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Optimally-sized magnetic resonance image-able theranostic nano-particles for quantitative surrogate imaging of chemotherapy accumulation and bio-distribution in solid tumor tissue interstitia

Hemant Sarin
Freelance Investigator in Translational Science and Medicine, USA

Novel innovative methodologies are needed to overcome the challenge for the effective treatment of primary and metastatic solid malignancies, which has to do with the trans-vascular delivery of nano-molar (nM)-to-micro-molar (uM) concentration of a small molecule chemo-xenobiotic selectively into solid tumor tissue foci and then the persistence of the chemo-xenobiotic in the tumor milieu for several hours. It is possible to accomplish this with optimally-sized magnetic resonance image-able DTPA/DOTA chelated Gadolinium (Gd)-dendrimer nano-particles bearing covalently attached small molecule chemo-xenobiotics with labile linkages and physiologic exterior functionality, as these 8-to-9 nanometer-sized nano-particles are free from intravascular protein interactions and have prolonged plasma half-lives by being resistant to proteolytic degradation in circulation, which results in functionalized dendrimer accumulation selectively in tumor tissue to milli-molar (mM) concentrations, without systemic side effects. For this purpose, the methodology of non-model-based quantitative dynamic contrast-enhanced magnetic resonance imaging (qDC-E MRI) has been developed, which permits the non-invasive determination of Gd concentration accumulation in tumor tissue as a surrogate measure of Gd-DTPA dendrimer-small molecule chemo-xenobiotic accumulation and specifically, the amount of chemo-xenobiotic, with a priori knowledge of the amount of percent Gd and ratio of Gd chelate-to-chemo-xenobiotic per functionalized dendrimer batch. Utilizing this qDC-E MRI methodology, real-time accumulation of Gd-DTPA-Generation 5-Doxorubcin in orthotopic RG-2 malignant gliomas has been quantitatively imaged and the significant regression of brain tumor has been demonstrated, after a single I.V. dose of the functionalized dendrimer. In this didactic session, this novel methodology will be discussed, as will the translational perspective towards its clinical application.

Biography

Hemant Sarin earned his Bachelor of Science in Biology with Highest Honors (1994) followed by a Medical Doctorate (1999) and went on to gain experience in Neurosurgery (2000-2003) prior to completing the NIH Imaging Sciences Program while developing his Translational Imaging-based Malignant Glioma Research Program concomitantly (2004-2009). He went on to gain additional intensive experience in Neurology for 6 months (2010), International Science Policy for 6 months (2011) and American Board Eligibility in Occupational and Environmental Medicine (2012-2014) while earning his Master of Science degree concomitantly on the conserved basis of toxin and toxicant interactions in the physiologic state.

hemantsarin74@gmail.com

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