Abstract: After almost two decades of active development optoacoustic tomography is entering the real world of clinical applications, with diagnostic imaging of breast cancer being the first major market niche for this technology where existing modalities have apparent drawbacks. We will present a number of system designs for optoacoustic mammography that show tissue structures in 2D and 3D with high sensitivity (contrast) / resolution, and discuss their advantages and limitations [1]. The main value of OAT is in its potential capability to provide functional and molecular information based on quantitatively accurate display of the optical absorption coefficient. However, quantitatively accurate OAT has not been demonstrated yet. We believe that only a full view three-dimensional tomography system that acquires complete set of forward data and uses rigorous solutions for inverse problem of image reconstruction have the potential for success in the breast cancer diagnostics. But even the full view design has challenges when providing quantitatively accurate information due to a large number of unknown parameters, separately distributed in the volume of tissue being examined. These parameters might be determined with sophisticated math-physics methods. As a step in this direction, we presently combine advantages of laser optoacoustics and ultrasound tomography as a hybrid dual-modality. The optoacoustic sub-system provides images based on distribution of molecular chromophores in the body absorbing near-infrared light, yielding functional images of the total hemoglobin [Hb] and blood oxygen saturation [SO2] as well as molecular images of targeted contrast agents. The ultrasound sub-system provides anatomical images of tissue structures and can also provide the speed of sound (SoS) and acoustic attenuation images, which can be used for iterative reconstruction of more accurate optoacoustic images. A review of our research efforts advancing biomedical applications of the three-dimensional optoacoustic tomography system in preclinical imaging using small laboratory animals and clinical application in diagnostic imaging of breast cancer will be presented and challenges of achieving further progress will be outlined.