1 Introduction

Photoacoustic (PA) imaging is poised to fill a large gap in clinical imaging; PA imaging can provide resolution far beyond ultrasound and comparable to magnetic resonance imaging or computed tomography, but with a small, relatively low cost device that can fit into a hand-held scanner. PA imaging has great potential for the visualization of physiology and pathology molecularity due to its superior tissue penetration depth and good spatial resolution.[1] Endogenous contrast agents with high optical absorption, such as hemoglobin and melanin, can be imaged with better spatial resolution than with pure optical imaging, and the imaging resolution is not limited by strong light scattering in deep biological tissues. In PA imaging, a short-pulsed laser is used to irradiate the tissue, and a focused ultrasonic transducer then detects the PA waves generated via thermoelastic expansion (Fig. 1). The acquired PA data are used to quantify the optical absorption distribution and then construct the tissue structure. In some situations, when endogenous contrast is unavailable (e.g., solid tumors and lymph nodes), exogenous contrast agents are employed to resolve such a problem. In addition to the improvement in imaging contrast, they can also enhance the imaging depth as they absorb light strongly in the near-infrared range (NIR, also known as an optical window or therapeutic window). Moreover, nanomaterials with strong NIR absorption have great potential to serve as PA contrast agents due to their preferential accumulation in tumor tissue, which is because of the enhanced permeability and retention effect. Nowadays, design of contrast agents that produce a sufficient PA signal in a low concentration is still challenging.

To date, the best existing exogenous contrast agents are based on gold nanoparticles (GNPs), which are potentially toxic in the 30 to 70 nm range that is optimum for PA imaging and suffers from the shape deformation upon high energy laser exposure.[3] Organic dyes are also extensively used in PA imaging, but their small size (<2 nm) leads to their nonspecific distribution to a wide range of tissue, causing a low imaging contrast in the region of interest against surrounding

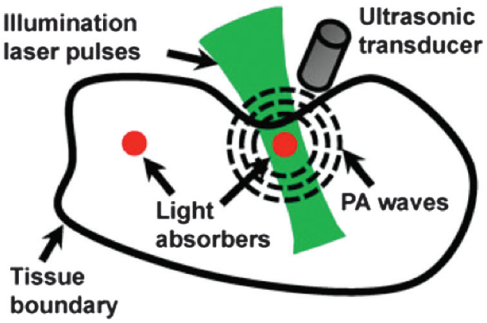

Figure 1 Illustration of the photoacoustic (PA) effect and PA imaging. Reproduced with permission from Ref. 2. Copyright 2011, John Wiley and Sons.