MS Thesis Presentation

Department of Biomedical Engineering

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Time: Friday, December 4th, 2015, 2:30 -4:00 pm
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Title of thesis: Optimization and Characterization of Multifunctional Polymer-based Nanoparticles Containing DTPA-Gd Contrast Agent for MRI Enhancement
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Summary

The lack of specific and accurate imaging is an urgent issue for the prevention, diagnosis, and treatment of diseases such as cancer and atherosclerosis. Magnetic resonance imaging (MRI) is a promising modality for disease imaging without ionizing radiation. Diethylenetriaminepentaacetic acid gadolinium (III) (DTPA-Gd) is a FDA-approved MR contrast agent used to improve the visibility of internal body structures. Conjugation of the DTPA-Gd onto macromolecular polymers leads to high relaxivity and prolonged retention in blood circulation. More importantly, polymers can be applied to improve spatial and temporal biodistribution of loaded contrast agents.

A “theranostic” contrast agent including a high payload of DTPA-Gd for cancer detection was synthesized on the basis of polytyrosine polymer. The polytyrosine-DTPA-Gd particles were formed with near-spherical morphology, smooth surfaces, Gd attachment efficiency of 34.75 +/-7.59%, Gd loading of 0.013 mg Gd per mg of particles, and an average size of 217.9 +/-12.8 nm. Future studies will focus on adding MicroRNA therapeutics and aptamer targeting on the surface of polytyrosine.

Adding environmental sensitivity to contrast agents an oxidative-stress sensitive MRI contrast agent for atherosclerosis was designed by using polyamidoamine generation 5 dendrimer (PAMAM G5). PAMAM G5 was partially PEGylated using methoxy-poly (ethylene glycol)-carboxymethyl (mPEG-CM), and the remaining amine groups were conjugated with DTPA-Gd. The acid groups of mPEG-CM were activated by using carbodiimide chemistry. The PEG chain was used to form interpolymer complexation (IPC), blocking the T1 contrast-causing ability of DTPA-Gd. The relaxivity of PEG-G5-DTPA-Gd (r1 = 16.57 $mM^{-1}s^{-1}$, r2 = 44.63 $mM^{-1}s^{-1}$) is much higher than that of Gd chloride alone (r1 = 16.57 $mM^{-1}s^{-1}$, r2 = 44.63 $mM^{-1}s^{-1}$), indicating PEG-G5-DTPA-Gd is suitable for MRI enhancement. Additionally, the relaxivity of IPC-Gd (r1 = 8.56 $mM^{-1}s^{-1}$, r2 = 23.15 $mM^{-1}s^{-1}$) is lower than PEG-G5-DTPA-Gd, suggesting that interpolymer complexation is able to block the relaxivity of contrast agents. Future work will focus on the signal recovery under oxidative stress as well as *in vitro* studies.