to the other HER2 targeting ^{177}Lu-radioconjugates.
Conclusions: Two libraries of ligands, targeting respectively ER and HER2 have been successfully synthesised and radiolabelled with [^{177}Lu]$LuCl_3$. Estradiol-based radioconjugates showed good stability and modification of their chemical structures are currently on going to increase their cell penetration. Biological evaluation of their affinity and therapeutic efficacy are currently on going and will be presented in due course. The extension of both libraries is already on going, notably by the development of peptide-based ligands targeting ER.

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PP10
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A RIGOROUS MONTE CARLO SIMULATION FRAMEWORK FOR ACTINIUM-225-PSMA-617 TARGETED ALPHA THERAPY IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Ali Alshehri [1]
[1] *Radiological Sciences Department | Collage of Applied Medical Science | Najran University*

Aims: This study presents a systematic comparison of MCNP6.3 and GATE Monte Carlo simulation codes for 225Ac-PSMA-617 dosimetry analysis, evaluating organ-level absorbed doses, microdosimetric parameters, and radiobiological endpoints.
Methods: Comprehensive Monte Carlo simulations were performed using both MCNP6.3 and GATE for 225Ac-PSMA-617 targeted alpha therapy dosimetry. Organ-level absorbed doses were calculated for critical organs including prostate, kidneys, bone marrow, and salivary glands. Microdosimetric parameters including S-values, linear energy transfer (LET) distributions, and DNA damage metrics were evaluated. Radiobiological parameters encompassing α/β ratios, relative biological effectiveness (RBE) values, and cell survival fractions were determined. Statistical agreement was assessed using correlation analysis, Bland–Altman plots, and percentage difference calculations.
Results: This comprehensive comparative analysis of MCNP6.3 and GATE Monte Carlo simulation codes for 225Ac-PSMA617 dosimetry demonstrates exceptional agreement across multiple analytical domains, establishing confidence in both platforms for targeted alpha therapy applications. The organ-level dosimetric comparison revealed strong statistical correlation ($R\ 2 = 0.987$, $p < 0.001$) with mean relative differences of $-2.8 \pm 4.1\%$, indicating systematic consistency well within clinically acceptable uncertainty ranges. Microdosimetric parameter comparisons showed excellent agreement for S values (mean difference: $1.2 \pm 3.8\%$) and LET distributions (mean difference: $-0.8 \pm 2.9\%$). DNA damage calculations demonstrated consistency between codes with double-strand break predictions differing by $2.3 \pm 4.2\%$. Radiobiological parameter analysis revealed mean relative differences ranging from -3.9% to 6.2% across tissue types, with α/β ratios showing the highest agreement ($-0.5 \pm 2.1\%$) and RBE values displaying slightly larger variations ($3.4 \pm 5.8\%$). Both MCNP6.3 and GATE Monte Carlo codes demonstrate excellent agreement for 225Ac-PSMA-617 dosimetry applications, with systematic differences well within clinically acceptable ranges ($< 5\%$).
Conclusion: In conclusion, this study establishes MCNP6.3 and GATE as equivalent and reliable tools for 225Ac-PSMA-617 dosimetric analysis, with systematic differences well within clinically acceptable ranges. The demonstrated agreement across organ-level, microdosimetric, and radiobiological domains supports the continued development and clinical implementation of both platforms for targeted alpha therapy applications. These findings provide essential validation for regulatory submissions, clinical trial design, and treatment optimization protocols in the rapidly evolving field of targeted radionuclide therapy. The integration of artificial intelligence and machine learning approaches with Monte Carlo simulations represents an emerging frontier that could benefit from the platform consistency demonstrated in this study. Standardized datasets generated using either MCNP6.3 or GATE could serve as reliable training inputs for AI-driven dosimetric models, expanding the clinical utility of both platforms.

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PP12
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IMPROVED QUALITY CONTROL OF [18F] FDG: OVERCOMING MATRIX EFFECTS WITH ADVANCED COLUMN AND RINSING STRATEGIES

Andreas Schildan [1], Hans-Ulrich Meinel [2], Osama Sabri [3], Jean-Pierre Chervet [4], Detlef Jensen [4]
[1] *University Hospital Leipzig - Department of Nuclear Medicine; University Hospital Leipzig, Department of Nuclear Medicine;* [2] *University Hospital of Leipzig, Department of Nuclear Medicine;* [3] *Department of Nuclear Medicine, University Hospital Leipzig;* [4] *Antec Scientific*

Aims: Precise quality control of [^{18}F]Fluorodeoxyglucose (FDG) using high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD) is complicated by matrix effects arising from saline-citrate buffers in routine FDG formulations. Although these buffers are necessary for maintaining pH and isotonicity, they reduce anion exchange column capacity and lead to unpredictable shifts in retention time during sequential analyses.
Methods: We tested a new column, the Antec Scientific SweetSep AEX18 (2.1×185 mm), to address these issues and developed a pharmacopeia-compliant analytical workflow suitable for pharmaceutical settings.
Results: The major challenge is that current system suitability requirements do not permit the inclusion of in-run high-ionic-strength rinsing steps, which are otherwise common in HPAEC. In response, we developed a measurement and cleaning protocol that clearly separates the analytical and maintenance phases. By leveraging the high eluting strength, long-term stability, and bacterial resistance of the methanesulfonate anion, we added a dedicated post-analytical rinsing step. This helps maintain column performance, prevent carryover, and avoid regulatory conflicts arising from the integration of non-pharmacopeial processes. Meanwhile, the time required for QC measurements remains unchanged.
Additionally, system automation was enhanced by integrating electrochemical KOH eluent generation with automated methanesulfonate rinsing, thereby eliminating the need for manual KOH solution preparation. This dual-eluent method simplifies operation and improves reproducibility.
Conclusion: The protocol consistently supports robust, precise, and pharmacopeia-compliant FDG analysis, maintaining resolution and retention across multiple sample runs. Our experience demonstrates that modern column technology, strategic rinsing with methanesulfonate, and eluent system integration significantly improve the practicality and reliability of HPAEC-PAD for FDG and other sensitive pharmaceutical applications.

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PP13
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PRODUCT QUALITY REVIEW OF THE [18F] FDG RADIOPHARMACEUTICAL

Marija Atanasova Lazareva [1], Maja Chochevska [2,3], Katerina Kolevska [4], Maja Velichkovska [5], Filip Jolevski [6], Nevena Manevska [7]
[1] *University Institute of Positron Emission Tomography of Republic of North Macedonia, Faculty of Medical Sciences, Goce Delcev University, Stip, and 3university Institute of Positron Emission Tomography, Skopje, North Macedonia;* [2] *University Institute of Positron Emission Tomography, Skopje; 3Department for Production of Radioisotopes and Radiopharmacy;* [4] *University Institute of Positron Emission Tomography;* [5] *University Institute of Positron-Emission Tomography of Republic of North Macedonia;* [6] *Public Health Institution University Institute For Positron-Emision Tomography Republic of North Macedonia;* [7] *Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine, University of Ss Cyril and Methodius, Institute of Patophysiology and Nuclear Medicine*

Aims: A Product Quality Review (PQR) is an essential tool for analysing and verifying the consistency of established and validated production processes as well as the quality of the produced radiopharmaceuticals. In accordance with European GMP requirements, PQR must be performed annually, to confirm the consistency and suitability of existing processes and to identify opportunities to improve both the product and processes. This study aims to present the annual PQR for [^{18}F]FDG radiopharmaceutical produced during the year 2024, at the University Institute for Positron Emission Tomography.
Methods: A retrospective study was performed on all [^{18}F]FDG batches produced in 2024. The PQR covered: (i) number of manufactured and released batches; (ii) starting materials/consumables and their compliance with

specification for starting materials; (iii) in process controls including decay-corrected radiochemical yield and bubble point test (BPT) results; (iv) quality control (QC) results of finished product and trending against final product specification (appearance, radionuclidic identity, pH, radiochemical purity/identity by TLC, residual solvents, radionuclidic purity, bacterial endotoxins and sterility); (v) out-of-specification (OOS) results and investigations; (vi) deviations; (vii) status of equipment qualification/calibration and preventive/corrective maintenance; (viii) complaints; and (ix) change control, including revised and newly introduced procedures.

Results: A total of 194 batches of [^{18}F]FDG were produced; only one batch was not approved for injection, indicating that 99.5% was released. The yield decay corrected was 64% (ranging from 50–78%), and the filter integrity test results were in the range of 4.00–4.56, indicating that the manufacturing process was stable and met the defined acceptance criteria. A review of the quality control results showed stable performance throughout the whole year and they were closely distributed around the mean value, with no out-of-trend values. All batches released were in accordance with the finished product testing specification. One OOS event was recorded and, following laboratory investigation, the root cause was identified as operator error with appropriate follow-up actions. During the year, 15 deviations related to the [^{18}F]FDG production process were opened, of which five were major, one critical and the others were minor. All were documented and closed in accordance with the deviation procedure. During 2024, no complaints were reported for [^{18}F]FDG or associated services. The equipment used for production and quality control was routinely maintained and qualified. Through change control, four standard operating procedures (SOPs) were revised, and four SOPs were implemented during the year.

Conclusion: From the annual Product Quality Review of the finished product [^{18}F]FDG radiopharmaceutical, it can be concluded that the production process is stable, consistent and GMP-compliant, ensuring that the finished product consistently meets the specifications for [^{18}F]FDG solution for injection, as well as the incoming material complies with approved specifications for the quality of starting materials.

Keywords: PQR, GMP, radiopharmaceutical preparations, pharmaceutical quality system:

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INTEGRATING RISK ASSESSMENT FOR EFFECTIVE PROCESS CONTROL IN RADIOPHARMACEUTICAL PRODUCTION FACILITY

Maja Chochevska [1,2], Katerina Kolevska [3], Marija Atanasova Lazareva [4], Maja Velichkovska [5], Filip Jolevski [6], Nevena Manevska [7]

[1] *University Institute of Positron Emission Tomography, Skopje; 2Department for Production of Radioisotopes and Radiopharmacy;* [3] *University Institute of Positron Emission Tomography;* [4] *University Institute of Positron Emission Tomography of Republic of North Macedonia, Faculty of Medical Sciences, Goce Delcev University, Stip, and 3university Institute of Positron Emission Tomography, Skopje, North Macedonia;* [5] *University Institute of Positron-Emission Tomography of Republic of North Macedonia;* [6] *Public Health Institution University Institute For Positron-Emision Tomography Republic of North Macedonia;* [7] *Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine, University of Ss Cyril and Methodius, Institute of Patophysiology and Nuclear Medicine*

Aims: Ensuring radiopharmaceutical product quality, patient safety, and regulatory compliance in radiopharmaceutical production and diagnostic facility requires robust process control systems aligned with Good Manufacturing Practice (GMP) and ISO standards. On the other hand, ICH Q10 emphasizes the integration of GMP regulations with ISO 9001:2015 quality management concepts to ensure consistency throughout the complete drug manufacturing process.

Methods: Risk identification focused on critical aspects of productivity, system reliability, and nonconformities, as well as on hazards related to radioisotope and radiopharmaceutical production, quality control activities, radiation exposure, equipment failures, and process variability. A risk assessment methodology compliant with ICH Q9, GMP, and ISO standards was applied to real data collected over a two-year period at the University Institute of Positron Emission Tomography. The approach included: systematic risk identification, risk evaluation based on probability of a risk and the severity of its potential consequences through risk scoring system and risk matrix, risk control through preventive and corrective action, risk analysis, risk review and communication to ensure continuous monitoring and improvement.

Results: The results of the risk analysis showed a 54% reduction in risk ratings over a two-year period. Among the risks that were reassessed, 72% were classified as medium-level risks, while 28%, were classified as high-level risks. No change in risk ratings was observed for 45% of the identified risks. Within this group, 54% had previously been assessed as medium and 46% as low-level risks, with no risks classified as high level. Importantly, no risks affecting product quality were identified during the observed period.

Conclusion: The established risk management process proved to be essential for improving operational performance and preventing disruptions throughout the entire radiopharmaceutical production process. The integration of risk assessment and risk management was demonstrated to be a fundamental component of effective process control in GMP-compliant radiopharmaceutical production facility.

Keywords: risk management; risk assessment, radiopharmacy, good manufacturing practice, ISO

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STEREOSELECTIVE SYNTHESIS OF 18F-LABELED SPECIALIZED PRO-RESOLVING MEDIATORS

Åshild Sørskår [1], Amalie Reinertsen [1], Syed Nuruddin [2], Charles Serhan [3], Trond Hansen [1]

[1] *University of Oslo, Department of Pharmacy;* [2] *Oslo Imaging and Therapy Laboratory;* [3] *Brigham and Women's Hospital, Harvard Medical School, Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine*

Aims: The aim of this study is to investigate the mechanisms underlying the observed sex-specific effects of the specialized pro-resolving mediator resolvin D5 (RvD5), which has been shown to reduce inflammatory pain in male mice but not in female mice.

Methods: To explore this sex dimorphism, a series of RvD5 analogs will be synthesized, including an ^{18}F-labeled analog. The radiolabeled compound is designed for use in positron emission tomography (PET) imaging studies to enable in vivo evaluation of the analogs.

Results: The synthesized ^{18}F-labeled RvD5 analog is expected to allow visualization of tissue distribution, pharmacokinetics, and target tissue engagement in vivo. These data may reveal sex-dependent differences in the biological behavior of RvD5 analogs.

Conclusion: PET imaging using an ^{18}F-labeled RvD5 analog may provide novel insights into the mechanisms underlying the sex-specific effects of RvD5 and contribute to a better understanding of its role in inflammatory pain resolution.

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SYNTHESIS AND PRECLINICAL EVALUATION OF GALLIUM-68 AND ZIRCONIUM-89 LABELED DESFERRIOXAMINE-B ANALOGUES FOR PET/CT IMAGING OF INFECTION.

Robin Maradan [1], Barbora Neuzilova [2], Julia Kronberger [3], Irene Feiner [3], Xabier Guarrochena [3], Ayfer Kılçar [4], Milos Petrik [2], Thomas Mindt [3]

[1] *University of Vienna, Institute of Inorganic Chemistry;* [2] *Palacký University;* [3] *University of Vienna;* [4] *Ege University*

Aims: We adapted a solid-phase peptide synthesis (SPPS) approach for the facile synthesis of oxoDFO* and DFO*^{sp}.[1] The complexation properties of the obtained chelators with Gallium-68 (^{68}Ga) and Zirconium-89 (^{89}Zr) are compared to those of the established Desferrioxamine-B (DFO) and DFO*. The resulting complexes were used for infection imaging applications based on the same principle as [^{68}Ga]Ga-DFO.[2]

Methods: DFO analogs were synthesized and labeled with ^{68}Ga and ^{89}Zr; the radiochemical yield (RCY) and radiochemical purity (RCP) were assessed via iTLC. In vitro characterization of the complexes was performed, including logP, protein binding, and stability in various media. In vitro uptake of all complexes was tested in selected microbial cultures under various conditions. In vivo biodistribution was studied in healthy mice. PET/CT imaging of [^{68}Ga]Ga-DFO and [^{89}Zr]Zr-DFO analogs was performed in a mouse model of bacterial myositis.