Biomaterials and Biomechanics in Bioengineering, *Vol. 3, No. 3 (2016) 129-140*
DOI: http://dx.doi.org/10.12989/bme.2016.3.3.129

Polymeric nanoparticles as dual-imaging probes for cancer management

Jyothi U. Menon[1,2], Parth Jadeja[1,2], Pranjali Tambe[1,2], Dheeraj Thakore[1,2], Shanrong Zhang[3], Masaya Takahashi[3], Zhiwei Xie[4], Jian Yang**[4] and Kytai T. Nguyen[1,2*]

[1]Bioengineering Department, The University of Texas at Arlington, Arlington, TX, USA 76019
[2]Graduate Biomedical Engineering Program, UT Southwestern Medical Center, Dallas, TX, USA 75390
[3]Advanced Imaging Research Center, UT Southwestern Medical Center, Dallas, TX, USA 75390
[4]Department of Biomedical Engineering, Pennsylvania State University, University Park, PA 16802

(Received June 29, 2015, Revised September 12, 2016, Accepted Accepted December 16, 2016)

Abstract. This article reports the development of biodegradable photoluminescent polymer (BPLP)-based nanoparticles (NPs) incorporating either magnetic nanoparticles (BPLP-MNPs) or gadopentate dimeglumine (BPLP-Gd NPs), for cancer diagnosis and treatment. The aim of the study is to compare these nanoparticles in terms of their surface properties, fluorescence intensities, MR imaging capabilities, and *in vitro* characteristics to choose the most promising dual-imaging nanoprobe. Results indicate that BPLP-MNPs and BPLP-Gd NPs had a size of 195±43 nm and 161±55 nm, respectively and showed good stability in DI water and 10% serum for 5 days. BPLP-Gd NPs showed similar fluorescence as the original BPLP materials under UV light, whereas BPLP-MNPs showed comparatively less fluorescence. VSM and MRI confirmed that the NPs retained their magnetic properties following encapsulation within BPLP. Further, *in vitro* studies using HPV-7 immortalized prostate epithelial cells and human dermal fibroblasts (HDFs) showed > 70% cell viability up to 100 µg/ml NP concentration. Dose-dependent uptake of both types of NPs by PC3 and LNCaP prostate cancer cells was also observed. Thus, our results indicate that BPLP-Gd NPs would be more appropriate for use as a dual-imaging probe as the contrast agent does not mask the fluorescence of the polymer. Future studies would involve *in vivo* imaging following administration of BPLP-Gd NPs for biomedical applications including cancer detection.

Keywords: nanoparticles; fluorescent; MRI; contrast agent; dual imaging

1. Introduction

Cancer imaging is an important aspect of cancer diagnosis as it can be used for relatively accurate and early detection of the tumor masses in the body, preferably before the start of metastasis (Frangioni 2008). Various imaging modalities have been employed in monitoring the effects of different therapeutic agents on tumor growth (Balu-Maestro *et al.* 2002). Commonly

*Corresponding author, Ph.D., E-mail: knguyen@uta.edu
**Corresponding author, Ph.D., E-mail: jxy30@psu.edu

http://www.techno-press.org/?journal=bme&subpage=7 ISSN: 2465-9835 (Print), 2465-9959 (Online)

targeting and imaging", *Biomater.*, **30**(36), 6947-6954.
Jennings, L.E. and Long, N.J. (2009), "Two is better than one'-probes for dual-modality molecular imaging", *Chem. Comm.*, (24), 3511-3524.
Ke, J.H., Lin, J.J., Carey, J.R., Chen, J.S., Chen, C.Y. and Wang, L.F. (2010), "A specific tumor-targeting magnetofluorescent nanoprobe for dual-modality molecular imaging", *Biomater.*, **31**(7), 1707-1715.
Laurent, S., Dutz, S., Häfeli, U.O. and Mahmoudi, M. (2011), "Magnetic fluid hyperthermia: focus on superparamagnetic iron oxide nanoparticles", *Adv. Colloid Interface Sci.*, **166**(1), 8-23.
Liao, A.H., Liu, H.L., Su, C.H., Hua, M.Y., Yang, H.W., Weng, Y.T., ... and Yen, T.C. (2012), "Paramagnetic perfluorocarbon-filled albumin-(Gd-DTPA) microbubbles for the induction of focused-ultrasound-induced blood–brain barrier opening and concurrent MR and ultrasound imaging", *Phys. Medicine Biol.*, **57**(9), 2787.
Liu, J. and Luijten, E. (2004), "Stabilization of colloidal suspensions by means of highly charged nanoparticles", *Phys. Rev. Lett.*, **93**(24), 247802.
Magda, D., Lecane, P., Miller, R.A., Lepp, C., Miles, D., Mesfin, M., ... and Karaman, M.W. (2005), "Motexafin gadolinium disrupts zinc metabolism in human cancer cell lines", *Cancer Res.*, **65**(9), 3837-3845.
Mandal, S.K., Lequeux, N., Rotenberg, B., Tramier, M., Fattaccioli, J., Bibette, J. and Dubertret, B. (2005), "Encapsulation of magnetic and fluorescent nanoparticles in emulsion droplets", *Langmuir*, **21**(9), 4175-4179.
Maroto, R., Kurosky, A. and Hamill, O.P. (2012), "Mechanosensitive Ca2+ permeant cation channels in human prostate tumor cells", *Channels*, **6**(4), 290-307.
Menon, J.U., Gulaka, P.K., McKay, M.A., Geethanath, S., Liu, L. and Kodibagkar, V.D. (2012), "Dual-modality, dual-functional nanoprobes for cellular and molecular imaging", *Theranostics*, **2**(12), 1199-1207.
Nam, T., Park, S., Lee, S.Y., Park, K., Choi, K., Song, I.C., ... and Kim, K. (2010), "Tumor targeting chitosan nanoparticles for dual-modality optical/MR cancer imaging", *Bioconjugate Chem.*, **21**(4), 578-582.
Runge, V.M. (2000), "Safety of approved MR contrast media for intravenous injection", *J. Magnetic Resonance Imag.*, **12**(2), 205-213.
Sahoo, B., Devi, K.S.P., Banerjee, R., Maiti, T.K., Pramanik, P. and Dhara, D. (2013), "Thermal and pH responsive polymer-tethered multifunctional magnetic nanoparticles for targeted delivery of anticancer drug", *ACS Appl. Mater. Interf.*, **5**(9), 3884-3893.
Townsend, D.W. (2008), "Dual-modality imaging: combining anatomy and function", *J. Nuclear Medicine*, **49**(6), 938-955.
Wadajkar, A.S., Kadapure, T., Zhang, Y., Cui, W., Nguyen, K.T. and Yang, J. (2012), "Dual-imaging enabled cancer-targeting nanoparticles", *Adv. Healthcare Mater.*, **1**(4), 450-456.
Wadajkar, A.S., Menon, J.U., Tsai, Y.S., Gore, C., Dobin, T., Gandee, L., ... and Hsieh, J.T. (2013), "Prostate cancer-specific thermo-responsive polymer-coated iron oxide nanoparticles", *Biomater.*, **34**(14), 3618-3625.
Waggoner, A. (2006), "Fluorescent labels for proteomics and genomics", *Current Opinion Chem. Biol.*, **10**(1), 62-66.
Wang, P., Zou, X.M., Huang, J., Zhang, T.L. and Wang, K. (2011), "Gadolinium inhibits prostate cancer PC3 cell migration and suppresses osteoclast differentiation *in vitro*", *Cell Biol. Int.*, **35**(11), 1159-1167.
Yang, J., Zhang, Y., Gautam, S., Liu, L., Dey, J., Chen, W., ... and Tang, L. (2009), "Development of aliphatic biodegradable photoluminescent polymers", *Proceedings of the National Academy of Sciences*, **106**(25), 10086-10091.

CC