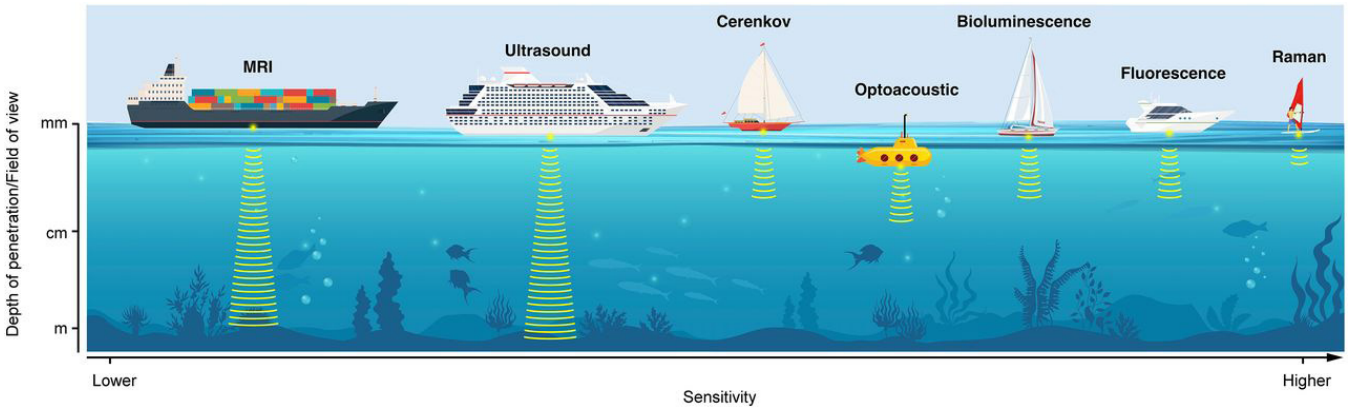
Comparing **In Vivo Optical Imaging** to Other Modalities (CT/PET/SPECT/MRI/US)

WHAT IS IN VIVO OPTICAL IMAGING?

In Vivo Optical Imaging is a non-invasive technique used to monitor and visualize biological processes, disease progression, and therapeutic efficacy of drugs in longitudinal preclinical studies involving small animal models. This modality primarily employs bioluminescent and fluorescent probes, but also offers crossover applications, such as Cerenkov imaging which utilizes the light emission from many commonly used medical isotopes.

WHAT ARE OTHER IMAGING TECHNIQUES USED IN PRE-CLINICAL RESEARCH?

- **MRI** - Magnetic Resonance Imaging provides high spatial resolution and is used for the detection and extraction of physiological, molecular, and anatomical information. However, it is both time consuming and cost prohibitive.
- **CT** - Computed Tomography imaging offers high spatial resolution and depth of penetration. However, CT uses ionizing radiation, can have limited throughput and limited sensitivity, and often requires contrast for soft tissues.
- **PET** - Positron Emission Tomography imaging is a quantitative, highly sensitive imaging technique that offers excellent penetration depth and spatial resolution. However, it is best suited to fast assay kinetics, requires radionuclide use, and has limited spatial resolution.
- **SPECT** - Single-Photon Emission Computed Tomography is a nuclear imaging technique that employs a radioactive tracer and computed tomography (CT). SPECT imaging allows different radioisotopes labeling simultaneously. It offers high penetration depth. However, it is limited to tracing slow assay kinetics, requires radionucleotide use, and offers limited spatial resolution.
- **US** - Ultrasound generates structural images via differing reflections of high-frequency sound waves. Ultrasound has limited sensitivity, and image quality is highly operator-dependent.



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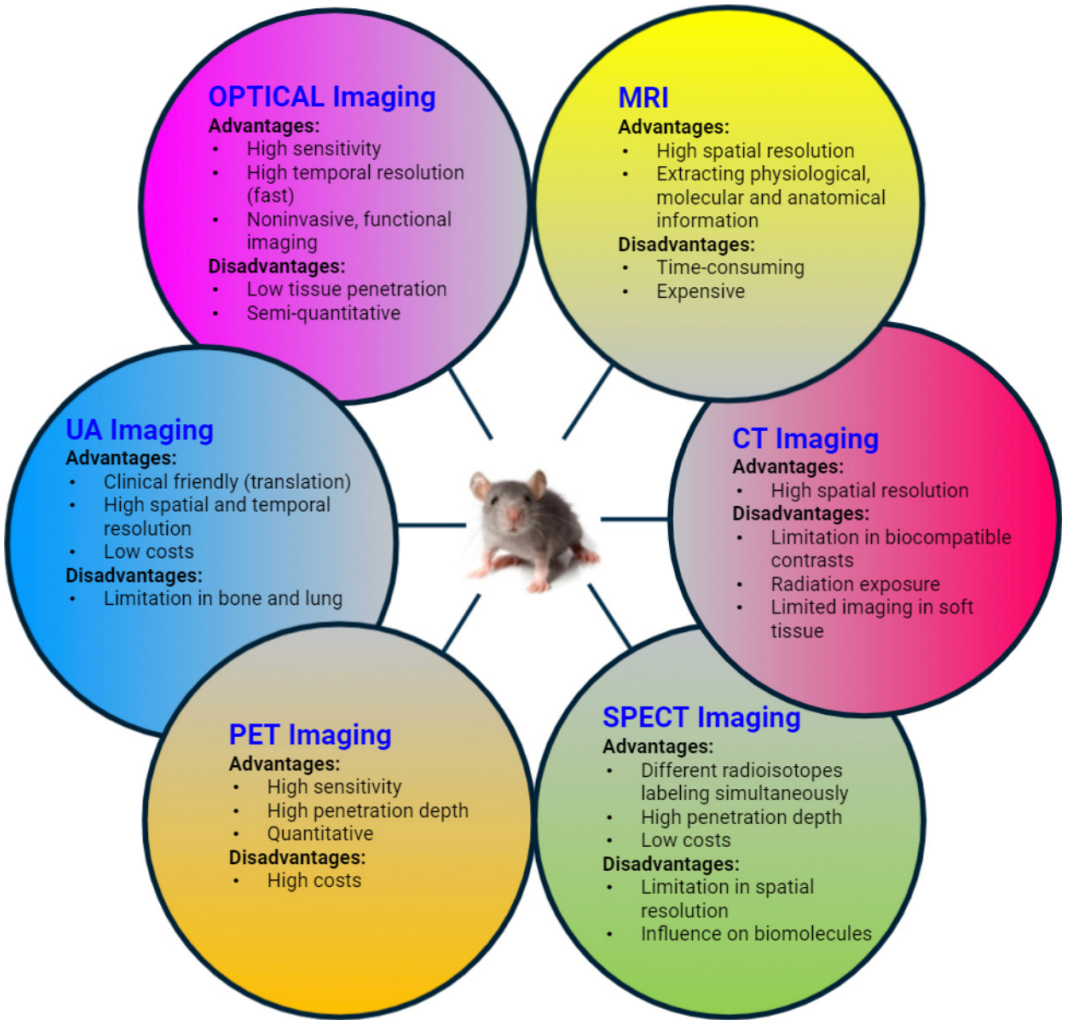
COMPARING PRECLINICAL IMAGING MODALITIES: PROS & CONS

All of these modalities offer in vivo , non-invasive tracking of cells, cellular process, and tissue changes - with pros and cons to each modality. Multimodality imaging can help overcome the limitations of an individual modality.



Huang Y., et al. 2012 Biomedical Nanomaterials for Imaging - Guided Cancer Therapy

HOW IS IN VIVO OPTICAL IMAGING DIFFERENT FROM OTHER MODALITIES?

The above mentioned modalities are very good for resolving cellular level structures. However, when a model system is initiated and cells are injected into it, it may take weeks to get to the point where you are looking at cellular level structures that are of a size that can be resolved with CT or MRI.

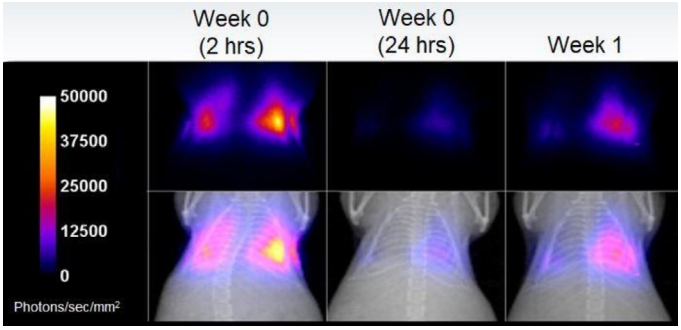
In Vivo Optical Imaging is different from other preclinical imaging modalities in a variety of ways that make it more efficient. Some of the features of *In Vivo* optical imaging that give it an edge over other modalities like CT, MRI, PET SPECT and US are as follows:

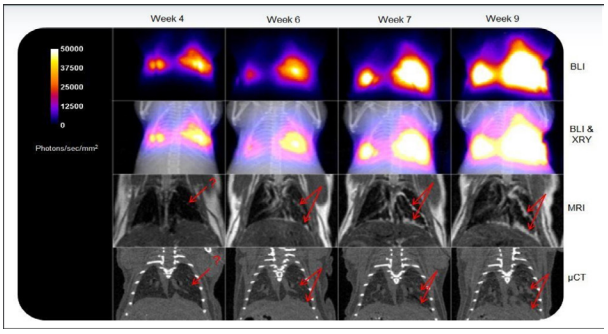
- **High Sensitivity**

  Cutting edge sensitivity - For instance in the Lago X imaging system, the minimum detectable radiance is 45 photons/sec/cm^2/sr. Furthermore, Bioluminescence in vivo imaging is sensitive enough to quantitate and detect signal for as low as 10–17 moles/L of luciferase enzyme.

  Early-onset Detection - Luciferase expression can be readily validated with in vitro assays prior to use in a model. Expression within the model can then be easily visualized shortly after introduction, particularly in orthotopic tumor models.

  In an experiment involving an orthotopic lung carcinoma model in mice, In Vivo Optical Imaging results were compared with that of µCT and MRI. After only 2 hours of injecting the labeled cells, light emitted from luciferase activity was detectable. In the following weeks signals keep growing stronger. In comparison, In MRI and µCT performed for the same experiment, lesions of tumor mass development became detectable after almost 4 weeks.



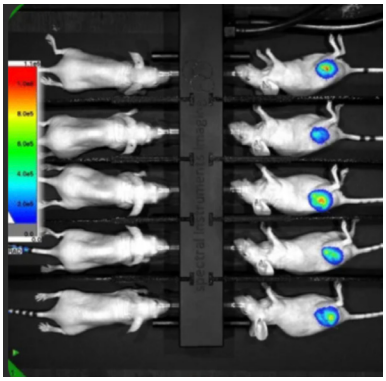


Van Praagh A., et al. 2017. Bruker BioSpin, World Molecular Imaging Conference, Abstract ID: 2730570

- **Screening Modality** - Early onset detection enables screening of mice early on in the experiment which is not possible in other techniques.

- **Fast, Real-time Data acquisition**
  With In Vivo Optical Imaging, the data acquisition is quite fast and enables the detection of biological processes in real-time. Data acquisition takes only between 5 to 20 seconds. By comparison PET and SPECT Imaging takes at least a few minutes upto half an hour, while data acquisition in MRI takes almost an hour.

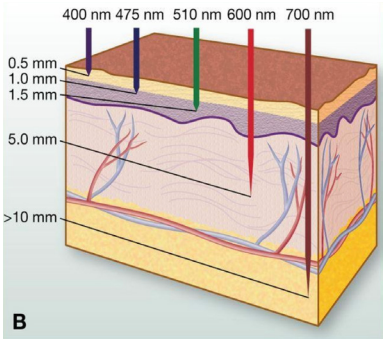
- **High Throughput Screening**
  In Vivo Optical Imaging offers a wider field of view (FOV) as compared to other imaging modalities such that 5 to 10 mice can be viewed at the same time. It enables you to create a large "n" data set for the accumulation of strong statistical data.



Courtesy of S. Hori, S. Lee, Sanjiv , and S. Gambhir. Canary Center at Stanford U. School of Medicine

LIMITATIONS OF IN VIVO OPTICAL IMAGING

A limitation of this technique is the limited penetration of light through the tissues due to absorption of light by oxygenated haemoglobin and melanin. Therefore, it is beneficial to select a probe that requires a light having a wavelength of 700 to 1000 nm for optimal imaging results.



Keereweer, S. et. al. 2013 Optical Image-Guided Cancer Surgery--Challenges and Limitations

CONCLUSION

Although In Vivo Optical Imaging has its own unique strengths, most preclinical investigations do require a combination of different imaging modalities to gather data. The high sensitivity, early onset detection, high throughput screening and fast real time data acquisition of In Vivo Optical Imaging give it an advantage over other imaging modalities.