



Targeting of Human Lung-Cancer xenografts with Technetium-99m glucarate

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Objectives: ^{99m}Tc -glucarate (GLA) offers great potential value in the targeting of several solid human cancers. In transplanted human tumors in mice, GLA showed high tumor/muscle and tumor/blood ratios at early times after injection, indicating that high target to not-target background ratios can be achieved. Lung cancer is one of solid tumors in which GLA may have favorable targeting potential. The purpose of this study was to determine the properties of GLA in targeting xenografted human A549 lung cancer in mice. First, we investigated the early kinetic characteristics of GLA in A549 cancer using a small-animal SPECT system called FASTSPECT with the capability of fast dynamic imaging. Second, we collected delayed GLA images to determine the late retention of GLA up to 24 hrs after injection in the tumors and optimize the suitable imaging time.

Methods: Twelve anesthetized SCID mice bearing A549 tumors on the right thigh or back were imaged using FASTSPECT. Immediately after intravenous injection of 185 MBq GLA via a jugular vein catheter, dynamic images were acquired in seven mice (Group 1) every minute for 30 min, followed by 5-min acquisition every 15 min until 2-hr. Other five animals (Group 2) received tail vein injection of GLA and subjected to repeated imaging at 10-min, 2-hr, 4-hr, 6-hr and 24-hr points by 10-15 min acquisition. Tomographic reconstructions were made using the ML-EM algorithm. Tumor time-activity curves of dynamic images were created by ROI analysis. Tissue samples were harvested at the end of the imaging session to determine GLA biodistribution.

Results: A549 tumors were well visualized initially by FASTSPECT imaging 1-10 min after injection. Dynamic images demonstrated that 2-hr GLA retention (% peak) of the tumor was $25.2 \pm 2.4\%$. GLA showed rapid clearance via kidneys and less retention in normal tissues. While activity in kidneys and bladder was reduced significantly 4-6 hrs after injection, the tumors became visible more clearly on delayed images. The tumor was detectable by FASTSPECT 24-hr after injection, but required much longer acquisition. The ratios of tumor to muscle activity was 3.370.12 at 2-hr and 2.51 ± 0.15 at 24-hr ($P > 0.05$).

Conclusions: The results in this study indicate that A549 lung cancer xenografts can be well detected by GLA imaging. It may enable visualization of the primary lung cancer

rapidly post administration in the clinic. Delayed imaging may provide more reliable information for localization of the tumors. This agent warrants further study.

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