EDITORIAL

AI in Nuclear Medical Applications: Challenges and Opportunities

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In the realm of resource allocation within the healthcare sector, numerous challenges exist that necessitate the automation of these processes for effective management [1]. The increasing demand for automation in healthcare is driven by a surge in patients, a need for enhancements in quality, such as early identification and tailored treatments, and the increasing burden on healthcare professionals like doctors and nurses. Artificial Intelligence (AI) is already demonstrating its potential in screening routines, rivaling human performance in tasks such as breast cancer screening. The integration of AI within the radiology departments has yielded notable advancements. This integration not only enhances resource utilization but also offers opportunities for further optimization, particularly in the realm of nuclear medical applications. The synergy between AI and radiology stands to significantly streamline operations related to radioactive isotopes, thereby enhancing overall efficiency and efficacy in clinical settings. The synergy between AI and radiology stands to significantly streamline operations related to radioactive isotopes, thereby enhancing overall efficiency and efficacy in clinical settings [2, 3].

The utilization of Artificial intelligence especially machine/deep learning into different aspects of nuclear medical applications advances exponentially, showcasing their potential roles in physics and clinical tasks including: **radiotherapy, medical imaging, radiopharmacy, and disease theranostics**. These four domains are outlined briefly as follows.

A) Radiotherapy, also called radiation oncology or therapeutic radiology, employs nuclear or ionizing radiation to damage and eradicate cancerous tumor cells. AI systems hold the capability to streamline various aspects of the intricate radiotherapy process including segmentation, planning, prediction of dose delivery, integration with radiomics, measuring radiation dosage, utilizing computer-aided detection, and forecasting outcomes. Nevertheless, viewing artificial and swarm intelligence as a "black box" raises concerns, as human operators might comprehend only the input, output predictions, and applying it to clinical practice poses challenges [4].

While AI holds transformative potential, challenges exist in its clinical implementation, including technical, ethical, and legal domains, such as patient data privacy. The limited transparency of the entire system raises ethical questions and warrants careful consideration from various perspectives [5, 6].

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Moreover, AI may be involved in various treatment stages, making it complex to establish a structured knowledge base. Transparency issues in routine machine learning implementation could be unsettling for patients and practitioners, impacting the trust inherent in clinical relationships. Unanswered questions regarding the responsibility of treatment decisions and the need for comprehensibility in clinical decision-making processes may hinder AI adoption. Despite these challenges, recognizing the possible benefits of AI is crucial for improving the therapeutic ratio and refining workflow effectiveness in radiotherapy.

Some propose increasing control over machine learning by allowing doctors to understand the inner workings of the devices and implementing additive controls if regulatory agencies demand algorithm disclosure [5]. The routine use of AI-based technologies in radiotherapy is expected to increase over the next 5–10 years, focusing on task replacement and decision support systems. The importance of clear interpretability of AI outputs and the need for well-educated and trained radiotherapy professionals are emphasized. The roles and responsibilities of professionals, including a core team led by radiation oncology and medical physics experts, need to be clearly defined. New training for professionals should cover organizing services with integrated AI tools, selecting and implementing AI applications, defining input for AI, and evaluating output competently [6].

The future of AI in radiotherapy encompasses innovative approaches, as evidenced by the integration of educational chatbots into the Internet of Things. Utilizing AI features like Natural Language Processing (NLP) through platforms such as IBM Watson Assistant, these chatbots exhibit humanlike characteristics, aiding users in diverse backgrounds to acquire information and guidance. Furthermore, the report underscores the current clinical use and anticipated expansion of AI-based auto-contouring in radiotherapy, while highlighting challenges such as the lack of consent regarding validation and ensuring quality. There's a pressing need for direction, learning, and instruction on secure AI tool usage, with concerns about equitable implementation across departments.

B) Medical imaging: Nuclear medical imaging relies on capturing gamma rays produced during the radioactive decay of introduced radioisotopes within the body. An external camera detects the emitted radiation, which is then reconstructed into an image. Common nuclear image acquisition technologies are Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) [7].

AI applications in the medical imaging sector can be categorized into several primary fields including image pre-and post-processing, image reconstruction, image denoising, estimation of full-count SPECT, and SPECT Attenuation Correction (AC) [6, 8].

In body oncology, nuclear medical imaging plays a crucial role in early therapy response evaluation, lesion characterization, and quantifying whole-body tumor volume, especially in challenging cases like prostate cancer metastases. In cardiac imaging, SPECT and PET are regularly employed to aid clinical decision-making, often combined with CT or MRI scans. For diffuse gliomas, advancements in genomics, epigenomics, and transcriptomics have influenced tumor classification, with MRI being the primary imaging method, occasionally complemented by PET using radiotracers like C methionine and Fluoro Ethyl Tyrosine (FET) [9].

One of the significant obstacles in creating attenuation maps from magnetic resonance imaging was differentiating via bone and air areas, like the mastoid in the temporal bone and bone fat in the pelvic areas. Ultrashort echo time and zero echo time show promise in addressing this challenge for brain imaging, although they experience elevated levels of noise and artifacts in the images. Scientists have explored various machine learning-based approaches such as random forest, support vector machines (SVMs), Markov network, and clustering algorithms to enhance the segmentation-based method of MR-based attenuation correction. However, the integration of convolutional neural networks with hand-crafted approaches allows for the preservation and extraction of richer detail information [7].

Future direction must furnish proof regarding the benefits of employing deep learning in image reconstruction, focusing on both the precision in qualitative and quantitative aspects in comparison to existing algorithms. The speed of execution, particularly with "direct reconstruction" DL approaches, is crucial, especially in the framework of positron emission tomography scan covering the entire body with substantially increased data volumes. Additionally, future research should compare DL's performance with post-processing reconstruction improvements like denoising or super-resolution tasks. The exploration of multimodality datasets for automatic image segmentation, combining PET, CT, and MR, is identified as a crucial direction. Moreover, the application of DL in image synthesis, specifically image harmonization, is highlighted as significant for addressing imaging technology-related variability in multicenter trials. Employing generative adversarial networks for translating images is seen as a potential major player in harmonization methodologies. The emphasis on large training datasets and harmonization approaches beyond standardization protocols underscores the evolving landscape of AI in nuclear medical imaging.

C) Radiopharmacy: or Nuclear Pharmacy is a specialized field in the pharmacy profession dedicated to the correct utilization of radiopharmaceutical drugs. The potential of Radiopharmaceutical Therapy (RPT) for predictive modeling, image analysis, and treatment optimization is further augmented by artificial intelligence and machine learning. Combining therapeutic and diagnostic technique, artificial intelligence techniques, predicting dose absorption and treatment results, could be pivotal in customizing radiopharmaceutical theranostic therapies [10, 11].

Advanced radiomics and artificial intelligence applications for the theranostic use of radioligands targeting somatostatin receptors and prostate-specific membrane antigen hold the substantial potential in enhancing diagnosis and treatment monitoring by supplementing visual analysis with quantitative information.

To substantiate the promising achievements, subsequent scientists should replicate and confirm these results using a sizable patient cohort. This step is crucial for establishing robust scientific evidence and translating the potential uses of radiomics and artificial intelligence into clinical trials. It will also broaden the utilization of therapies guided by dosage measurements for those individuals' receiving radiopharmaceuticals. To address challenges related to reproducibility and generalization in radiomics and AI research, conducting multi-center studies through data sharing and harmonization is imperative. Emphasizing the incorporation of radiomic signatures, biological characteristics, and physical models into the training of architectures is essential. In summary, these applications have immense potential to further improve patient outcomes [12]. Moreover, the future of theranostics and the clinical advancements in RPTs should involve utilizing new isotopes and biological targeting methods. This includes refining personalized dosimetry and introducing innovative therapy approaches that integrate RPTs with external beam radiotherapy or methodical treatment [13].

D) Disease theranostics: In medical nuclear imaging of non-malignant conditions, AI approaches are primarily employed for automated or assisted image categorization and clinical decision support, particularly in spanning thoracic imaging to diagnose some diseases including tuberculosis, lung cancer, the identification of emerging infections, and a range of cardiovascular conditions as well as other diseases like Alzheimer and Parkinson [7]. In addition, the automated selection of features, segmentation, and classification in myocardial perfusion scintigraphy can aid in pinpointing individuals eligible for intervention and predicting clinical outcomes.

AI-driven analysis of nuclear medical images can be categorized into three main categories for disease theranostics [9]:

1) AI categorizes predefined body subregions with specific labels, aiding in histological classification from segmented tumor PETs and diagnosing neurodegenerative diseases through cerebral metabolic PET.

2) AI assists nuclear medical experts in analyzing total-body nuclear medical data, commonly used to quantify entire tumor volumes in positron emission tomography. It semi-automatically eliminates physiological uptake, facilitating the quantification of whole-body tumor volumes.

3) AI processes entire-body image data to automatically identify all pathological tracer accumulations, integrating aspects from previous trends. This is commonly applied in oncological examinations like FDG-PET, PSMA-PET, or bone scintigraphy, enabling patient stratification based on overall survival. This approach may facilitate early therapy intensification and improve outcomes. The estimation of pathological status from predefined anatomical subregions is relevant for diagnosing benign diseases, while fully automated delineation of pathological tracer foci is more applicable for monitoring oncological diseases. AI models can undergo pre-training on PET/CT images and then be fine-tuned using SPECT/CT data. The transfer of knowledge across modalities for lesion segmentation in SPECT images, utilizing PET segmentations, can be achieved through unsupervised adversarial training, similar to adapting from the magnetic resonance domain to the computed tomography domain. By estimating a probability map using diagnostic PET images and incorporating it into the segmentation model for SPECT/CT images, the model gains insights into the likelihood that a voxel in a SPECT image is part of a tumor or Organ at Risk. While the probability map may lack the precision required for complete SPECT/CT segmentation due to tumor variations, it serves as an initial guide, enhancing the likelihood of detecting smaller tumors [10].

Besides neurooncological conditions, artificial intelligence is frequently applied in nuclear medicine for neurodegenerative disorders. Various neural networks are utilized to automatically classify Alzheimer's disorder, employing FDG PET with T1-weighted MR images, FDG PET images alone, or amyloid PET images. The buildup of Ab amyloid in the brain is anticipated to occur before the onset of Alzheimer's signs. Although pharmaceutical treatments are not yet approved, early theranostics, facilitated by automated assessment of PET images of the brain, could be crucial in recognizing candidates for potential therapeutic intervention when targeted therapies become available. Future research can employ AI and big data in theranostic approaches for pretreatment and diagnostic staging/re-staging of aggressive tumors expecting to enhance image reconstruction and reduce noise in theranostic images [9, 13].

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