

Diffuse optical tomography (DOT) is emerging as a viable new biomedical imaging modality. Using visible and near-infrared light, in the range of 500 to 900 nm, this technique can probe absorption as well as scattering properties of biological tissues. The main applications are currently in brain, breast, limb, and joint imaging; however, the area of optical tomographic imaging of small animals is attracting increasing attention. This interest is mainly fueled by recent advances in transgenic manipulation of small animals that has led to many models of human diseases. Using these models it is possible to link specific genes, proteins, and enzymes to molecular, and cellular processes that underlie various disorders. In addition, the advent of novel biochemical markers that are sensitive to molecular processes, defect genes, and cell receptors, makes it for the first time possible to detect diseases on a molecular level long before actual phenotypical symptoms appear.

Small animal optical tomography has several advantages over other, more traditional, imaging modalities. For example, optical markers emit low-energy near-infrared photons that are less harmful than more energetic gamma rays emitted from radioactive markers (used in SPECT and PET, for instance). This simplifies synthesis procedures and experimental designs and will be of particular importance for future applications in humans. Furthermore, optical methods typically offer higher sensitivity (as compared to MRI and SPECT) and are relatively inexpensive (as compared to PET, SPECT, and MRI).

In this paper we will review underlying principles in optical tomographic imaging as they apply to studies involving small animals. We will describe the basic contrast mechanism involved in imaging of endogenous as well exogenous contrast agents. In addition we will discuss specific features and advantages of different types of optical instrumentation currently available, such as steady-state, frequency-domain, and time-resolved imaging systems. Furthermore we will describe in detail the structure of commonly used image reconstruction schemes and algorithms and point to still existing challenges. Finally, we will provide an overview of the most recent literature in optical small animal imaging, specifically in the areas of blood oximetry, fluorescence and bioluminescence imaging.

**Educational Objectives:**

1. To understand significance, potential, and limits of optical tomographic small animal imaging.
2. To understand the contrast mechanisms that underlie optical tomographic imaging.
3. To understand the basic measurement instrumentation used in optical tomographic imaging.
4. To understand the fundamental concepts and problems involving optical tomographic image reconstruction algorithms.
5. To learn about the major applications of this novel technology.