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Tumour Radionuclides Therapy: in vitro and in vivo Dose Distribution Study

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Abstract : Introduction: Heterogeneity of dose distributions across a tumour is problematic for targeted radiotherapy. Gold nanoparticles (AuNPs) enhance dose-distributions of targeted radionuclides. The aim of this study is to demonstrate if tumour dose-distribution of targeted AuNPs radiolabelled with either of two radioisotopes (^{177}Lu and ^{90}Y) in breast cancer cells produced homogeneous dose distributions. Moreover, in vitro and in vivo studies were conducted to study the importance of receptor level on cytotoxicity of EGFR-targeted AuNPs in breast and colorectal cancer cells. Methods: AuNPs were functionalised with DOTA and OPPS-PEG-SVA to optimise labelling with radionuclide tracers and targeting with Erbitux. Radionuclides were chelated with DOTA, and the uptake of the radiolabelled AuNPs and targeted activity in vitro in both cell lines measured using liquid scintillation counting. Cells with medium (HCT8) and high (MDA-MB-468) EGFR expression were incubated with targeted ^{177}Lu-AuNPs for 4h, then washed and allowed to form colonies. Nude mice bearing tumours were used to study the biodistribution by injecting ^{177}Lu-AuNPs or ^{90}Y-AuNPs via the tail vein. Heterogeneity of dose-distribution in tumours was determined using autoradiography. Results: Colony formation (% control) was 81 ± 4.7% (HCT8) and 32 ± 9% (MDA-MB-468). High uptake was observed in the liver and spleen, indicating hepatobiliary excretion. Imaging showed heterogeneity in dose-distributions for both radionuclides across the tumours. Conclusion: The cytotoxic effect of EGFR-targeted AuNPs is greater in cells with higher EGFR expression. Dose-distributions for individual radiolabelled nanoparticles were heterogeneous across tumours. Further strategies are required to improve the uniformity of dose distribution prior to clinical trials.

Keywords : cancer cells, dose distributions, radionuclide therapy, targeted gold nanoparticles
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