Detection and removal of melanoma, before it has metastasized, dramatically improves prognosis and survival. The purpose of this chapter is to (1) summarize current methods of melanoma detection and (2) review state-of-the-art detection methods and technologies that have the potential to reduce melanoma mortality. Current strategies for the detection of melanoma range from population-based educational campaigns and screening to the use of algorithm-driven imaging technologies and performance of assays that identify markers of transformation. This chapter will begin by describing state-of-the-art methods for educating and increasing awareness of at-risk individuals and for performing comprehensive screening examinations. Standard and advanced photographic methods designed to improve reliability and reproducibility of the clinical examination will also be reviewed. Devices that magnify and/or enhance malignant features of individual melanocytic lesions (and algorithms that are available to interpret the results obtained from these devices) will be compared and contrasted. In vivo confocal microscopy and other cellular-level in vivo technologies will be compared to traditional tissue biopsy, and the role of a noninvasive "optical biopsy" in the clinical setting will be discussed. Finally, cellular and molecular methods that have been applied to the diagnosis of melanoma, such as comparative genomic hybridization (CGH), fluorescent in situ hybridization (FISH), and quantitative reverse transcriptase polymerase chain reaction (qRT-PCR), will be discussed. KEYWORDS: Atypical nevi; Dermoscopy; Fluorescence in situ hybridization (FISH); Gene expression profiling; Hyperspectral imaging; In vivo confocal microscopy; Melanoma detection; Melanoma digital photography; Melanoma prevention; Melanoma screening; Optical biopsy; Optical coherence tomography; Quantitative real-time PCR (qRT-PCR) PMID: 26601859