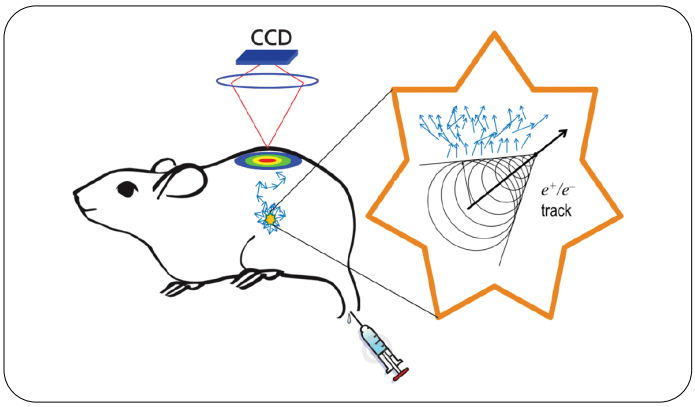
Cerenkov emission from radioisotopes in tissue.

Optical imaging detects photons in the visible range of the electromagnetic spectrum. PET and SPECT imaging instruments are sensitive to photons in the much higher energy range of x-rays and gamma rays. While the PET and SPECT probes which can generate Cerenkov light in tissue will continue to produce the relevant gamma- and x-rays, visible photons will be produced from the Cerenkov emission, which the IVIS® optical imaging platform will detect.

In beta decay emitters such as PET probes and isotopes such as ^{90}Y, ^{177}Lu, ^{131}I and ^{32}P, the beta particle will travel in the tissue until it either annihilates with an electron or loses momentum due to viscous electromagnetic forces.

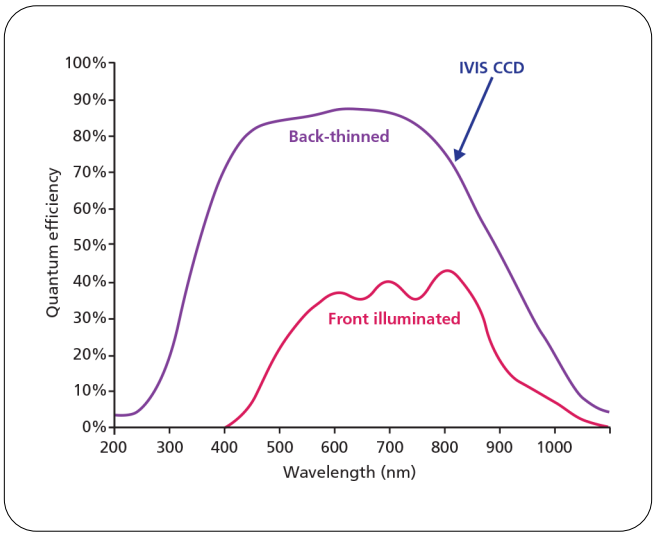
It is possible that the beta (electron or positron) is relativistic, traveling faster than the speed of light in the tissue. While it is impossible to travel than the speed of light in a vacuum (c), the speed of light in tissue is $v = c / n$, where n is the tissue index of refraction and $n \geq 1$. Cerenkov photons will be generated by a relativistic charged particle in a dielectric medium such as tissue.



Highly sensitive CCD's

As these photons are in the visible wavelength band, the imaged photons are subject to scattering and absorption by the tissue to the degree that their propagation can be approximated as a diffuse process. The photons eventually reach the animal surface and are imaged by the highly sensitive CCD camera.

IVIS CCD cameras are optimal for imaging the low photon counts generated by Cerenkov emission from radioisotopes as the CCD's are cooled to -90 °C, and back-thinned with a high quantum efficiency (>80%) over 450 nM – 750 nM. These characteristics offer a low read noise of ~ 3 e RMS and a dark current of $< 4 \times 10^{-4}$ e/sec/pixel at -90 °C. The high resolution CCD's are 1024 or 2048 pixels on a side with 13 µM pixel size. For improved sensitivity necessary for Cerenkov imaging, the pixels can be binned up to 16 x 16, and integration times range from 0.5 seconds to 10 minutes.



Radioisotope biodistribution optical imaging with DyCE

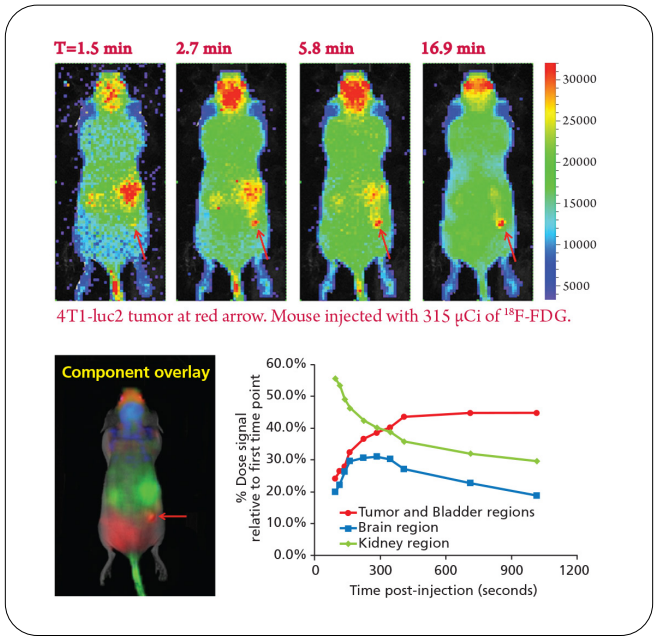
Biodistribution curves of radioisotopes can be determined by imaging in the IVIS and analyzing the images in DyCE™ software.

^{18}F-FDG kinetics

A mouse bearing a subcutaneous 4T1-luc2 tumor in its right flank was injected with 315 µCi of ^{18}F-FDG intravenously. 55 seconds post-injection, the animal was imaged dynamically starting 55 seconds post-injection to capture the distribution of ^{18}F-FDG in the mouse body via Cerenkov light from positron emission. No luciferin was administered to the mouse to avoid contamination of luciferase signal into the Cerenkov signal.

DyCE was applied to the series of 2D time-domain 'Open' filter images of Cerenkov light emission from positron emission. DyCE characterizes the temporal change in pixel intensities of the 2D images.

Without a priori identification of organ regions, the unmixed component amplitudes map to pixel regions in the 2D image which can be associated with anatomical features. By corresponding pixel color-mapping to component temporal evolution, kinetics of ^{18}F-FDG can be characterized.

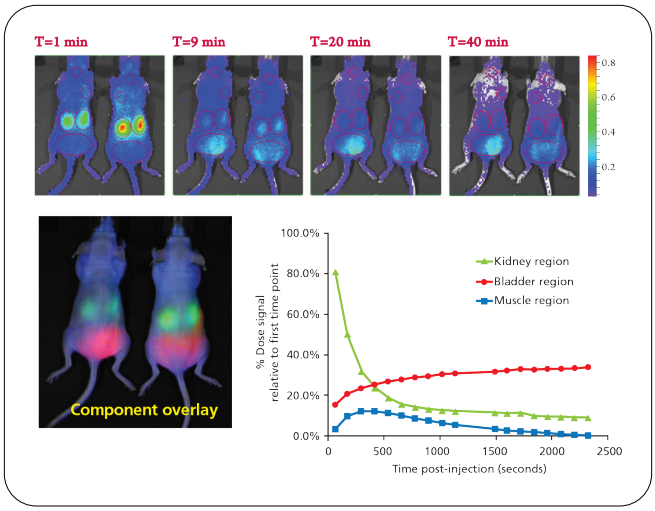


^{90}Y-AABD kinetics

Mice injected with 10 µCi of ^{90}Y-AABD and imaged dynamically in optical imaging system starting 55 seconds post-injection. Imaging parameters: 60 second exposures at bin level 16 and f-stop 1, dorsal imaging using the 'Open' filter.

^{90}Y is a beta-minus emitting isotope where optical imaging of Cerenkov radiation is the only means for *in vivo* characterization of biodistribution in small animals. DyCE was performed to determine kinetics of ^{90}Y-AABD. Relative abundances of tracer uptake are associated in the kidneys, muscle and brain regions in the 2D component overlay image.

Cerenkov emission from radioisotopes in tissue.



Summary

Cerenkov imaging of radiopharmaceuticals injected in small animals is a low-cost solution to PET and SPECT instrumentation.

IVIS systems have highly sensitive CCD camera required for the low signal Cerenkov light, and offer high signal to noise ratios.

High animal throughput is also available in all IVIS systems, where up to 5 animals can be imaged in 2D simultaneously.

Kinetics of PET probles and radio-therapeutics such as ^{90}Y and ^{131}I can be followed with optical imaging and analyzed with DyCE.

Table 1: List of radioisotopes produced and distributed by Revvity. Those which will produce Cerenkov Light *in vivo* are highlighted in green. Through its worldwide distribution capabilities, Revvity can assure delivery of materials to many areas of the world soon after production. If you require additional information on a specific isotope or information on a product that is not listed below, please contact us at www.revvity.com

Isotopes suitable for Cerenkov imaging	Half-life	Radiation	Kinetic energy (keV)	Application
Iodine-124	4.2 days	Beta+ (β^+)	686 974	*In Vivo* Imaging-Cerenkov Immuno-PET
Iodine-131	8.04 days	Gamma (γ) Beta- (β^-)	364 637 284 606	β- Therapy *In Vivo* Imaging-Cerenkov & SPECT
Phosphorus-32* No Carrier Added in water	14.29 days	Beta- (β^-)	1710	*In Vitro* assays *In Vivo* Imaging-Cerenkov
Yttrium-90	64.1 hours	Beta- (β^-) Beta+ (β^+)	2.28	β- Therapy PET Calibration *In Vivo* Imaging-Cerenkov & PET
Zirconium-89* No Carrier Added in 1M Oxalic Acid pH <4	78.41 hours	Beta+ (β^+)	396	*In Vivo* Imaging-Cerenkov & Immuno-PET
Lutetium-177	6.64 days	Beta- (β^-) Gamma (γ)	0.50 208	β- Therapy *In Vivo* Imaging-SPECT Cerenkov

* Available from Revvity

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