Contribution ID: **156** Type: 口头报告

小鼠体内 ^{177}Lu-FAP 临床前吸收剂量评估：基于 SPECT-CT 图像的 GATE 蒙特卡洛全粒子输运与 MIRD 近似模型物理差异

摘要

摘要

背景：成纤维细胞激活蛋白（FAP）是放射性药物治疗（RPT）的重要靶点，在多种实体瘤中高表达。随着 ^{177}Lu 标记 FAP 药物的快速发展，准确评估临床前模型中的吸收剂量对疗效、安全及临床转化至关重要。目前，基于 MIRD 的器官水平剂量估算与基于蒙特卡罗（MC）的体素水平剂量计算在物理模型上存在本质差异，其一致性尚需系统比较。本研究旨在比较 GATE 蒙特卡罗模拟与 MIRD 方法在荷瘤小鼠中的剂量计算结果，重点探讨 MC 在粒子输运、次级电子沉积、组织非均匀性及边界效应等物理过程中的优势。

方法：基于 U87 荷瘤 BALB/c 裸鼠模型，尾静脉注射三种 177Lu-FAP 药物。于注射后进行小动物 SPECT/CT 显像，手动勾画主要器官 VOI，获取各时间点器官放射性活度。采用 OLINDA/EXM、Odam 及 PKAD 算法计算 TIAC 并归一化，结合 S 值获得 MIRD 体系器官吸收剂量。同时，将 SPECT/CT 图像导入 3D Slicer 进行格式转换，利用 Python 进行空间坐标变换，作为 GATE 模拟输入。基于 GATE v9.0（Geant4）进行体素级 MC 模拟，以 CT 图像（0.25 mm 体素）构建体素化体模，SPECT 图像定义体素化源。物理过程包含光电效应、康普顿散射、韧致辐射，无能量削减及方差减少。放射源为 177Lu，DoseActor 输出能量沉积与剂量分布。模拟时间为实际采集的 1/10–1/100，统计不确定性 <5%，每只小鼠耗时 3.5 小时。基于 VOI 计算各器官剂量率，积分拟合得总吸收剂量，并分析能量剖面及剂量等高线。

结果：三种放射性药物在肿瘤中均显示出较高的放射性摄取与滞留。在器官吸收剂量方面，基于 MIRD 方法（OLINDA/EXM、Odam、PKAD）计算得到的肾脏和肿瘤吸收剂量分别为 19.78—45.94Gy/GBq 和 670.27—744.43 Gy/GBq，不同计算工具之间结果较为接近/存在一定差异。GATE 蒙特卡罗模拟获得的体素级剂量分布显示，肿瘤内剂量呈现明显异质性，平均吸收剂量为 713.51—840.10Gy/GBq，与 MIRD 方法相比差异为 12%—25%。肾脏剂量在体素水平同样表现出局部热点，最高与平均剂量比值可达 2.5。

结论：MIRD 方法提供器官平均水平剂量，适用于快速评估，但无法反映内部剂量异质性。GATE-MC 通过精确模拟粒子输运、次级电子沉积及边界效应，揭示肿瘤及肾脏内部的剂量异质性，更接近真实物理分布。两者物理本质互补，联合使用可为 RPT 药物临床前剂量学表征及临床转化提供更全面的物理依据。

关键词

吸收剂量；MIRD；蒙特卡洛；辐射剂量学；医学物理

Abstract

Abstract

Background: Fibroblast activation protein (FAP) is an important target for radionuclide radiotherapies (RPT) and is highly expressed in various solid tumors. With the rapid development of ^{177}Lu-labeled FAP agents, accurate assessment of absorbed dose in preclinical models is essential for efficacy, safety, and clinical translation. Currently, MIRD-based organ-level dosimetry and Monte Carlo (MC)-based voxel-level dose calculations have fundamental differences in physical models, and their consistency requires systematic comparison. This study aims to compare GATE Monte Carlo simulations with MIRD-based methods for dose calculation in tumor-bearing mice, with an emphasis on the advantages of MC in physical processes such as particle transport, secondary electron deposition, tissue heterogeneity, and boundary effects.

Methods: Based on a U87 tumor-bearing BALB/c nude mouse model, three ^{177}Lu-FAP agents were injected via the tail vein. Small-animal SPECT/CT imaging was performed at multiple time points post-injection, and VOIs of major organs were manually delineated to obtain organ radioactivity at each time point. OLINDA/EXM, Odam, and the PKAD algorithm were used to calculate TIACs followed by normalization, and organ absorbed

doses were obtained based on the MIRD framework combined with S-values. Meanwhile, SPECT/CT images were imported into 3D Slicer for format conversion, and spatial coordinate transformation was performed using Python to generate input for GATE simulations. Voxel-level MC simulations were performed using GATE v9.0 (Geant4). CT images (0.25 mm voxel size) were used to construct a voxelized phantom, and SPECT images were used to define a voxelized source. The physical processes included photoelectric effect, Compton scattering, and bremsstrahlung, without energy cuts or variance reduction. The radioactive sources were ^{177}Lu. DoseActor was used to output energy deposition and dose distributions. The simulation time was set to 1/10–1/100 of the actual acquisition time, with statistical uncertainty <5%. Each mouse simulation took 3.5 hours on a computing cluster. Based on the delineated VOIs, dose rates of each organ were calculated, and total absorbed doses were obtained by integral fitting. Energy profiles and dose contour lines were also analyzed.

Results: All three radiopharmaceuticals showed high radioactive uptake and retention in tumors. In terms of organ absorbed doses, the kidney and tumor absorbed doses calculated by the MIRD-based methods (OLINDA/EXM, Odam, PKAD) were 19.78–45.94 Gy/GBq and 670.27–744.43 Gy/GBq, respectively. The results from different calculation tools were relatively close / showed some differences. Voxel-level dose distributions obtained from GATE Monte Carlo simulations revealed significant intratumoral dose heterogeneity, with mean absorbed doses ranging from 713.51 to 840.10 Gy/GBq, showing a difference of 12%–25% compared to the MIRD-based methods. At the voxel level, the kidneys also exhibited local hotspots, with a maximum-to-mean dose ratio reaching 2.5.

Conclusion: The MIRD-based methods provide organ-level mean doses suitable for rapid assessment but fail to reflect internal dose heterogeneity. GATE-MC, by accurately simulating particle transport, secondary electron deposition, and boundary effects, reveals dose heterogeneity within tumors and kidneys, which is closer to the true physical distribution. The two approaches are physically complementary, and their combined use can provide a more comprehensive physical basis for preclinical dosimetry characterization and clinical translation of RPT agents.

Keywords

Absorbed dose; MIRD; Monte Carlo; Radiation dosimetry; Medical physics

Authors: Mr 瑞磊, 庞 (中国药科大学); Mr 鹤霖, 王 (中国药科大学); Ms 月清, 顾 (中国药科大学); Mr 智豪, 韩 (中国药科大学)

Presenter: Mr 瑞磊, 庞 (中国药科大学)

Session Classification: 核技术及应用、医学物理与工程

Track Classification: 口头报告: 核技术及应用、医学物理与工程