

(188)Re-loaded lipid nanocapsules as a promising radiopharmaceutical carrier for internal radiotherapy of malignant gliomas

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Résumé en anglais	<p>PURPOSE: Lipid nanocapsules (LNC) entrapping lipophilic complexes of (188)Re ((188)Re(S(3)CPh)(2)(S(2)CPh) [(188)Re-SSS]) were investigated as a novel radiopharmaceutical carrier for internal radiation therapy of malignant gliomas. The present study was designed to evaluate the efficacy of intra-cerebral administration of (188)Re-SSS LNC by means of convection-enhanced delivery (CED) on a 9L rat brain tumour model. METHODS: Female Fischer rats with 9L glioma were treated with a single injection of (188)Re-SSS LNC by CED 6days after cell implantation. Rats were put into random groups according to the dose infused: 12, 10, 8 and 3Gy in comparison with blank LNC, perrhenate solution (4Gy) and non-treated animals. The radionuclide brain retention level was evaluated by measuring (188)Re elimination in faeces and urine over 72h after the CED injection. The therapeutic effect of (188)Re-SSS LNC was assessed based on animal survival. RESULTS: CED of (188)Re perrhenate solution resulted in rapid drug clearance with a brain T (1/2) of 7h. In contrast, when administered in LNC, (188)Re tissue retention was greatly prolonged, with only 10% of the injected dose being eliminated at 72h. Rat median survival was significantly improved for the group treated with 8Gy (188)Re-SSS LNC compared to the control group and blank LNC-treated animals. The increase in the median survival time was about 80% compared to the control group; 33% of the animals were long-term survivors. The dose of 8Gy proved to be a very effective dose, between toxic (10-12Gy) and ineffective (3-4Gy) doses. CONCLUSIONS: These findings show that CED of (188)Re-loaded LNC is a safe and potent anti-tumour system for treating malignant gliomas. Our data are the first to show the in vivo efficacy of (188)Re internal radiotherapy for the treatment of brain malignancy.</p>

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