Intratumoral Distribution and Retention of Gold Nanoparticles Characterized by Computed Tomography in a Non-Small Cell Lung Cancer Model

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Lung cancer produces the highest number of cancer-related deaths worldwide. Currently, Non-Small Cell Lung Cancer (NSCLC) accounts for more than 85% of those cases. To date, achieving an early and precise diagnosis of NSCLC remains challenging due to extensive intratumor heterogeneity, which concerns not only to tumor epithelial cells but also the diverse microenvironment with which the tumor cells interact. In addition, genetic and phenotypic tumor heterogeneity and consequent non-uniform spatial drug distribution can lead to therapy resistance in cancer treatment. Therefore, visualization of the tumor microenvironment using morphological imaging techniques such as computed tomography (CT) can better clarify structure, vasculature, and biodistribution, making possible optimization of applications in the fields of diagnostics as well as individualized treatment.

In this study, we aim to evaluate the intratumoral distribution of Gold Nanoparticles (GNPs) in Lewis Lung Carcinoma (LLC) tumor-bearing mice using high resolution CT preclinical imaging. We hypothesize that by exploiting the adsorption of molecules on the GNP surface, we can influence the intratumoral distribution and retention of the particles. In fact, GNPs exhibit high X-Ray attenuation and optimal biocompatibility, compared to the common side effects associated with the administration of standard contrast agents.

GNPs approximately 34 nm in diameter are synthesized and surface passivated with Bovine Serum Albumin (BSA) to reduce opsonization and improve colloidal stability. CT phantom imaging is used to determine X-ray attenuation as a function of GNP concentration and surface functionalization. Particle uptake in vitro within the LLC cells was dependent on surface passivation. An in vivo study is performed by injecting intratumorally, concentrated GNPs into LLC-solid tumors grown on the right flank of 6-week old female C57BL/6 mice. Ten days post-injection, follow-up assessments with CT imaging and quantifications show the intratumoral distribution and retention of the particles.

In vivo results show significant heterogeneity in the intratumoral biodistribution of GNPs dependent on surface passivation. BSA-GNPs perfuse predominately along the tumor periphery, allowing the visualization of the tumor boundaries, with few depositions throughout the entire tumor volume over time. This response suggests perfusion rather than permeability as the limiting factor for tumor accumulation of the GNPs.