

# What is Optical Imaging?

Optical imaging uses light to interrogate cellular and molecular function in the living body, as well as in animal and plant tissue. The information is ultimately derived from tissue composition and biomolecular processes. Images are generated by using photons of light in the wavelength range from ultraviolet to near infrared.

Contrast is derived through the use of:

- exogenous agents (i.e., dyes or probes) that provide a signal
- endogenous molecules with optical signatures (i.e., NADH, hemoglobin, collagens, etc.)
- reporter genes.

## Florescence Imaging

Fluorescence protein imaging uses endogenous or exogenous molecules or materials that emit light when activated by an external light source such as a laser. An external light of appropriate wavelength is used to excite a target molecule, which then fluoresces by releasing longer-wavelength, lower-energy light.

Fluorescence imaging provides the ability to localize and measure gene expression including normally expressed and aberrant genes, proteins and other pathophysiologic processes. Other potential uses include cell trafficking, tagging superficial structures, detecting lesions and for monitoring tumor growth and response to therapy.

## Bioluminescent Imaging (BLI)

Bioluminescent imaging uses a natural light-emitting protein such as luciferase to trace the movement of certain cells or to identify the location of specific chemical reactions within the body.

Bioluminescent imaging is being applied to both gene expression and therapeutic monitoring.

## Optical Imaging Technologies

**Near-infrared fluorescence imaging** involves imaging fluorescence photons in the near-infrared range (typically 600–900 nm). A fluorochrome is excited by a lower wavelength, light source and the emitted excitation is recorded as a slightly higher wavelength with a high sensitivity charge-coupled-device (CCD) camera.

**Diffuse optical tomography (DOT)** is based on diffuse light that penetrates tissue at multiple projections yielding tomographic images. DOT uses arrays of lasers and detectors in multiple geometric configurations around the object.

An important milestone for in vivo optical imaging, DOT can provide quantitative information about light absorption, scatter and uptake of fluorescence contrast agents. The most widely used type of DOT, which offers a spatial resolution of several millimeters, measures changes in blood oxygenation caused by neural activity.

**Diffuse optical spectroscopy (DOS)** combines multi-frequency intensity-modulated and continuous-wave nearinfrared light to quantify tissue absorption and scattering spectra from 650 to 1000 nm. DOS allows quantitative analysis of tissue chromophore concentrations of oxyhemoglobin, deoxyhemoglobin, methemoglobin, water, and lipid.



**Confocal microscopy** is a method of optical microscopy by which structures in the focal plane are visible and those outside the focal plane are suppressed. The scanning of the focal plane through the object being imaged enables the collection of three-dimensional microscopic image data sets. It offers several advantages over conventional optical microscopy, including controllable depth of field, the elimination of image degrading out-of-focus information and the ability to collect serial optical sections from thick specimens.

Other optical imaging systems technologies include:

- Coherent anti-Stokes Raman scattering (CARS)
- surface-weighted imaging
- phase-array detection
- multiphoton imaging
- intravital microscopy

## Clinical Applications

- fluorescence imaging is entering initial clinical testing in areas such as breast imaging and endoscopy
  - using ultrasound localization, diffuse optical tomography is able to measure light absorption within breast tissue to quantify hemoglobin content and blood oxygen levels to help differentiate early state cancers from benign lesions.
  - diffuse optical spectroscopy of hemoglobin and deoxyhemoglobin in breast tumors also shows promise as a biomarker for effective neoadjuvant chemotherapy in cancer patients.
- detection of:
  - ovarian cancer
  - superficial malignant skin lesions
  - lymphoma
  - intestinal adenoma
- intraoperative scanning
- stem cell trafficking
- monitoring treatment response

## Advantages

- confocal microscopy is able to provide real-time information to help guide surgeons during endoscopy and surgery
- exquisite sensitivity and resolution.

## Limitations

- able to penetrate only few centimeters deep
  - absorption and scatter
  - lack of mainstream clinical instrumentation.
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## Research

The application of optical imaging to date has been largely in animal and in vitro models, although clinical use is increasing, especially when endoscopic evaluation is possible and in the study of gynecologic malignancies, the colon and heart.

A great deal of basic research is performed with cellular and animal models of disease. Optical molecular imaging techniques have become essential tools for studying small-animal models, providing unique insights into disease pathogenesis, drug development and the effects of therapy.

In practice, molecular imaging can complement and in some cases, replace conventional laboratory techniques. Optical imaging allows for noninvasive, repetitive in vivo imaging of dynamic biological processes.

Both bioluminescence and fluorescence imaging have been used to assay pharmacodynamics of therapeutic agents in vivo, establishing dosing parameters to guide initial clinical trials and eventual clinical applications.

## Optical Imaging on the Horizon

Under development within the field of optical imaging are:

- new molecular probes and nanomaterials, including:
  - imaging probes based on near-infrared fluorescence that detect lesions a few centimeters deep in tissue
  - contrast agents targeted to specific molecules, especially agents in which fluorescence is quenched until released by a specific enzyme or defined target.
  - tissue-specific multi-modal imaging molecules that can be used in hybrid imaging systems, combining optical with PET or SPECT
  - quantum dots, fluorescent nanoparticles that emit light when exposed to ultraviolet light, for use in treating cancer and other diseases
- dynamic mapping of cellular transformations at the molecular level, providing a visual picture of the dynamics of proteins, DNA, RNA and lipids during cell disintegration.
- photoablation therapy, in which gold nanospheres are heated with near-infrared light to treat melanoma
- the use of diffuse optical tomography to distinguish malignant from benign breast lesions
- photodynamic therapy
- photoacoustic tomography or laser-induced ultrasound

## Photoacoustic Tomography (PAT)

In photoacoustic tomography, a short-pulsed laser beam is directed at the area of the body being studied. Some of the



light is absorbed and partially converted to heat, which causes a thermo-elastic expansion and a rise in pressure. This rise in pressure creates an ultrasonic or photoacoustic wave, which can be detected by a transducer. Ultrasonic scattering in biological tissue is much weaker than optical scattering, allowing for high spatial resolution at depths beyond the optical diffusion limit.

Potential clinical applications of PAT include:

- melanoma cancer screening
- gastrointestinal tract and colon endoscopy
- neonatal and adult brain imaging
- breast cancer imaging
- prostate cancer imaging
- image-guided sentinel lymph node needle/core biopsy for cancer staging
- early prediction of response to chemotherapy
- dosimetry in thermal therapy
- blood flow, oxygenation and tissue metabolism imaging.

#### **About SNMMI**

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Society of Nuclear Medicine and Molecular Imaging  
1850 Samuel Morse Drive  
Reston, VA 20190  
[www.snmmi.org](http://www.snmmi.org)  
[www.discovermi.org](http://www.discovermi.org)

