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Artificial intelligence in nuclear cardiology: Technical perspectives, strategic directions, and recommendations from an IAEA expert working group

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Artificial intelligence (AI) is increasingly permeating nuclear cardiology and offers the possibility to enhance diagnostic accuracy, prognostic stratification, and operational efficiency. AI is demonstrating applicability across the imaging workflow—from individualized patient selection and adaptive image reconstruction to denoising of low-dose datasets, automated attenuation and motion correction, calcium scoring, and the integration of imaging with clinical and functional variables for enhanced diagnosis and comprehensive risk assessment.

But the translational trajectory of AI in nuclear cardiology is challenged by the lag in fundamental AI knowledge among researchers and clinicians, the quality of the target data regarding heterogeneity in acquisition protocols, scanner platforms, and patient populations, and by infrastructural disparities that constrain the generation of large, representative datasets needed for training and validation, particularly in low-resource settings. Additionally, necessary regulatory and legal frameworks remain in early stages of harmonization.

This white paper, developed by an International Atomic Energy Agency (IAEA) working group, provides a succinct overview of the technical basis, areas of deployment, clinical value and unmet challenges of AI in nuclear cardiology. It makes punctual suggestions to aid maturation in this area while maintaining a sober interaction with the overwhelming nature of the field. These include promoting standardized acquisition and reporting practices, establishing globally representative reference datasets, promoting imaging multimodality frameworks and developing AI-proficient clinical and technical personnel. Under these conditions, AI may meaningfully enhance the diagnostic and prognostic value of

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nuclear cardiology while supporting equitable implementation and preserving clinical accountability.
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Introduction and objectives

The emergence and development of artificial intelligence (AI) is reshaping the field of nuclear cardiology. AI-enabled analyses are optimizing workflows while enhancing the diagnostic and prognostic value of nuclear cardiology techniques. However, the unprecedented growth of AI is also saturating the channels of knowledge dissemination,[1] making it increasingly difficult to maintain an overview of the state-of-the-art, assess the robustness of AI approaches, and contextualize their performance and generalizability in clinical practice.

In its international role supporting the safe, effective, and equitable access to and use of nuclear medicine, the International Atomic Energy Agency (IAEA) has established a working group to assess the current landscape of AI implementation in nuclear cardiology and identify its most relevant challenges. The present white paper resulted from this process. It aims to provide a succinct overview of the technical basis of AI, the areas of deployment in nuclear cardiology, the documented clinical value and the emerging challenges in this utilization. Simultaneously, it makes punctual suggestions to aid maturation in this area and to maintain a sober interaction with the overwhelming nature of this field. Finally, it proposes the creation of a high-quality nuclear cardiology reference dataset to serve as a structural contribution to the training and improvement of novel AI models in nuclear cardiology.

The basis of AI and its place in nuclear cardiology

Modern machine learning (ML)-based AI relies on mathematical models (or algorithms) that iteratively improve their classification or predictive performance through exposure to new data. ML extends traditional statistical modeling as it can accommodate a large amount of input variables and capture complex, non-linear relationships within the data. Among ML techniques, artificial neural networks—featuring various processing mechanisms such as convolutions and transformers—have demonstrated remarkable success in analyzing and generating images, text, and video. These advancements fall under the umbrella term of deep learning (DL). (See Fig. 1) The most notable breakthroughs in this domain are foundational models, including large language models (LLMs) such as Chat GPT and emerging vision-language models (VLMs).[2]

Usually, ML-based AI benefits from large datasets which are randomly parcellated to subject the models to several runs of representative data, allowing its progressive refinement (i.e. training-testing process). Nevertheless, technical advancements in AI model functions, model pre-training and transfer learning have opened the door to data economization. This makes it increasingly equitable to generate useful AI models.

At the core of AI lies the quality of the data used for training, testing, and validation. Regardless of whether a model is simple or complex, it learns patterns and relationships from the data to optimize its output. In essence, AI models are designed to converge on a solution based on the algorithms they employ. However, these models have not inherent understanding of whether the learned dependencies are mechanistically related to the problem at hand. As a result, outputs can be heavily biased or overfitting when trained on low-quality or unrepresentative datasets. For a clinically oriented explanation of ML-based AI principles in nuclear cardiology, readers are encouraged to consult the accompanying references. Nuclear cardiology entails the use of single-photon emission computed tomography (SPECT) and positron emission tomography (PET) to assess myocardial perfusion, function, and metabolism.[3] These techniques generate vast amounts of data—qualitative, semi-quantitative, quantitative and pixel-based images—on top of an already substantial set of clinical variables. This abundance of data types underlies the relevance and applicability of AI in this domain. Whether through simpler AI models that integrate clinical and imaging input variables, or through complex DL approaches, nuclear imaging provides a rich substrate for effective and comprehensive data analysis.[4-6] As a result, key advancements of AI in nuclear cardiology include improvement in patient selection, image acquisition and processing, image interpretation and report generation, as well as the integration of nuclear cardiology data with other clinical and imaging information for diagnostic and prognostic purposes. (Fig. 2) The state-of-the-art in these areas will be discussed in the following section.

AI domains of implementation

Appropriate use of imaging and patient selection

Accurate patient selection and adherence to *appropriate use criteria* are essential to maximize diagnostic yield, minimize

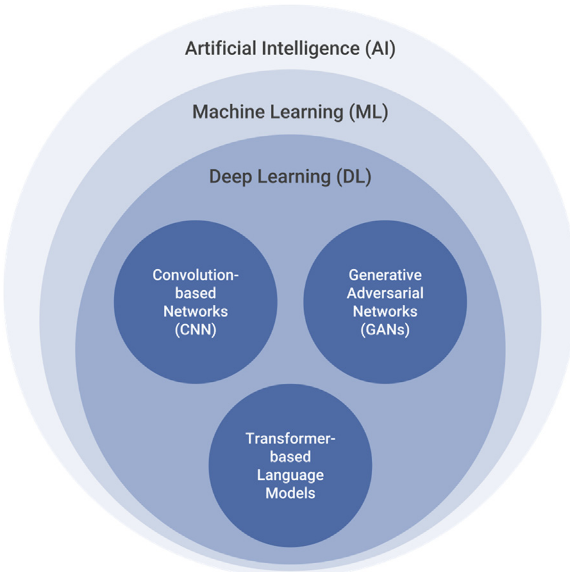

Fig. 1 Hierarchical relationship between artificial intelligence (AI), machine learning (ML), and deep learning (DL), with key DL architectures relevant to medical imaging, including convolutional neural networks (CNNs), generative adversarial networks (GANs), and transformer-based language models.

unnecessary procedures, reduce radiation exposure, and optimize resource utilization. AI enables a highly individualized approach by integrating clinical, imaging, and risk factor data to identify patients most likely to benefit from advanced imaging techniques, thereby improving diagnostic efficiency. ML models can support the prediction of abnormal myocardial perfusion imaging (MPI) based on pre-test variables.[4,7-10] These data-driven approaches go beyond traditional dichotomous appropriateness criteria, offering a more nuanced assessment that may enhance patient selection.

Stress-only imaging

The stress-only SPECT protocol is an established approach to reducing both radiation exposure and imaging costs while improving patient throughput and maintaining prognostic value comparable to standard stress-rest acquisition protocols. Building on the concepts discussed in the previous section, after a normal stress MPI, AI models can assist in identifying patients suitable for stress-only imaging by selecting appropriate patients for rest scan cancellation with a high prognostic safety. Hu et al.[11] developed a ML model using data from the REFINE SPECT registry to identify low-risk patients who could forgo rest scans, demonstrating lower MACE rates among AI-selected individuals. Eisenberg et al. validated a similar model based on stress-only imaging and clinical variables, achieving an area under the curve (AUC) of 0.84 for detecting obstructive CAD and outperforming expert interpretation (AUC 0.70) and total perfusion deficit (TPD) analysis (AUC 0.78)[12] Liu et al. developed a DL model trained on over 37,000 stress-only SPECT studies, achieving an AUC of 0.872 for predicting perfusion abnormalities, with robust performance across patient subgroups.[13] Wang et al. trained six ML models on rest-stress SPECT data and demonstrated that stress-only models based on selected key features—such as summed stress score, summed wall thickness score of stress, and end-diastolic volume—achieved diagnostic performance (AUC 0.863) equivalent to full rest-stress MPI in detecting CAD.[14] Complementing these image-based strategies, Martineau et al. developed a binomial logistic regression model based solely on clinical data available at the time of scheduling, predicting normal MPI with an AUC of 0.81 and reducing unnecessary imaging by 56.5 %.[15] Collectively, these studies support the role of AI in expanding the use of stress-only imaging protocols and suggest that AI-guided rest scan cancellation could become standard practice, enhancing both safety and the overall quality of nuclear cardiology care.

Image acquisition and processing

Image reconstruction

Image reconstruction in nuclear cardiology has traditionally relied on algorithms like filtered back projection (FBP) and

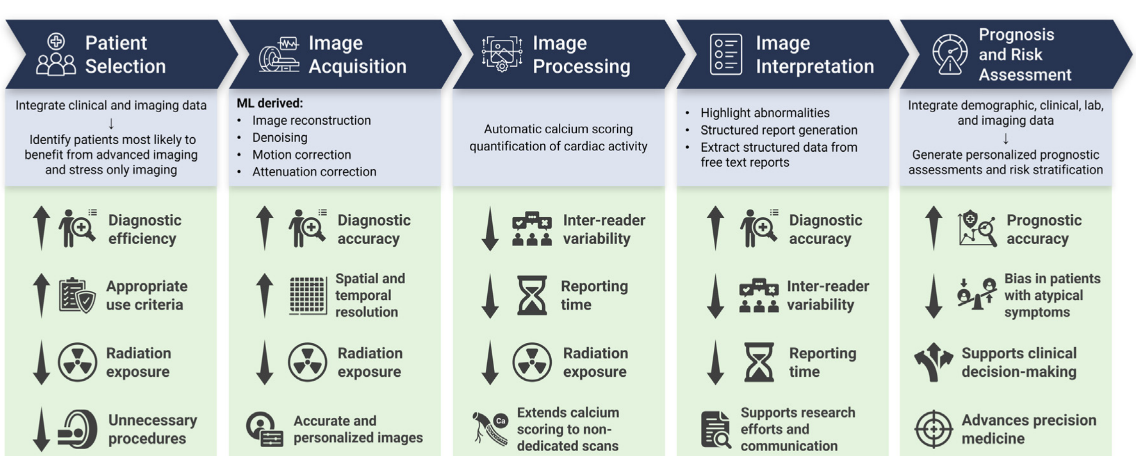

Fig. 2 Summary of machine learning (ML) applications (Light blue boxes) and its advantages (light green boxes) across different stages of nuclear cardiology workflow.

iterative techniques such as ordered-subset expectation-maximization (OSEM). While effective, these techniques are constrained by fixed assumptions about noise and system behavior, resulting in trade-offs between resolution, noise levels, and scan duration. Recent advances in DL are transforming reconstruction by introducing data-driven, patient-specific algorithms that overcome many of these limitations.[16,17] Unlike conventional approaches, AI models learn directly from empirical data, capturing complex noise patterns and scanner characteristics to generate more accurate and personalized images.

AI has been used to reconstruct diagnostic-quality images directly from low-count shortened imaging datasets.[18,19] Convolution-based DL models leverage large-scale learned priors, enabling reliable performance even under suboptimal conditions. Although promising, AI-based reconstruction remains largely in the research phase or early stages of clinical adoption, rather than routine practice. Studies have demonstrated improvements in spatial and temporal resolution, particularly in dynamic PET and gated SPECT, where models trained to recognize anatomical features—such as valve planes or ischemic regions—better preserve detail compared to traditional methods. In addition, AI-driven segmentation and automated reorientation tools have been increasingly applied to standardize myocardial perfusion imaging analysis, improving reproducibility and reducing operator dependency in tasks such as polar map generation and left ventricular axis alignment.[17,20,21] A key advantage of AI is its adaptability: rather than applying a fixed algorithm to every patient, AI models can personalize reconstruction based on factors such as body size, attenuation profiles, and scanner type.[22] For example, larger patients may benefit from AI models trained on similar body types, maintaining image quality at lower radiation doses. This aligns with the emerging paradigm of "adaptive reconstruction," in which processing is dynamically tailored to individual patient characteristics.[23]

Of note, image quality alone does not validate these methods. They must also demonstrate diagnostic and prognostic accuracy in complex clinical scenarios such as multi-vessel disease or balanced ischemia.[24] Hybrid approaches combining physical modeling and AI such as physics-informed DL may offer a balance of interpretability and performance. Although not yet used clinically, attention-based architectures and transformer models also hold promise in refining resolution without amplifying noise.[25] Cloud-deployed reconstruction pipelines could democratize access, enabling high-quality nuclear imaging in low-resource settings through scalable and secure platforms.[26]

Denoising

AI offers a transformative approach for denoising low-dose nuclear cardiology images, addressing a key limitation in image quality and diagnostic reliability. DL algorithms—particularly convolution-based and generative adversarial networks (GANs)—have demonstrated a strong potential to reconstruct high-quality images from noisy or under-sampled data. Typically trained on paired low-dose and full-dose datasets, these models can preserve critical features such as perfusion defects even at significantly reduced doses (e.g., 1/8 or 1/16 of standard). For example, Ramon et al. demonstrated that a supervised DL model outperformed conventional methods like OSEM, while Aghakhan Olia et al. used a U-Net GAN architecture to recover full-dose-equivalent image quality[18,19] used a U-Net GAN architecture to recover full-dose-equivalent image quality These approaches produce images nearly indistinguishable from standard protocols in terms of spatial resolution and quantitative metrics like TPD. Notably, clinical validation has shown that DL denoising of SPECT MPI can yield significantly better detection of perfusion defects than conventional reconstructions.[27,28]

Despite these advances, DL-based denoising is not yet standard clinical practice due to regulatory hurdles and the need for broader validation, although pilot studies are ongoing in multiple centers. Next-generation efforts aim to integrate denoising into real-time reconstruction pipelines and explore hybrid AI models that combine denoising, segmentation, and outcome prediction.[22] Emerging strategies also focus on task-specific tuning—such as preserving ischemic patterns—and on AI-driven dose optimization to minimize radiation and scan time while maintaining diagnostic accuracy.[29] Personalization efforts are growing, using patient-specific factors (e.g., BMI, gender, coronary calcium scores) to tailor scan parameters and uphold the "as low as reasonably achievable" (ALARA) principle for radiation.[29]

Motion correction

Motion artifacts—whether due to cardiac contraction, respiratory cycles, or patient movement—can significantly degrade the diagnostic accuracy of MPI. AI, particularly DL, has introduced new paradigms for correcting these artifacts without the need for external sensors or complex gating protocols.

AI-based motion correction is often approached through frame-by-frame registration using convolutional or recurrent architectures such as convolutional long short-term memory (CLSTM) networks. For instance, Shi et al. used CLSTM to correct motion in dynamic cardiac PET, significantly improving myocardial blood flow quantitation compared to traditional methods.[30] Similarly, Li et al.[31] developed a deformation field estimation model integrated into iterative PET image reconstruction for enhanced correction fidelity.[32]

Accurate motion correction improves perfusion quantification, functional parameters, and overall diagnostic accuracy. AI methods have outperformed conventional rigid and affine techniques, particularly for non-linear, variable motion. Clinical readiness is advancing, with tools under validation in multicenter settings such as the REFINE SPECT registry, which is assessing reproducibility and real-world performance.[33] Ultimately, AI-driven motion correction is expected to become a real-time, embedded feature of acquisition and reconstruction systems, eliminating the need for external tracking hardware and streamlining workflows.

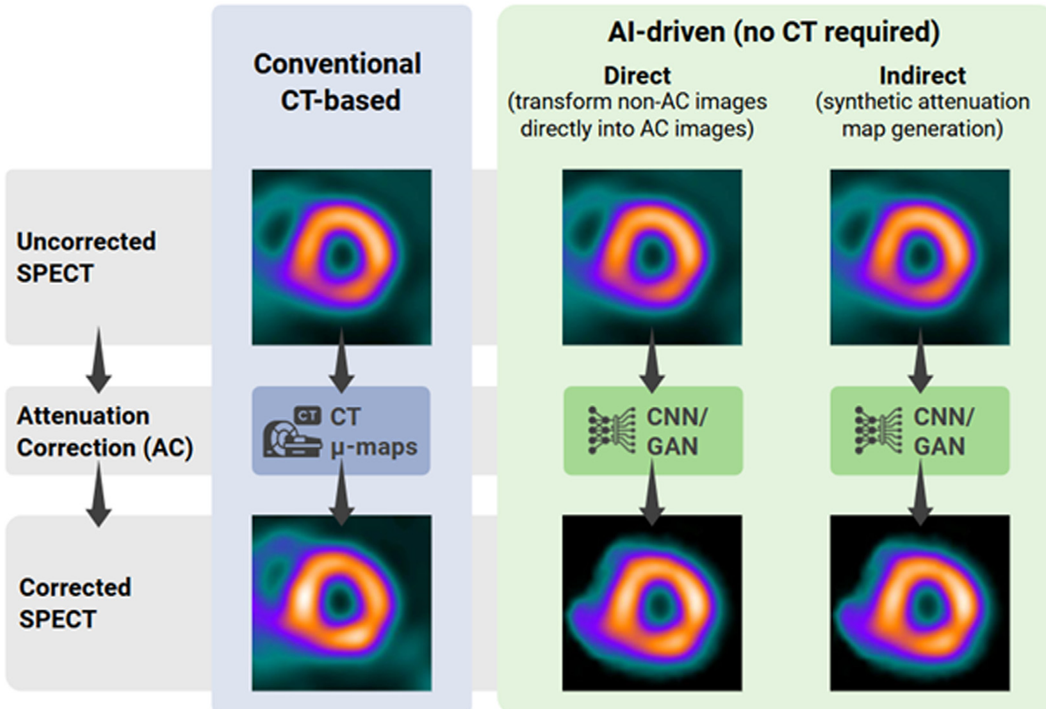

Fig. 3 Comparison of conventional CT-based attenuation correction (AC) and AI-based CT-less direct AC in SPECT imaging- Convolutional neural networks (CNNs) and generative adversarial networks (GANs) can generate attenuation-corrected images without the need for CT-derived μ-maps. All images shown are from the same patient.

Attenuation correction

Soft tissue and diaphragmatic attenuation frequently introduce artifacts that impair the diagnostic and prognostic performance of MPI. While traditional CT-based attenuation correction (AC) improves image quality, it requires hybrid SPECT/CT or PET/CT systems, which are not universally available—particularly in low resource settings—and add radiation exposure and procedural complexity. As a result, many MPI studies are still performed without attenuation correction. These are labelled non-attenuation corrected (NAC).[23,34]

Convolutional and generative deep learning can generate synthetic AC images directly from NAC data, eliminating the need for CT. These models are trained on large, paired datasets of NAC and AC images from the same patients. This allows the AI models to map the relationships between the scans through maximization of structural similarity to apply these to unseen NAC data (see Fig. 3). Some approaches also incorporate clinical variables to further enhance prediction accuracy. For example, the DeepAC model uses a conditional GAN to convert NAC short-axis images into high-fidelity simulated AC images, outperforming CT-based methods in cases of emission−CT misregistration.[23]

Clinical validation has shown that AI-based AC reduces false perfusion defects and improves diagnostic accuracy for obstructive CAD. In a multi-center trial of 722 patients, deep learning-based AC improved the AUC from 0.717 (NAC) to 0.752 ($p = 0.016$), increased specificity by 6.2 %, and improved accuracy by 4.3 %, performing comparably to expert readers. Similarly, Prieto Canalejo et al. demonstrated that AI-generated AC maps achieved over 96 % accuracy for attenuation defect localization and significantly enhanced interpretability. Furthermore, Hagio et al. reported a multicenter, multivendor validation of deep learning AC in the context of the international Flurpiridaz 301 trial, supporting its potential for broader clinical adoption.

AI-based AC is now transitioning into clinical use, especially in settings without hybrid SPECT/CT systems. These tools offer near-instantaneous correction and can be seamlessly integrated into clinical workflows without altering acquisition protocols, enhancing accessibility and adherence to best practices in nuclear cardiology.

Automated calcium scoring

Coronary artery calcium scoring is an established tool for risk stratification in patients with suspected CAD, guiding preventive strategies such as lipid-lowering therapiesBeyond CAD risk, AI-enabled calcium scoring has demonstrated improved prediction of non-coronary events such as heart failure and stroke.[35] Traditionally, calcium scoring uses non-contrast ECG-gated CT scans, with the Agatston score serving as the primary metric.[36] Recent advances, including iterative reconstruction and deep learning-based image reconstruction, have enabled significant reductions in radiation dose while maintaining image quality.[37] AI algorithms now automate coronary artery segmentation, plaque detection, and the calculation of Agatston, volume, and mass scores, achieving excellent agreement with expert readings—often with intraclass correlation coefficients often above 0.98.[35,38] These tools accelerate analysis, reduce inter-reader variability, and facilitate integration with cardiac function assessment. Importantly, AI is extending calcium scoring to non-dedicated scans such as low-dose chest CT or PET/CT attenuation images, enhancing screening possibilities and expanding access to risk assessment in low-resource settings.[38-40] This aligns with the IAEA's mission to promote equitable access to medical imaging and facilitate research and innovation in developing countries. Despite rapid progress, further validation across diverse populations and imaging platforms remains essential to ensure reliable clinical adoption worldwide.

Quantification of metabolic activity

Cardiac nuclear imaging extends beyond perfusion assessment. Techniques such as PET/CT with 18F-fluorodeoxyglucose (FDG) and SPECT/CT with 99mTc-labeled bone seeking agents are increasingly used to evaluate cardiac inflammation and amyloidosis, respectively. While quantitative parameters have long supported diagnosis, follow-up, and prognostication—particularly in cardiac sarcoidosis—the integration of AI is enhancing reproducibility through automation.[41] Recent studies have shown that deep learning models can segment cardiac chambers on non-contrast CT for attenuation correction and automatically quantify SUVmax-derived measures, such as cardiac metabolic volume and activity. For example, Miller et al. developed a fully automated FDG PET pipeline for cardiac sarcoidosis, achieving high diagnostic performance (AUC up to 0.92) for cardiometabolic activity and inflammation volume.[42] The same segmentation framework was applied to 99mTc-pyrophosphate imaging for transthyretin (ATTR) cardiac amyloidosis, successfully identifying positive cases and predicting risk.[43] In parallel, DL has shown high accuracy in detecting and grading radiotracer uptake on scintigraphy. Halme et al. trained a DL model to classify Perugini grades on bone scintigraphy, achieving AUCs $\geq$ 0.88 for ATTR detection and up to 0.94 for high-grade uptake.[44] These models focus on clinically relevant myocardial features and outperform traditional visual interpretation, potentially enabling earlier and more reliable diagnosis.

Image interpretation and diagnostic performance

Most of the clinical evaluation of AI use centers on improving diagnosis and reporting of CAD. AI models now match or exceed expert performance by integrating imaging data with clinical variables to enhance diagnostic accuracy and risk assessment. For instance, Betancur et al. demonstrated that ML algorithms combining perfusion, functional, and clinical data outperform traditional scores in predicting MACE.[45] Otaki et al. developed explainable AI models that highlight image regions associated with abnormalities, improving transparency and clinical confidence.[46] ML techniques also improve consistency in scoring perfusion defects and estimating ischemic burden, helping reduce inter-reader variability, especially in settings with limited access to expert interpreters. DL tools further harmonize imaging outputs across different SPECT systems, supporting multi-center research and standardization efforts.

Recently, Large language models (LLMs) have shown value in complementing diagnostic ML by automating report generation. Garcia et al. demonstrated how natural language generation systems can integrate MPI findings into structured, coherent reports,[47] describing perfusion patterns, vascular territories, and management recommendations.[48] LLMs also assist in verifying report completeness and flagging inconsistencies, although very careful oversight is required to mitigate risk associated with AI-generated hallucinations.[47]

Structured reporting has advanced through systems like the AI-driven Structured Reporting System (AIsR), which applies rule-based logic to create guideline-compliant narratives from imaging data, improving standardization and communication. Natural language processing (NLP) enables the extraction of key details from free-text reports and their transformation into structured data for automated classification and reporting.[49] Hybrid systems that combine NLP with ML can operate in both retrospective and real-time reporting settings.[50]

Successful implementation of AI in nuclear cardiology requires integrated infrastructure, including large, annotated datasets, advanced DL/ML platforms, rule-based inference decision engines, NLP tools, PACS / DICOM, secure cloud or federated learning systems, and regulatory validation. When carefully implemented, AI and LLMs have the potential to significantly improve diagnostic interpretation and personalized care in nuclear cardiology. Clinical leadership will be essential to ensure these technologies translate into meaningful and measurable patient outcomes.

Prognostication and risk assessment

Prognostic estimations at the individual-patient level represents one of the most challenging clinical exercises in cardiology. By integrating different data sources, AI may significantly enhance risk stratification in patients undergoing nuclear cardiology imaging. In MPI, AI can also automate the quantification of myocardial blood flow and flow reserve—key metrics for diagnosing CAD and predicting cardiovascular outcomes.[10,51,52] AI is being directed to refine individualized risk profiling through incorporation of demographics, symptoms, ECG findings, laboratory results, and (complementary) imaging such as detection of high-risk CT plaque features.

AI is increasingly central to prognostication and risk assessment in ischemic heart disease. By combining imaging, clinical, and laboratory data, AI algorithms can produce individualized risk scores that outperform conventional models in predicting adverse cardiovascular events.[53] This approach is especially valuable for groups that are often difficult to assess—such as older adults, women, and patients with atypical symptoms—where AI reduces diagnostic bias and uncovers subtle prognostic markers.[54] Importantly, AI supports risk stratification in both obstructive and non-obstructive coronary artery disease, including ischemia with no obstructive coronary artery disease (INOCA). In these cases, it aids in detecting coronary microvascular dysfunction, abnormal myocardial flow reserve, and transient ischemic dilation, all of which are recognized indicators of prognosis and treatment guidance.[54] Beyond this, AI-driven quantification of myocardial blood flow, plaque burden, and ventricular function enhances the prediction of outcomes such as heart failure, arrhythmias, and major adverse cardiovascular events. International consensus statements highlight that these applications can advance precision medicine, broaden equitable access to accurate risk assessment, and help clinicians tailor therapy more effectively.[55]

Intrinsic challenges for artificial intelligence in nuclear cardiology

Over the past decade, several intrinsic challenges have emerged in the rapid development of AI in clinical medicine. These include algorithm bias, lack of transparency and interpretability, data privacy and security concerns, over-reliance and automation bias, challenges in clinical validation and generalizability, and regulatory and ethical uncertainties. Furthermore, nuclear cardiology presents a unique set of challenges for AI implementation and clinical integration. This section explores these obstacles and where appropriate, offers structural approaches to address them. Notably, given the rapidly evolving nature of AI, it is anticipated that new challenges will continue to arise. In such cases, grounding responses in the guiding principles of medical ethics and research integrity remains a sound approach.

Historically, progress in nuclear cardiology has been constrained by the need for substantial on-site technological and personnel resources—such as cyclotron facilities and radiochemistry expertise— as well as by heterogeneity in imaging protocols and comparisons in performance with other imaging modalities. As AI continues to expand its applications in nuclear cardiology, it is expected that new challenges will emerge. These challenges often mirror existing structural and operational complexities within the field and can therefore be framed within the same domains. These include:

a) Infrastructure Dependence: AI tools often require high-quality, standardized imaging data, which may be difficult to obtain in settings lacking advanced infrastructure.
b) Data Heterogeneity: Variability in imaging protocols, equipment, and patient populations can hinder the generalizability of AI models.
c) Comparative Performance: AI-enhanced nuclear cardiology must demonstrate added value over other modalities such as echocardiography, CT, and MRI, especially in terms of diagnostic accuracy, cost-effectiveness, and clinical outcomes.

Addressing these challenges requires a multidisciplinary effort involving clinicians, data scientists, regulatory bodies, and industry partners. Establishing robust validation frameworks, promoting transparency in AI algorithms, and ensuring equitable access to AI-enhanced diagnostics are essential steps toward responsible and effective integration.

Significant need for on-site technological and personnel resources

Given the specialized nature of both nuclear cardiology and AI, a substantial investment in resources is essential for the successful establishment, initiation, consolidation and maintenance at capabilities local sites. Financial resources are primarily allocated to building the infrastructure of an imaging centre, including the physical space, the IT infrastructure, scanners, the radiopharmacy components and where feasible, cyclotrons. Beyond infrastructure, highly specialized human resources—such as nuclear medicine physicians and technologists, medical physicists and radiopharmacists/radiochemist are required to sustain operations, manage hardware and optimize the clinical workflow. This resource-intensive environment directly affects the availability of nuclear cardiology studies for training and validating AI models. This is especially true for PET imaging, where conventional clinical research studies often involve limited sample sizes—typically smaller by nearly an order of magnitude compared to other modalities. Consequently, factors influencing access to nuclear imaging facilities (e.g., socioeconomic disparities) can significantly bias emerging imaging datasets. This raises concerns about the generalizability of AI models and the potential for reduced accessibility to AI-driven solutions in underrepresented populations.

Additionally, a lack of awareness and understanding of the principles and functioning of modern machine learning-based AI can hinder the development of local AI competence. While specialized hardware (e.g. GPUs for DL model training) is necessary, the associated costs represent only a fraction of the overall expenses involved in maintaining a nuclear cardiology-capable centre. Moreover, online training resources for AI proficiency—covering both model development and maintenance—are increasingly accessible.

We believe that the growing capabilities of AI offer promising strategies to mitigate these challenges. For example, AI-powered interfaces using virtual reality (VR) and augmented reality (AR))—as already employed by the IAEA in the development of VR models for external beam radiotherapy, two-dimensional (2D) brachytherapy, and three-dimensional (3D) brachytherapy —can accelerate and enhance the training of essential personnel in nuclear cardiology. Furthermore, we propose the development and promotion of imaging repositories that ensure broad representation across populations, imaging techniques, scanner types, radiotracers and acquisition protocols. These repositories should adhere to the highest possible standards of data quality to serve as reference datasets for AI model validation. The IAEA could take a leading role in promoting these reference-standard datasets through globally visible and impactful channels, while ensuring full compliance with data privacy and protection regulations.

Heterogeneity in Nuclear Cardiology processes

Nuclear cardiology imaging is characterized by substantial variability due to differences in radiotracers, scanner types, acquisition protocols, reconstruction software, and reporting standards. This heterogeneity poses a challenge for AI models, which may struggle to interpret subtle differences in imaging data and, as a result, may have reduced capacity to make accurate pathological attributions (i.e., identifying disease-related features) or mechanistic attributions (i.e., linking those features to underlying physiological processes).

To address this, promoting high-quality data—defined by completeness and standardization in both technical and clinical reporting—is essential. Emerging evidence suggests that some AI models demonstrate a degree of generalizability that helps mitigate the impact of such variability. Nonetheless, continued efforts to harmonize imaging practices and enhance dataset quality remain critical for the reliable development and deployment of AI in nuclear cardiology.

Integration with other cardiovascular imaging modalities to boost value

The true value of advanced imaging lies in its potential for integration across domains, AI may play a key role. In fact, it enables the seamless combination of nuclear cardiology modalities with other advanced imaging techniques such as MRI and echocardiography, and invasive imaging,—including quantitative coronary angiography and intracoronary imaging,—in the therapeutic decision-making process. This incorporation principle has been already displayed in hybrid modalities such as SPECT/CT and PET/CT, where both anatomical and functional analyses complement each other to enhance diagnostic and prognostic performance in ischemic heart disease.

The standalone value of nuclear imaging may sometimes be perceived as limited compared to modalities with greater accessibility (e.g., echocardiography) or higher spatial resolution (e.g., MRI). This perception is often exacerbated by communication barriers among the various medical specialists involved.—This, in turn, can constrain the analytical insights gained at both diagnostic and prognostic levels. Currently, the integrated value of multimodality is increasingly promoted through multidisciplinary teams (MDT), such as Imaging Teams or the Heart Teams. In this context, AI should be designed to facilitate the translation of complex imaging insights in a way that fosters effective cross-specialty communication.

Additionally, disparities in nuclear cardiology infrastructure and workforce expertise across centers and countries contribute to uneven adoption of AI technologies, particularly in resource-constrained settings. Advances in AI applications in NC through international collaboration in data collection, sharing, and model validation will further enhance NC role as a precise, efficient and patient-centered discipline. Intrinsic challenges for AI in Nuclear Cardiology and their possible solutions are summarized in Table 1.

Legal implications

AI holds immense promise for nuclear cardiology, however, the enthusiasm surrounding these advancements must be

Table 1 Summary of intrinsic challenges for AI in nuclear cardiology and their possible solutions.

Type of challenge	The challenge	Possible solutions
Infrastructure dependence and resource demands	Need for advanced facilities, equipment, IT systems, and trained staff → limit access to nuclear cardiology studies à reduced size and quality of training datasets. → AI bias and reduced model generalizability.	Develop high quality global imaging repositories with diverse. populations, scanners, tracers and protocols for AI training.
Data heterogeneity	Variability in tracers, scanners, and protocols → inconsistent data inputs → Reduces AI's reliability and accuracy.	Standardize imaging practices and reporting. Promote complete and standardized datasets. Leverage AI models resilient to variability.
Need for specialized human resources	- Need for high specialized – highly trained personnel. - Lack of understanding of the principles of ML based AI hinder the development of local AI competence.	Use AI powered VR/AR platforms to train personnel. Expand online AI training programs to build workforce competence.
Comparative performance and clinician perception	- Nuclear imaging is often perceived as limited and less cost-effective in comparison to other accessible or higher resolution modalities. - Communication barriers among medical specialists → limiting analytical insights.	AI driven multimodality data integration for richer diagnostic and prognostic insights. AI tools designed to enhance cross-specialty collaboration.

tempered by a strong commitment to safe, ethical and legally sound implementation. The rapid pace of AI innovation demands vigilant oversight to prevent unintended consequences and to protect the interests and to safeguard the rights and interests of both patients and healthcare professionals.

Data privacy and security

AI medical devices rely on sensitive data—including imaging, clinical records, and demographic information—that are protected by strict legal frameworks such as the General Data Protection Regulation (GDPR) in the EU and the Health Insurance Portability and Accountability Act (HIPAA)[56] in the U.S. Compliance with this regulations is essential to uphold ethical standards,[57] maintain public trust, and ensure responsible innovation. Central to this framework is the principle of data minimization, which dictates that only the information strictly necessary for a given purpose is processed.[58] Technical safeguards such as encryption and robust access controls are equally vital to prevent unauthorised access and data breaches.[59] These measures align with broader legal requirements that prioritise patient autonomy, including the obligation to obtain explicit, informed consent before personal data is used in AI systems. Patients must be clearly informed about how their data will be used— whether for algorithmic training, clinical decision support, or other purposes—ensuring transparency at every stage.[60,61] Certain legal exceptions apply in scientific research conducted for non-commercial, public health purposes. In such cases, data may be used with reduced subject rights if it is anonymized or pseudonymised, and the research is conducted under ethics committee oversight. However, these exceptions do not permit uses that could harm individuals or affect care outside approved research protocols.[62]

The legal basis for data processing must be clearly defined.[63] For sensitive healthcare data explicit consent remains essential and must include transparent explanations of how the data will be used. Emerging privacy-preserving methods such as federated learning and differential privacy offer promising solutions. Federated learning enables decentralized model training without transferring raw data, while differential privacy introduces statistical noise to protect individual identities—both enhancing privacy while maintaining model performance

Attribution of responsibility and liability

Under prevailing tort law, physicians retain primary responsibility for diagnostic decisions, even when relying on AI outputs. Courts globally, have continuously emphasised and upheld the physician's duty to exercise independent clinical judgement.[64] Following AI advice that aligns with established clinical care guidelines typically reduces liability risk. However, rejecting AI suggestions without sound clinical justification, especially when it results in unintended consequences or patient harm, exposes physicians to malpractice claims. Crucially, physicians are under strict expectations to verify AI outputs against raw data and other clinical information to avoid delegation of duty for judgement exercise. As AI tools become more integrated and validated within clinical workflows, the standard of care is evolving. There is a growing legal expectation that physicians utilise validated AI systems for timely and accurate diagnoses, and failure to adopt these tools may itself constitute negligence. While regulatory guidance remains in flux, regulatory clearance of AI devices increasingly informs what is considered reasonable clinical practice. Physicians can mitigate liability risks by demonstrating awareness of AI limitations-such as biases in training data and maintaining thorough documentation of their decision-making processes.[65]

Additionally, post deployment monitoring is critical to ensure continued model accuracy. As dynamic imaging equipment evolves, patient demographics shift, and diagnostic protocols change. These factors can cause model drift, where AI performance degrades over time. Without regular evaluation, such drift may go unnoticed, potentially resulting in clinical errors or legal liability.[16]

Technical foundations for safe and legally compliant AI in nuclear cardiology

As AI becomes routine in nuclear cardiology, ensuring legal and clinical safety is critical. AI tools differ from traditional software because they adapt to new data, requiring thorough testing before use and continuous monitoring afterward. Three core areas are essential: pre-deployment testing, post-deployment monitoring, and record-keeping.

1. *Testing Before Use*

AI tools must undergo verification (checking if the system works as intended) and validation (testing on real clinical data). The EU AI Act now mandates pre-market testing[66] for all high-risk medical AI systems. Skipping this step can expose hospitals and clinicians to legal liability.

2. *Ongoing Monitoring*

AI performance can decline over time due to model drift caused by changes in clinical environments. For instance, a UK hospital's sepsis AI tool failed after lab methods changed. Continuous performance checks and alerts are essential to avoid unsafe or negligent use.

3. *Traceability and Explainability*

Maintaining logs[67] of AI use, decisions, and any clinical overrides is vital for legal defense. Addressing the "black box" problem through explainable AI improves trust, accountability, and compliance in clinical decisions.

Technical methods that help explain AI decisions

To follow rules and protect against legal risk, developers and hospitals can use technical solutions that make AI more understandable: Feature attribution methods like SHAP or LIME provide a feature importance ranking, identifying which specific input variables - such as heart rate, stress test metrics, or image-derived features - had the greatest impact on the model's output in a given case. Visual explanations such as heatmaps highlight areas on an image (e.g., a nuclear scan) that the AI used to make its prediction. This helps doctors double-check the system's logic. Simplified model outputs can explain complex algorithms in easier forms, like showing a decision tree that roughly follows the AI's internal reasoning. Audit logs can record what model version was used, what data was entered, what result came out, and whether the result was followed or overridden. This makes later review possible. These methods don't make AI fully transparent, but they offer enough insight to help clinicians make informed choices and regulators assess legal compliance. The legal implications of using AI in Nuclear Cardiology and their possible solutions are summarized in Table 2.

Future perspectives

Given the unique profile of AI development, it is considerably taxing to provide an overview of upcoming developments regarding its future uses without high levels of speculation. Therefore, we provide a view on the directions where stewardship is both likely and desirable from the clinical-and-data research community.

Firstly, the implementation of AI in nuclear cardiology may prove crucial in the effort to advance the principles of multimodality. Here, the driving notion should be maximum value extraction from individual imaging techniques. This is meant to overcome their well-known drawbacks by optimizing value through feature extraction and integration with features from alternative imaging modalities, clinical and functional data, and even genetic insights at the individual level. A finely tuned AI approach to extract all the relevant patterns from a SPECT or PET MPI scan can be merged with another AI approach oriented to pre-test clinical data and complementary CT (even if from low-dose scans structurally meant for attenuation correction) or MRI data. This overarching example AI structure could be repeated as necessary considering the availability of imaging modalities. We believe that early research signals are beginning to accrue,[68-70] building upon previously championed concept of hybrid imaging (applied in infiltrative diseases such as cardiac sarcoidosis) (71).

Secondly, AI implementations can meet a more seamless integration into clinical practice through the training of human resources able to facilitate, use, query, adapt and interpret AI models. AI-capable nuclear researchers, technicians and clinicians could bridge the evident gap between pure data researchers and clinical personnel in a unique way.

Table 2 Summary of legal implications of using AI in Nuclear Cardiology and their possible solutions.

Type of implication	The implication	Possible solutions
Privacy & security	- AI relies on sensitive imaging and clinical data governed by GDPR, HIPAA, etc. - Risks of data breaches and misuse can erode public trust.	Apply encryption, federated learning, and differential privacy for safer model training. Ensure transparent consent processes with clear patient communication.
Attribution of responsibility	Physicians remain legally liable for AI-assisted diagnoses. → Not verifying AI outputs or ignoring AI recommendations without justification lead to malpractice risk.	Use validated AI systems. Maintain physician oversight and thorough documentation of decisions. Post deployment monitoring to ensure continued model accuracy.
Safety foundations	- AI model drift caused by changes in clinical environments. Without monitoring, this can lead to unsafe or inaccurate outcomes.	Pre-deployment testing: verification and validation. Post-deployment monitoring: continuous checks. Record keeping: Logs of AI use, decisions, and any clinical overrides.
AI transparency	- Deep learning models function as "black boxes," making it difficult for clinicians to understand how decisions are made.	Feature attribution methods (e.g., SHAP, LIME): Rank input variables by importance. Visual explanations (e.g., heatmaps): Highlight image regions used in prediction to allow clinical validation. Simplified model outputs: Translate complex algorithms into interpretable forms. Audit logs: Record model version, inputs, outputs, and physician actions.

Additionally, this could tackle the concerns regarding "replacement" of humans by AI approaches, which constitutes a documented barrier in AI development and integration.

Thirdly, it is like that emerging efforts in AI modelling will try to integrate as much data as possible from as many sources a feasible in the initial general modelling of cardiovascular disease (the underlying phenomenon being studied in this case). This poses the risk of imaging overuse with intrinsic disadvantages in terms of radiation exposure and costs. Nevertheless, this may be a temporary effect after which more selective use of imaging can be achieved as witnessed around foundational models where once model pre-training has been achieved, selective finetuning can be performed at a minimal cost. It will be vital to oversee/regulate these processes with the aim of preventing and expansion in the inequality seen between healthcare systems around the world.

Finally, as suggested in the previous section a reference dataset structure should emerge for the training-validation of novel AI models in nuclear cardiology. This initiative can be undertaken through international collaboration and should provide an information based on high-level quality, representing the status of nuclear cardiology studies and populations worldwide.

Declaration of competing interest

The authors declare no conflicts of interest related to the submission of the manuscript titled "Artificial Intelligence in Nuclear Cardiology: Technical Perspectives, Strategic Directions, and Recommendations from an IAEA Expert Working Group" to Seminars in Nuclear Medicine. All authors have contributed to the work in accordance with ethical standards and affirm that there are no financial, personal, or professional affiliations that could be perceived as influencing the content of this manuscript.

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