International Journal of Nanomedicine

Dovepress

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ORIGINAL RESEARCH

Effect of intratumoral administration on biodistribution of ^{64}Cu-labeled nanoshells

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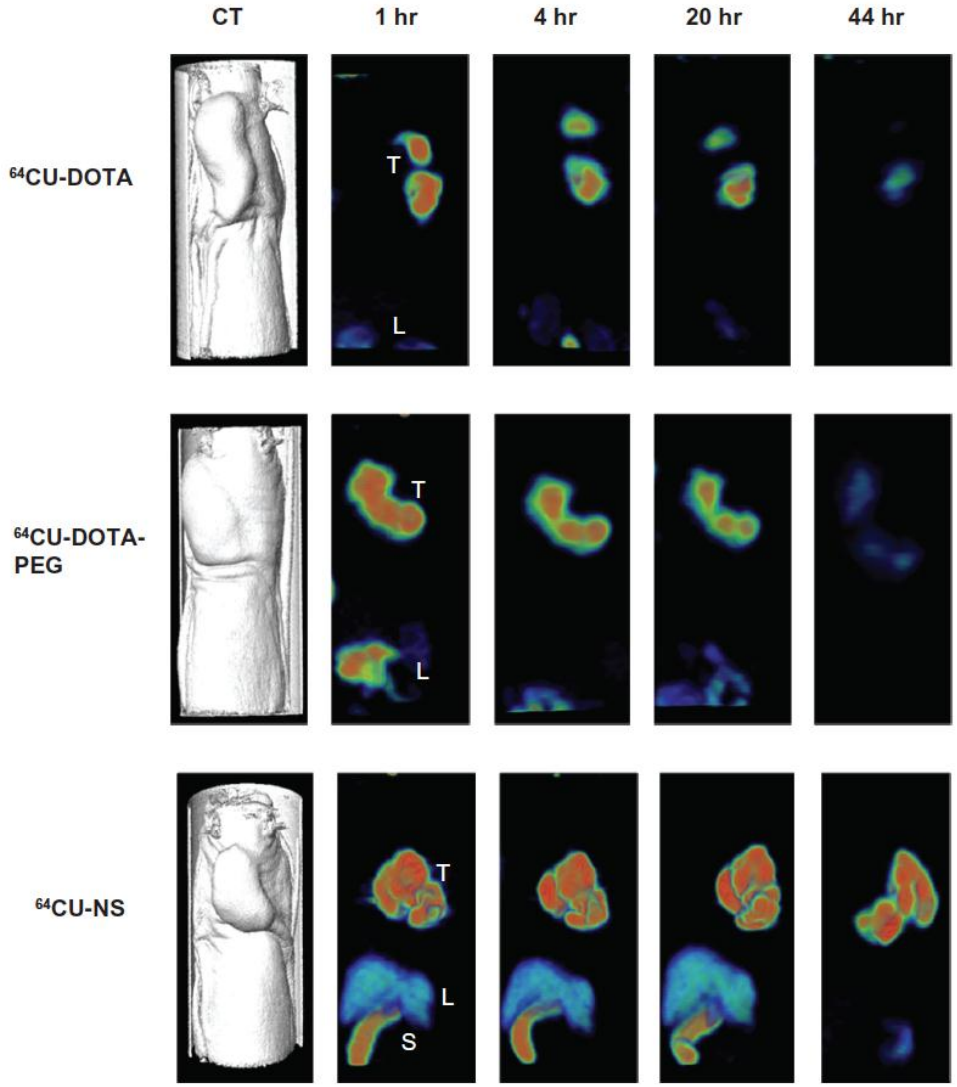
Background: Gold nanoshells are excellent agents for photothermal ablation cancer therapy and are currently under clinical trial for solid tumors. Previous studies showed that passive delivery of gold nanoshells through intravenous administration resulted in limited tumor accumulation, which represents a major challenge for this therapy. In this report, the impact of direct intratumoral administration on the pharmacokinetics and biodistribution of the nanoshells was systematically investigated.

Methods: The gold nanoshells were labeled with the radionuclide, copper-64 (^{64}Cu). Intratumoral infusion of ^{64}Cu-nanoshells and two controls, ie, ^{64}Cu-DOTA (1,4,7,10-tetraazaciclododecane-1,4,7,10-tetraacetic acid) and ^{64}Cu-DOTA-PEG (polyethylene glycol), as well as intravenous injection of ^{64}Cu-nanoshells were performed in nude rats, each with a head and neck squamous cell carcinoma xenograft. The pharmacokinetics was determined by radioactive counting of serial blood samples collected from the rats at different time points post-injection. Using positron emission tomography/computed tomography imaging, the in vivo distribution of ^{64}Cu-nanoshells and the controls was monitored at various time points after injection. Organ biodistribution in the rats at 46 hours was analyzed by radioactive counting and compared between the different groups.

Results: The resulting pharmacokinetic curves indicated a similar trend between the intratumorally injected agents, but a significant difference with the intravenously injected ^{64}Cu-nanoshells. Positron emission tomography images and organ biodistribution results on rats after intratumoral administration showed higher retention of ^{64}Cu-nanoshells in tumors and less concentration in other healthy organs, with a significant difference from the controls. It was also found that, compared with intravenous injection, tumor concentrations of ^{64}Cu-nanoshells improved substantially and were stable at 44 hours post-injection.

Conclusion: There was a higher intratumoral retention of ^{64}Cu-nanoshells and a lower concentration in other healthy tissues, suggesting that intratumoral administration is a potentially better approach for nanoshell-based photothermal therapy.

Keywords: gold nanoshells, intratumoral administration, positron emission tomography, biodistribution



The ^{64}Cu-labeled nanoshells are retain in the Tumor to a dramatically greater extent compared to Free radiolabels of ^{64}Cu-DOTA or ^{64}Cu-DOTA-PEG