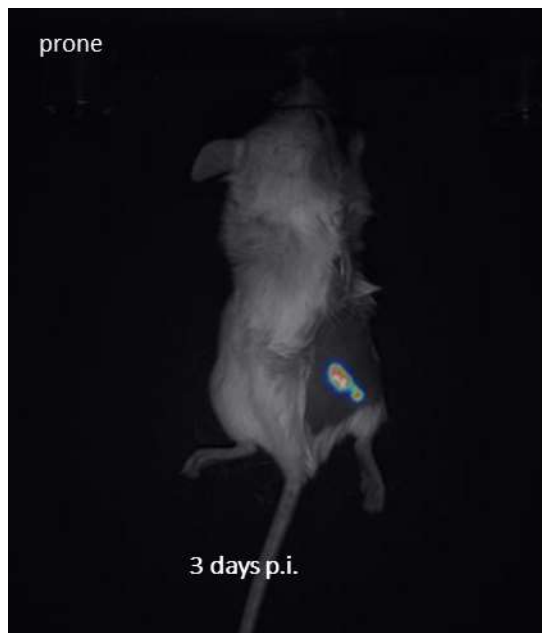
Fluorescent dye	Cy5
Infarction surgery	Thoracotomy and ligation at the level of the left-anterior descending (LAD) coronary artery (CA) approx. 4mm from the left auricle
Animal depilation	Depilation of fur over thorax and abdomen with cream, prior to imaging
Administration route	Intracardiac injection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



## Bioluminescence studies

### ○ U87MG-Luc2 cells – *in vivo* imaging

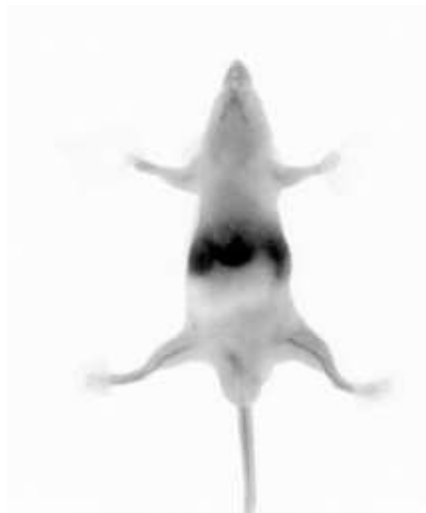
<b>Bioluminescent probe</b>	Luc2
<b>Mouse model</b>	Inoculation of $10^6$ U87MG-Luc2 cells to female SCID mice
<b>Animal depilation</b>	Depilation of fur over spine with cream, prior to imaging
<b>Administration route</b>	3mg of D-luciferin in 200ul saline (VivoGlo Luciferin) were administered intraperitoneally (IP)
<b>Imaging</b>	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**

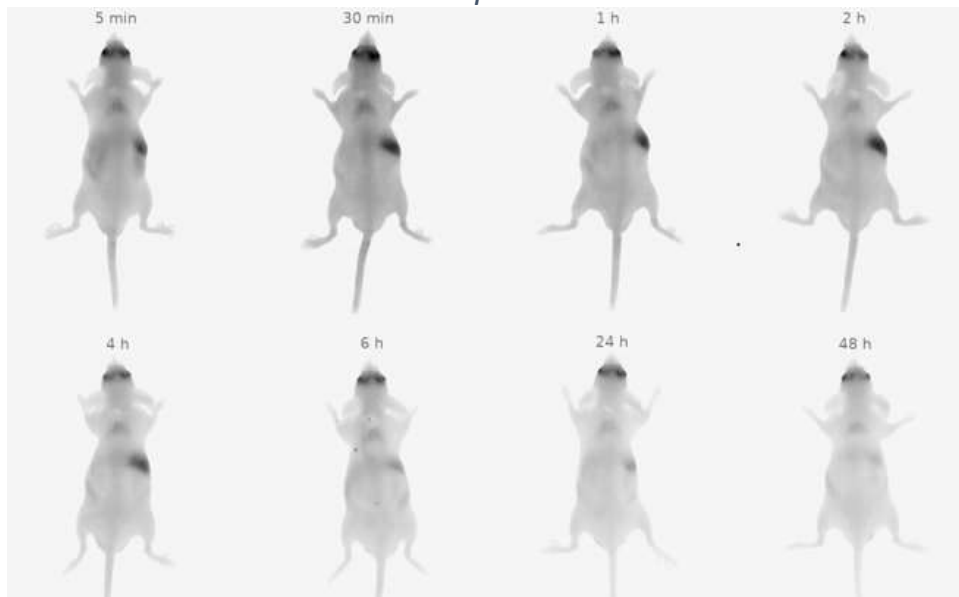
<b>SWIR probe</b>	ICG
<b>Model</b>	SKH-1 hairless albino
<b>Administration route</b>	500uM @ 100uL; Intravenous
<b>Imaging</b>	1 min post-injection
<b>Exposure time</b>	5 ms



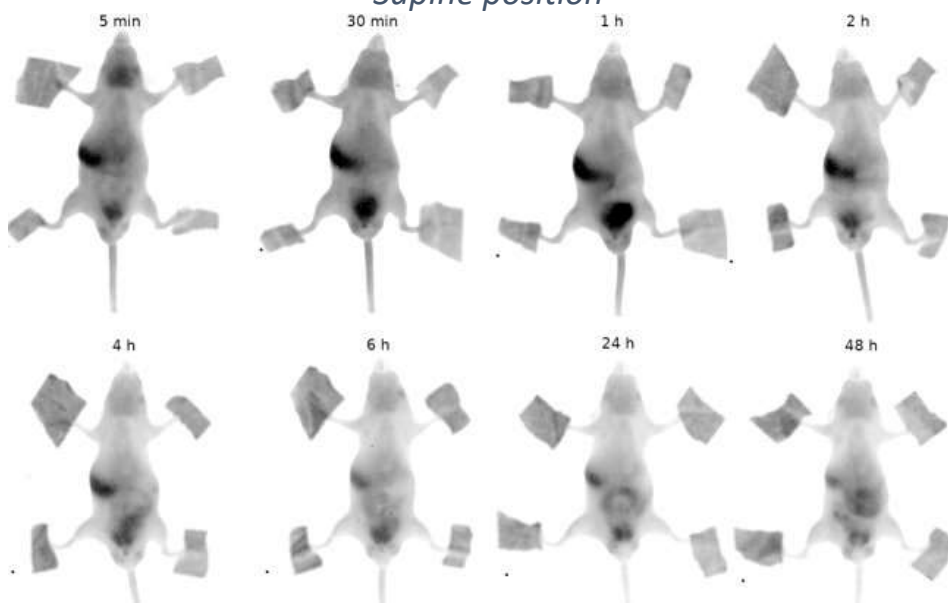
- **IRDye 800CW *in vivo* imaging**

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

*Prone position*



*Supine position*





  
BIOEMTECH

Lefkippos Attica Technology Park-N.C.S.R Demokritos, Greece

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