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Future Perspectives of Artificial Intelligence in Bone Marrow Dosimetry and Individualized Radioligand Therapy

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Radioligand therapy is an emerging and effective treatment option for various types of malignancies, but may be intricately linked to hematological side effects such as anemia, lymphopenia or thrombocytopenia. The safety and efficacy of novel theranostic agents, targeting increasingly complex targets, can be well served by comprehensive dosimetry. However, optimization in patient management and patient selection based on risk-factors predicting adverse events and built upon reliable dose-response relations is still an open demand. In this context, artificial intelligence methods, especially machine learning and deep learning algorithms, may play a crucial role. This review provides an overview of upcoming opportunities for integrating artificial intelligence methods into the field of dosimetry in nuclear medicine by improving bone marrow and blood dosimetry accuracy, enabling early identification of potential hematological risk-factors, and allowing for adaptive treatment planning. It will further exemplify inspirational success stories from neighboring disciplines that may be translated to nuclear medicine practices, and will provide conceptual suggestions for future directions. In the future, we expect artificial intelligence-assisted (predictive) dosimetry combined with clinical parameters to pave the way towards truly personalized theranostics in radioligand therapy.

Introduction

Radiopharmaceutical therapy (RPT) is a treatment modality in nuclear medicine that utilizes radiopharmaceuticals to selectively irradiate specific target tissues. The cytotoxic radiation from β- or α-particles is delivered directly to the cancer cell or the tumor microenvironment via vehicles that bind endogenously or via physiological accumulation mechanisms characteristic in neoplasia, and which allow for targeted therapeutic approaches. RLT is an effective option in the treatment of a variety of cancers, including thyroid cancer, neuroendocrine tumors, and prostate cancer.[1]

In extensively treated patients, however, hematotoxicity is considered a relevant dose limiting morbidity. The Netter I trial reported lymphopenia of grade ≥3 according to Common Terminology Criteria of Adverse Events in 10/111 patients with advanced, progressive, somatostatin-receptor-positive neuroendocrine tumors treated with [^{177}Lu]Lu-DOTATATE.[2] In the VISION-trial, the largest prospective trial investigating [^{177}Lu]Lu-PSMA-617 in castration resistant metastatic prostate cancer patients in conjunction to standard of care treatment, the most frequent adverse event of grade ≥3 was anemia occurring in 12.9% of patients.[3] In patients with hormone refractory

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prostate cancer with skeletal metastases treated with the α-emitter ^{223}Ra-dichloride, grade $\geq$3 anemia was reported in 13%, thrombocytopenia in 6%, and neutropenia in 3% of patients (ALSYMPCA trial).[4] These marketing approval leading phase III trials highlight the intrinsic nature of hematotoxic responses to RLT. Therefore, one of the upcoming obligations of the nuclear medicine community will lie on optimization in patient management based on predictive risk-factors. Careful patient selection will potentially reduce the number of adverse effects and broaden the applicability of theranostic treatment options.

Dosimetry of blood and bone marrow (BM) is essential in RLT for predicting hematological and BM toxicity, such as myelosuppression. This is due to its intricately linked dose-response relationship that has been extensively studied for various radiopharmaceuticals in the past decades.[5-9] In the era of precision medicine, there are, however, several factors including segmentation accuracy, computational capacities, the presence of skeletal metastases and total tumor burden, as well as specific binding of unlabeled nuclides to the BM or daughter migration in unbound α-particles that may affect the accuracy of dosimetry calculations, potentially restricting their predictive value.

Advances in artificial intelligence (AI) methods that are increasingly applied in the field of nuclear medicine[10] hold promise to overcome today's challenges to enable more accurate assessment of absorbed doses to blood and BM. In this context, leveraging machine learning (ML) and deep learning (DL) algorithms, may play a crucial role by heightening dosimetry accuracy, enabling early identification of potential hematological risk-factors, and paving the way for personalized and adaptive treatment optimization. This review delves into the literature available by now on AI in BM and blood dosimetry, exemplifies inspirational success stories from neighboring disciplines that may be translated to nuclear medicine practices, and provides conceptual suggestions for future directions.

What About It

Internal Dosimetry

Internal dosimetry is the science that focuses on the measurement and calculation of energy imparted to matter from radionuclides within both organs and tissues. The study of internal dosimetry also takes into account the spatial and temporal distributions, which are sampled with gamma-cameras and other detectors used in conventional and PET nuclear medicine. Dosimetry provides the fundamental quantities needed for occupational exposures in radiation protection, waste and environmental exposures, risk assessment and treatment planning. Most relevant for the practice of nuclear medicine is that for the approval of new radiopharmaceuticals, the regulatory agencies for medicine, such as European Medicines Agency (EMA) or the US Food and Drug Administration (FDA) require that dosimetric evaluations are performed in human subjects.[11]

The classical models used for radiopharmaceutical dosimetry Medical Internal Radiation Dosimetry (MIRD) or International Commission for Radiation Protection (ICRP) are computational methodologies that facilitate absorbed dose calculations to target organs based on the number of radioactive decays that occur in source organs. The general formulation $D = \widetilde{A} \times S$, reflects the organ-specific kinetics combined in the time-integrated activity ($\widetilde{A}$) and the spatial radiation transport combined in the S-value (S). The S-values are radionuclide− and anatomic model−specific.[12] In this formulation, most organs are source and target organ simultaneously, with an absorbed fraction depending on the target mass, gamma-radiation yield per decay and beta-radiation energy distribution. The remaining energy that is imparted outside of the source region is summed up as cross radiation and contributes to the exposure of neighboring organs and tissues. When considering organs that have a particularly wide extension in the body, such as the blood and bone marrow, it is necessary to consider the different contributors to the total absorbed dose.[13]

Current developments in imaging modalities such as Psitron Emission Tomography (PET) / Computed Tomography (CT) and Single Photon Emission Computed Tomography (SPECT) / Computed Tomography (CT) allow for accurate assessment of absorbed doses in small volume elements. Voxel-based dosimetry presents an alternative to the classical dosimetry models. These are based on the calculation of a voxel S-value by simulating the radionuclide corresponding monochromatic photon and electron sources in different homogeneous tissues.[14] The voxel S-value is then convoluted with the activity distribution, which can be worked out to display a dose−volume histogram of the volume of interest.

AI in Medicine

In recent years, AI has emerged as an essential tool in medical applications, revolutionizing various aspects of healthcare through advanced computational techniques. First, the breakthrough of AI methods in computer vision was enabled by large, preannotated datasets like ImageNET[15] and COCO,[16] where different machine learning models were tested, validated, and compared. In addition, the introduction of convolutional neural networks that could independently learn the patterns from raw data partially eliminated the need for human programmers to elaborately design imaging features.[17] For the medical image segmentation tasks, especially U-Net[18] and self-configuring nnU-Net[19] have been successfully trained and validated on various imaging modalities and tasks.

Medical AI research commonly follows a similar pattern. The studies typically employ supervised training methods and rely on limited labeled datasets due to privacy concerns associated with real medical data and the need for annotation from domain experts. While these models perform remarkably well on specialized tasks, they often struggle to generalize beyond their specific training data. This limitation highlights the need for more versatile AI approaches to handle diverse medical challenges.[20,21]

The emergence of foundation models marks a notable shift in AI development. Unlike traditional supervised models, foundational models utilize self-supervised learning, enabling them to train on large, heterogeneous data without or with very little need for expert annotation.[22] This approach allows foundational models to attain high accuracy across various medical tasks, particularly when adapted for specific applications.

In the coming years, we anticipate the emergence of several foundational models tailored to the medical field, which can seamlessly process data from multiple data modalities, quickly learn new tasks, and use medical domain knowledge.[22] Given these advancements, we propose using supervised models as an initial proof-of-concept to validate the feasibility and efficacy of AI solutions for medical tasks. Subsequently, the focus should shift towards collecting large, diverse, multicentric, multinational harmonize datasets versus data sets and fine-tuning and adapting medical foundation models. This dual approach would combine the advantages of the AI models, such as accessibility, easier validation of supervised models, and better generalization of foundation models.

Integrating AI in Bone Marrow Dosimetry

In dosimetry, data collection and calculations are labor-intensive and complex procedures that require medical physics expertise and proper dosimetry software tools. One of the focus-areas within the current research landscape has been the optimization of the time-consuming data acquisition process from serial imaging as well as multiple blood and urine sampling measurements. Several approaches for minimizing sampling time points via inclusion of population-based biokinetic data (single time-point dosimetry) have been introduced.[23-25] These simplifications provide access to routinely feasible and moderately accurate organ dosimetry in individuals encompassing similar excretion kinetics as the population used for respective model development. However, with the rapid development of DL algorithms, leveraging the calculation speed and automation capabilities of various dosimetry steps has become increasingly attractive by prioritizing accuracy of dosimetry calculations at clinically feasible computational effort.[26] In the following, the specific challenges of BM dosimetry will be addressed as well as the possibility to overcome these challenges with AI methodologies, in order to facilitate segmentation, fitting procedures, and radiation transport and energy deposition calculations.

Bone Marrow Segmentation

BM segmentation "in bone metastatic diseases" or similar. Otherwise, no malignant cells poses a unique challenge in nuclear medicine due to the presence of healthy and malignant cells. Therefore, delineation of metastatically affected BM tissue is not straightforward. Its complexity differentiates it from other organs-at-risk like kidneys, where the focus is solely on protecting healthy tissue from radiation.[27] In BM, the primary goal of RPTs or RLTs is often to eliminate the metastases while preserving or allowing for regeneration of healthy tissue. Typical methods have made use of surrogate radiopharmaceuticals to specifically target active BM. Delker et al.[28] used ^{99m}Tc-anti-granulocyte antibody SPECT/CT for active BM segmentation in [^{177}Lu]Lu-PSMA-617 therapy. Peterson et al.[29] presented a methodology to calculate the absorbed dose to hematopoietically active cells using ^{99m}Tc-sulfur colloid imaging for red marrow localization and quantification. Dalvand et al.[30] conducted a study to calculate the BM absorbed dose of [^{141}Ce]Ce-EDTMP complex and compared it with that of ^{89}Sr-dichloride using Monte Carlo simulations.

In recent years, DL models have been increasingly used for automated segmentation of organs and tumors from medical images, such as CT or PET/CT scans, with ever-increasing speed and accuracy.[31-35] DL network architectures most commonly used for image segmentation are fundamentally similar, and according to their backbone, can be classified into U-Net-based networks and vision transformer-based networks.[18,36] Importantly, the accessibility of freely available segmentation networks, such as TotalSegmentator, has led to a wide adoption of such tools in the field of clinical research[37] and increasingly in commercial tools[38] In the field of BM dosimetry, this will probably significantly reduce the time and effort required for manual or semi-automatic segmentation of bone sites or even the spongiosa, which is a crucial step in imaging-based dosimetry calculations and is particularly extensive for BM due to its distribution throughout the body.[39,40]

A simple way of dealing with intra- and inter-individual tumor burden in close vicinity to the BM could be the separation of macroscopic ligand-specific tumor sites from the total BM volume. In external beam radiotherapy, numerous studies have reported on DL methods for clinical target volume segmentation in different cancers, such as prostate cancer,[37,41] non-small cell lung cancer,[42] breast cancer,[43] rectal cancer[44] cervical cancer,[45] head and neck cancer,[46] pancreatic cancer,[47] and stomach cancer.[48] These DL tools also hold significant promise for application in RLT. For example, Zhao et al.[49] proposed an automated prostate cancer lesion characterization method with DL to determine tumor burden on [^{68}Ga]Ga-PSMA-11 PET/CT in PSMA-directed RLT. Li et al.[50] developed an automated DL-based framework that segments and classifies uptake on PSMA-PET/CT to automate quantification of whole-body tumor burden. Another multicenter study demonstrated strong performance and generalizability of a multiple 3D U-Net approach for total tumor volume segmentation from FDG-PET/CTs in lymphoma.[116] A recent review conducted by Brosch-Lenz et al.[51] discussed established and emerging segmentation techniques, along with their potential utilization in RLT.

Interestingly, in histopathological analyses, DL models with a 3-layer hierarchical framework were previously used in whole-slide BM images to detect BM cells and cellular trails and to identify the right cell-type.[52,53] In addition, a multi-step ML approach with individual DL-models was reported to accurately distinguish between acute myeloid leukemia and healthy tissue.[54,55] Although single cell-based disease status prediction was not reliable, these efforts illustrate how beneficial DL models may become in differentiating

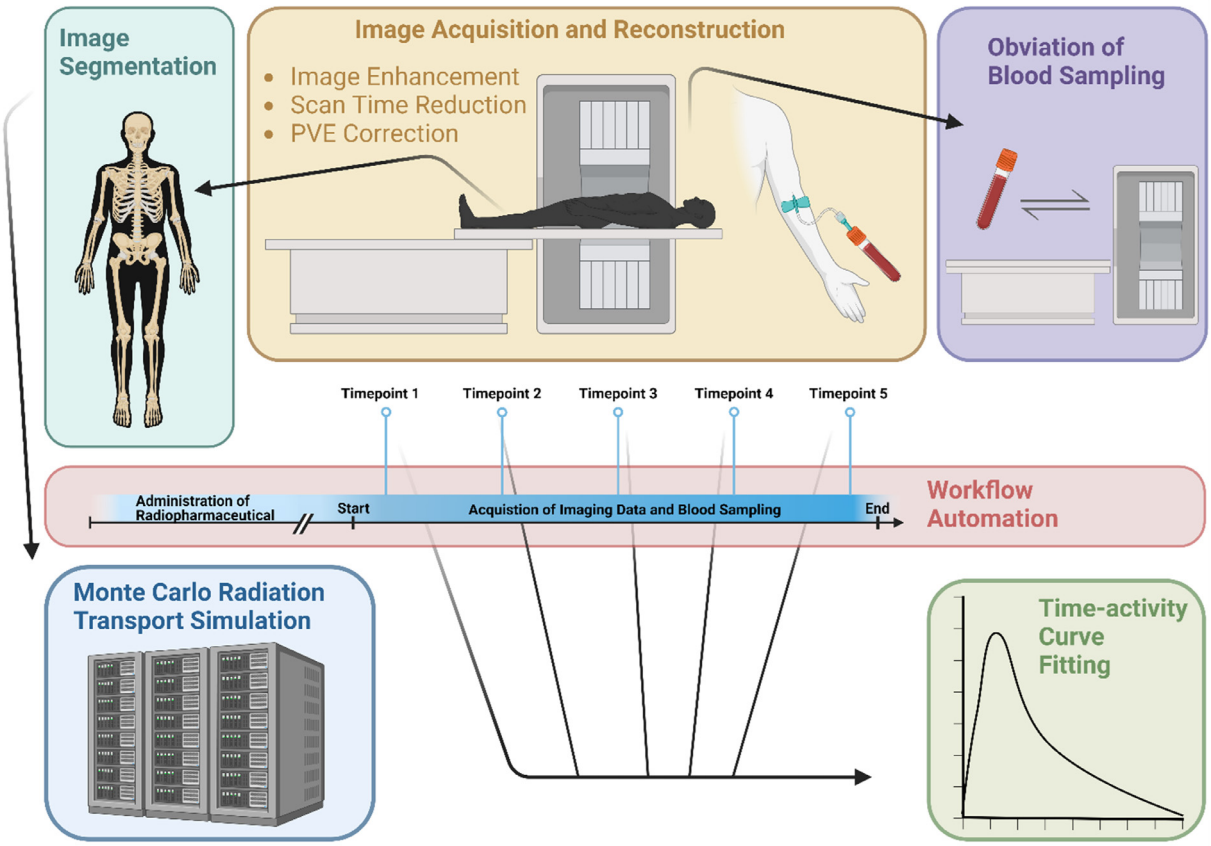

Figure 1 Conceptual illustration of potential use-cases for implementing AI methodologies in BM dosimetry protocols.

malignant from healthy BM tissue and should inspire the nuclear medicine community to dare exploration of such novel methodologies for dosimetry purposes.

Bone Marrow Dosimetry Workflow

The complex structure and spatial distribution of BM within the body, coupled with the generally low uptake of radiopharmaceuticals in this region, present a number of challenges to the current methodology of BM dosimetry. These limitations preclude its broader clinical implementation.[13] One potential solution could be the integration of AI into the methodology of BM dosimetry. This could, for example, facilitate data acquisition (e.g., accelerated image acquisitions) or enhance the accuracy of dosimetry calculations and their comparability between different sites. Another potential avenue for exploration lies in the integration of AI methodologies into the BM dosimetry workflow, particularly in dosimetry software platforms. This could improve access to the methodology, and make it more suitable for routine clinical practice. Besides segmentation, which was addressed earlier, a number of steps in the dosimetry workflow, including image registration, curve fitting, and dose calculation, could be simplified or even automated. Examples for potential ways of AI-integration in BM dosimetry are shown in Figure 1. The aspects with the highest potential are listed and briefly outlined below:

Enhancement of imaging: the low uptake of most radiopharmaceuticals in the BM results in very low count rates during imaging, which in turn leads to a high noise level. Similar to traditional signal processing techniques, artificial intelligence methods could be employed to reduce the noise level of the images before (e.g., in the projection domain) or after reconstruction.[56-58] Alternatively, convolutional neural networks have been employed to reduce scan time while preserving image quality.[59] This has been achieved, for instance, by generating synthetic projections that have never been recorded. Recently, deep learning approaches have also been used to correct for the partial volume effect, which strongly deteriorates the quality of SPECT/CT images by blurring the activity between bone sites, which can lead to errors in quantification, especially for therapeutic radionuclides such as ^{177}Lu and ^{131}I.[60,61]

Time-activity curve fitting: AI techniques can be employed to fit time-activity curves (e.g., those derived from quantitative imaging data), which represents a pivotal step in the estimation of time-integrated activity coefficients (formerly: residence times) and, thus, in the calculation of absorbed doses. Particularly in instances of complex biodistribution kinetics or when incorporating population-based models, AI approaches could enhance conventional analytical methodologies.[39,62]

Monte Carlo radiation transport simulation: AI can be employed to expedite radiation transport simulations, which are typically conducted using Monte Carlo simulations that serve as the foundation for calculating patient-specific dose

distributions. For instance, post-injection image data can be utilized to inform Monte Carlo simulations of dose distributions. Convolutional neural networks can be trained in a supervised manner to accelerate Monte Carlo simulations of dose distributions or even replace them entirely, thereby reducing the computational effort required to perform full Monte Carlo simulations. This can be achieved, for example, by the time-efficient estimation of tissue-specific convolutional kernels.[26,63-65] An example for the architecture of a convolutional neural network used for organ dosimetry is shown in Figure 2. This algorithm was applied on serial [^{68}Ga]Ga-NOTA-RGD-PET/CT data and revealed mean absorbed dose errors at organ level of less than 1.5% at almost 4000 times faster computational time compared to the reference Monte Carlo simulation. In addition, hybrid approaches combining DL algorithms with multiple voxel-S-value have recently allowed for voxel-wise absorbed dose mapping considering heterogeneous uptake patterns in a Monte-Carlo wise manner.[66,67] Mansouri et al.[67] employed a U-Net Transformer model combined with multiple voxel-S-value to evaluate organ- and voxel-wise absorbed dose errors in [^{177}Lu]Lu-DOTATATE therapy and reported less than 1% mean error for tumors and most investigated organs at risk including kidneys, liver and spleen. In this approach, processing time was only around 3 seconds per single-bed SPECT/CT. In BM dosimetry in particular, the microdistribution of the volume fractions of trabecular bone, fat and hematopoietic tissue plays a major role. AI might be used here to estimate these volume fractions from other imaging modalities and derive a corresponding composition-dependent dose prediction.

Direct estimation of bone marrow dose: the type of BM uptake of a radiopharmaceutical (specific or nonspecific in the context of blood flow) plays an important role in BM dose calculation, as does the activity concentration in the blood. In the future, image-based AI algorithms may be employed to estimate the dose absorbed to the BM directly from the imaging data, potentially obviating the necessity for blood sampling or the use of surrogate organs such as the whole body (which is often employed in planar whole-body images) or the lumbar spine (which is typically utilized in 3D imaging).[40,63]

Workflow automation: as previously stated, the integration of AI into dosimetry software platforms could facilitate the automation of various steps within a dosimetry workflow. This could, in turn, enhance the efficiency and accuracy of the BM dosimetry workflow, potentially eliminating the necessity for the majority of manual steps. This would, in turn, reduce the time and effort required for dosimetry, thereby facilitating wider clinical adoption.

Enhanced Biodosimetry

Peripheral blood mononuclear cells can be used to determine radiation damage in patients or to investigate differences in radiosensitivity between patients by biological methods. There are numerous cytogenetic studies on blood samples from patients undergoing nuclear medicine therapy, e.g. on dicentric chromosomes,[68-72] on translocations,[73] or on micronuclei.[74-76] A summary of the most important studies on this topic can be found in a review by Schumann et al.[77] An advantage of these cytogenetic methods is that they can detect radiation-induced effects of therapies at the cellular level. However, the disadvantage of all these methods is their low sensitivity in the range of absorbed doses below 100 mGy. This is an absorbed dose to the blood delivered during many radionuclide therapies, especially in the first few hours after the start of therapy.[77] By combining the absorbed dose determination in the blood with specific biomarkers, possible dose-effect relationships can be generated. However, most of the studies mentioned before, did not directly determine the

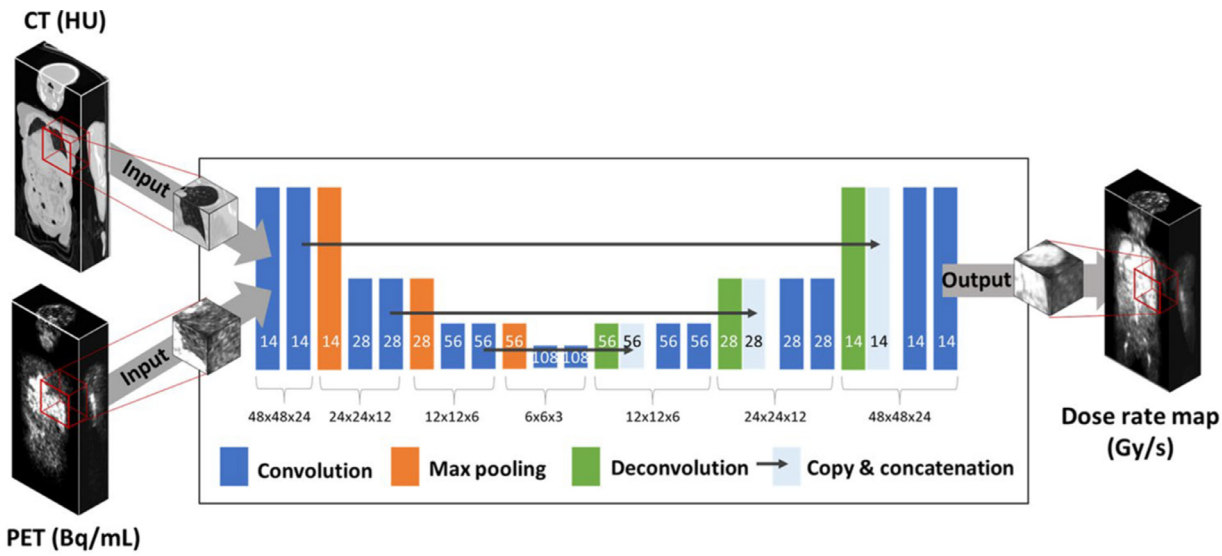

Figure 2 Example of a U-Net architecture for internal dose calculation. The Deep-dose algorithm/method applies a convolutional neural network to estimate voxel dose rate values (output) from quantitative hybrid imaging data (input). The matrix dimensions of each feature map (box) are indicated below the respective map. Monte Carlo simulation-based dose rate maps served as reference. Re-printed from.[115]

absorbed dose in the blood, so there is little data available to determine dose-effect relationships.

For absorbed doses in the low-dose range below 100 mGy the biomarkers γ-H2AX and 53BP1 are frequently used as a surrogate measure of DNA double strand breaks (DSBs).[78,79] Using this assay several studies have shown that there is a linear correlation between the absorbed dose to the blood and the number of radiation-induced γ-H2AX and 53BP1 DSB foci in the first hours after radiopharmaceutical administration.[80-83] At time points >24 h, the number of radiation-induced DSB foci decreases, even though the absorbed dose increases, most likely because DNA DSB repair competes with ongoing foci induction (>24 h) due to the non-negligible absorbed dose rate of residual activity in the body. These data may be indicative of what happens in normal tissues exposed to internal radiotherapy, and of tumor response in patients with neuroendocrine tumors[84] and prostate cancer.[85]

In most cases foci numbers from images obtained by confocal microscopy are manually counted in 100 cells. However, due to the low numbers of events in the absorbed dose range below 100 mGy, it would be advantageous to analyse a higher number of cell nuclei in order to minimise statistical uncertainties. This could be achieved by using special automated programmes for image analysis. A further advantage of an automated analysis is that the uniform counting method, independent of the observer, would also allow larger and multicentre studies, as well as simple routine analyses. This image analysis could be further improved by applying AI methods for automated image analysis. However, no automated programme has yet delivered reliable results in the range of low absorbed doses expected in the blood during radionuclide therapies. Most programmes were initially developed for higher absorbed doses (e.g. >1 Gy) and a correspondingly larger number of foci. In recent years, however, there have been publications on automated programmes that, according to the authors, are also suitable for the low absorbed dose range, such as AutoFoci[86] or use promising new methods, such as FocAn[87] or Foci-Xpress.[88] FociRad[89] applies methods for deep learning to these images, however, it was optimised for absorbed doses of more than 1 Gy.

To further enhance the potential of biodosimetry and to describe patient-specific absorbed-dose dependent DNA damage response in peripheral blood mononuclear cells a linear one-compartment model was developed using data from patients with differentiated thyroid carcinoma receiving their first radioiodine therapy.[90] This model could be extended to other therapies to significantly reduce the number of blood samples required to describe the *in vivo* induction and repair of DSBs. It is expected that this model could also be used for retrospective dosimetry of other radionuclides in radiation accidents.

Another step in linking biodosimetry data obtained from experiments is to use them to validate Monte Carlo simulations of radiation damage to DNA, e.g. with "Geant4-DNA".[91-94] These results in combination with experimental data could be used to further improve dosimetry and to establish dose-response relationships in radionuclide therapies.

Adaptive Treatment Planning

Most RLTs use fixed administered activities and treatment cycles – a historically driven approach. However, given the interindividual variability of tumor uptake patterns, and the generally low toxicity profile observed so far, it has been suggested that many if not most patients are being undertreated at this empiric regime.[95] This, in turn, has led to the development of dose escalation strategies following two basic principles: a) extend the number of treatment cycles to obtain a fixed cumulative administered activity and b) increase the administered activity per cycle based on individual dosimetry of organs at risk to obtain a fixed cumulative organ absorbed dose (toxicity threshold dose). The first concept was recently successfully applied in PSMA-targeted RLT therapy,[96,97] as well as ^{177}Lu- and/or ^{90}Y-based peptide receptor radiotherapy.[98] The feasibility of latter principle was demonstrated in the P-PRRT trial[95,99] and a combination of both approaches was used in the Uppsala observational study.[100] Interestingly, both studies used kidney dosimetry to individually tailor the cumulated activity per patient/cycle, and obtained grade three kidney toxicity in ≤0.5% of patients, while at least grade three subacute hematological/BM toxicity was observed in 5.8% (leukopenia and thrombocytopenia) and 15% (BM) of patients, respectively. In patients with healthy kidney function, individualized treatment planning based on blood and BM dosimetry could, therefore, become a key component for optimizing patient management in RLT.

Foremost among relevant parameters for individualized RLT is the determination of reliable dose-effect relations.[7,101-104] The development and increasing accessibility of DL architectures may further increase predictive accuracy by incorporating clinical- and patient-specific data to achieve satisfactory generalizability of training models. Such novel approaches have not yet been used in nuclear medicine, but the concept of DL-enhanced adaptive treatment planning is already known from external radiotherapy. In here, DL approaches have been utilized for adaptive radiation therapy by modifying treatment parameters based on up-to-date patient anatomy and treatment response. For example, task- and patient-specific adaptive radiation therapy has been implemented by overfitting DL models to patient-specific data and which resulted in more accurate autocontouring in CT used for treatment re-planning.[105] Dose adaptation with DL methods has been demonstrated for various entities, including lung cancer,[106,107] and prostate cancer.[108] Although the application of DL in adaptive RLT has yet not been explored, it could be a promising tool to, for example, automatically adjust the activity and the time between cycles by considering potential changes in the physiological biodistribution, tumor volume, and uptake patterns, as well as time-dependent cellular repair mechanisms after initial treatment.

Clinical Perspectives

In the era of personalized medicine, nuclear medicine has evolved from offering standardized RLT to customizing

treatments based on individual factors such as tumor heterogeneity and therapeutic responses.[109,110] Broader application of RLT presents significant potential; however, it is crucial to monitor potential severe hematotoxic or nephrotoxic side effects. Although serious adverse events are infrequent and most of them are well manageable, identifying at-risk patients is essential. For example, in patients responding to PSMA-targeted therapy for mCRPC or PRRT for neuroendocrine tumors, extended treatment cycles require monitoring of cumulative doses due to potential bone marrow depletion.[97,98,111] This risk is heightened in patients previously treated with chemotherapy, as their hematopoietic recovery capacity can be compromised, increasing the likelihood of severe adverse events. Here, dosimetry can play a vital role. Dosimetry of tumor lesions and safety organs facilitates the customization of RLT through tailored regimens that aim to minimize toxicity and enhance tumor responses.[112]

Specifically, correlation of the absorbed dose to the BM with a reduction in platelet count and decrease in hemoglobin levels has been observed.[7] Additionally, it is crucial to consider the absorbed dose in the spleen, as it is the most irradiated organ during PRRT and serves as a significant reservoir of blood cells.[113,114] It is also recognized that treatment response varies among patients with similar clinical conditions who receive identical activities, which is largely attributed to differences in the absorbed doses to target lesions. With regards to dosimetry, several aspects could be significantly enhanced and streamlined by applying AI methods. The application of AI methods in BM dosimetry is particularly noteworthy for its clinical implications. The reduced time requirements can lead to broader implementation in clinical practice and greater availability and applicability in larger patient cohorts. This advancement may bring dosimetry offerings closer to routine clinical use. Furthermore, AI can facilitate the linkage between macrodosimetry and microdosimetry, ultimately enabling the generation of a comprehensive dose profile for individual patients.[15] Additionally, higher standardization can enhance the reliability of dose-response relationships, thereby strengthening clinical confidence in dosimetry results and further promoting wider adoption. It is also likely that user dependency will decrease, which results in improved comparability of dosimetry methods and results across different centers, and which facilitates multicenter studies, contributing to further generation of evidence.

Conclusion

This review was designed to inspire and motivate the nuclear medicine research community on the opportunities for integrating artificial intelligence methodologies in blood and bone marrow dosimetry-guided RLT. Leveraging machine learning and deep learning algorithms are expected to play a crucial role in internal dosimetry by heightening accuracy and standardization at low computational effort, and enabling early identification of potential hematological risk-factors. In the future, we expect artificial intelligence-assisted (predictive) dosimetry combined with clinical parameters to pave the way towards truly personalized theranostics in RLT.

Declaration of competing interest

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