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*Invited Perspective*

# In a "nutshell": intrinsically radio-labeled quantum dots

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**Abstract:** Quantum dots (QDs) have many intriguing properties suitable for biomedical imaging applications. The poor tissue penetration of optical imaging in general, including those using QDs, has motivated the development of various QD-based dual-modality imaging agents. In this issue of AJNMMI (http://www.ajnmmi.us), Sun et al. reported the synthesis and in vitro/in vivo characterization of intrinsically radio-labeled QDs (r-QDs), where $^{109}$Cd was incorporated into the core/shell of QDs of various compositions. These r-QDs emit in the near-infrared range, have long circulation half-life, are quite stable with low cytotoxicity, exhibit small size and low accumulation in the reticuloendothelial system, and can allow for accurate measurement of their biodistribution in mice. With these desirable features demonstrated in this study, future development and optimization will further enhance the biomedical potential of intrinsically radio-labeled QDs.

**Keywords:** Quantum-dots (QDs), nanoparticle, positron emission tomography (PET), single-photon emission computed tomography (SPECT), near-infrared (NIR), optical imaging

The first decade of the 21st century has witnessed an explosion of biomedical research based on various nanomaterials, which hold tremendous potential to revolutionize disease diagnosis and treatment [1-3]. In the second decade of this century, clinical translation is the key in this vibrant research area and it is expected that nanotechnology will advance into clinical trials and eventually the day-to-day clinical practice in the near future. In this blooming nanotechnology arena, one of the most extensively studied classes of nanomaterials is quantum dots (QDs) [4, 5]. Due to the many intriguing properties that are more advantageous than traditional organic dyes, QDs are desirable fluorophores for biomedical imaging applications. Since the first demonstration of the biomedical potential of QDs in 1998 [6, 7], QD-based research has increased exponentially and QDs have become powerful tools in an array of research disciplines such as molecular biology, cell biology, molecular imaging, and medical diagnostics. For imaging applications, QDs have been investigated in a wide variety of scenarios in both cells and live animals. Aside from applications based on non-specific distribution/accumulation of QDs such as vasculature imaging, lymph node mapping, etc. [4, 5, 8], active tumor targeting using QD-based probes has also been achieved by several research groups [9-13].

One of the major limitations for optical imaging in general is poor tissue penetration, even in the relatively optically clear near-infrared (NIR, 700-900 nm) window [14-16]. Since magnetic resonance imaging (MRI) has no limit in tissue penetration, a wide variety of QD-based dual-modality agents have been reported for both optical imaging and MRI [17, 18]. However, the very low sensitivity of MRI severely limits the potential applications of these QD-based dual-modality agents. Furthermore, whether combination of optical imaging and MRI is a desirable approach is questionable, since neither imaging technique is highly quantitative. On the other hand, radionuclide-based imaging techniques, such as single-photon emission computed tomography (SPECT) and positron emission tomography (PET) [19, 20], are very sensitive and highly quantitative with virtually no limit in tissue penetration. Clinically, PET/SPECT imaging has been widely used in oncology for cancer staging and monitoring the therapeutic re-