Chemistry of Contrast Media

Particles and Polymers

Particles and Polymers for Optical Imaging

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Learning Objectives:

- Understand the advantages and disadvantages of various imaging modalities
- Understanding of established optical probes and their uses, both clinical and preclinical
- Understand the synthesis and unique characteristics (e.g. preparation, spectral properties, doping and size) of quantum dots for optical imaging
- Understand the biocompatibility aspects (e.g., toxicity of metals and coatings) of quantum dots compared to other contrast agents used for optical imaging

Despite the limitations of poor tissue penetration and high scatter (relative to PET/PECT, CT, and MRI) optical imaging is relatively inexpensive, portable, and offers the potential for high sensitivity and spatial and temporal resolution. Near-infrared (NIR) light 700-900 nm propagates through tissues due to minimal DNA and water absorption. Most in vivo applications for optical imaging employ NIR fluorescent dyes, but gold nanoparticles, carbon nanotubes and quantum dots are also important. For optical imaging, cyanine dyes are important synthetic molecules since many fluoresce in the NIR. Of these Indocyanine Green (ICG) has the longest history and continues to garner interest because it is FDA approved for systemic delivery. However, the qualities that make it good for cardiac output measurement, i.e., plasma binding and fast plasma clearance, are poor for in imaging. It also suffers from poor stability in aqueous solutions. To improve plasma residence, stability and tissue targeting, the dyes can be loaded into polymer nanoparticles and liposomes. A strong size dependent localized Surface Plasmon Resonance (SPR) absorption is observed with many metallic nanoparticles. Gold, due to its inertness and surface functionalization, has attracted much interest for imaging. Single walled carbon nanotubes (SWCNT) are also attractive for imaging. They are basically hollow cylindrical molecules of carbon atoms, open or capped at the ends, with high aspect ratios of as small as one nm in diameter to as much as several cm in length. In general, they are non-toxic and hydrophobic but can be made water soluble by surface modifications reducing the tendency to agglomerate. Surface modification can also be exploited for targeting. They possess strong absorbance in the NIR, but they have low fluorescent quantum yield relative to fluorescent dyes, gold and quantum dots, and concerns persist regarding their long-term toxicities, particularly if inhaled. Quantum dots (QDs), semiconductor crystal materials, offer the advantages of very high quantum yield, stability, almost no quenching or bleaching, and can be produced in a rainbow of colors, from visible to the NIR, depending on their size. Emission frequencies increase as QD size decreases, causing a color shift from red to blue in the emitted light and they can be made in tunable emission/excitation combinations. QDs have been studied extensively for in vitro cell imaging, but to be translated to human in vivo use problems associated with the general toxicity of semiconductor materials must be overcome. QDs tend to be hydrophobic and cannot be used in aqueous solutions unless their surfaces are modified. With surface modification their hydrophilicity can be increased and their toxicity decreased. This talk will focus on comparing imaging modalities, concentrating on optical imaging, and go into greater depth regarding the application of quantum dots and efforts to reduce their toxicity and translation to in vivo use.

Relevant Publications:

1. Srinivasan, S. R. Manchanda, A. Fernandez-Fernandez*, T. Lei*, A. J. McGoron. Near-Infrared Fluorescing IR820-Chitosan Conjugate for Multifunctional Cancer Theranostic Applications, Journal of Photochemistry and Photobiology B: Biology 119:52-59, 2013.
2. Manchanda, R., A. Fernandez-Fernandez, D.A. Carvajal*; T. Lei*, Y. Tang, A.J. McGoron. Nanoplexes for Cell Imaging and Hyperthermia: In vitro Studies. J of Biomedical Nanotechnology. 8:699-707, 2012.
3. Fernandez-Fernandez, A, R. Manchanda, T. Lei, D. Carvajal, Y. Tang, S. Kazmi*, A.J. Mcgoron. A Comparative Study of Optical and Heat Generation Properties of IR820 and Indocyanine Green. Mol Imaging. 11(2):99-113. 2012. DOI 10.2310/7290.2011.00031
4. Fernandez-Fernandez, A., R. Manchanda, A.J. McGoron. Theranostic Applications of Nanomaterials in Cancer: Drug. Delivery, Image-Guided Therapy, and Multifunctional Platforms. Appl Biochem Biotechnol. 165(7-8):1628-51, 2011.
5. Lei, T., S. Srinivasan, Y. Tang*, R. Manchanda, A. Nagesetti, A. Fernandez-Fernandez, A.J. McGoron. Comparing Cellular Uptake and Cytotoxicity of Targeted Drug Carriers in Cancer Cell Lines with Different Drug Resistance Mechanisms. Nanomedicine: Nanotechnology, Biology and Medicine. 7(3):324-332, 2011 doi:10.1016/j.nano.2010.11.004. NIHMS 254071
6. Tang, Y., T. Lei, R. Manchanda*, A. Nagesetti, A. Fernandez-Fernandez, S. Srinivasan, A.J. McGoron. Simultaneous Delivery of Chemotherapeutic and Thermal-Optical Agents to Cancer Cells by a Polymeric (PLGA) Nanocarrier: an In Vitro Study. Pharm Res (2010) 27:2242-2253. DOI 10.1007/s11095-010-0231-6.
7. Manchanda, R., A. Fernandez-Fernandez, A. Nagesetti, and A.J. McGoron, Preparation and characterization of a polymeric (PLGA) nanoparticulate drug delivery system with simultaneous incorporation of chemotherapeutic and thermo-optical agents. Colloids and Surfaces B: Biointerfaces, 2010, 75:260-267.

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