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Intelligent Imaging: Artificial Intelligence Augmented Nuclear Medicine

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Footline: AI in nuclear medicine

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Abstract

Artificial intelligence (AI) in nuclear medicine and radiology represents a significant disruptive technology. While there has been significant debate about the impact of AI on careers of radiologists, the opportunities in nuclear medicine enhance the capability of the physician and at the same time impact on the responsibilities of physicists and technologists. This transformative technology requires an insight into principles and opportunities for seamless assimilation into practice without the associated displacement of human resources. This article introduces the current clinical applications of machine learning (ML) and deep learning (DL); laying a platform for the subsequent continuing education article outlining the foundations of AI, ML and DL.

Introduction

The emergence of artificial intelligence (AI) in nuclear medicine and radiology has occurred over the last 50 years (e.g. auto-contouring). Typically, AI has been involved with problem solving associated with logic and reasoning. The more recent developments in deep learning have increased research and publication in radiology and nuclear medicine journals due to new capabilities in AI driven image segmentation and interpretation. As early as 1976, AI commentators and experts predicted that AI would bring careers in medicine to an end (*1*). While Geoffrey Hinton has been widely attributed as predicting AI would put radiologists out of a job (*2*), his more conservative perspective predicts significant changes to health care delivery and the way medicine is practiced (*3*). While the 'doomsday" predictions may be exaggerated, there is no denying that AI, neural networks and deep learning represent the greatest disruptive technology to confront radiology and nuclear medicine since the early days of Roentgen, Becquerel and Curie. AI is both the vehicle for transport into the next century of sustainable medical imaging and, if ignored, a potential extinction level competitor. The key to sustainable co-existence lies in understanding and exploiting the capabilities of AI in nuclear medicine while mastering those capabilities unique to the human health professional.

Artificial Intelligence

Precision nuclear medicine heralds an exciting era with the re-engineering of clinical and research capabilities. The term AI was first used in 1955 to broadly describe the use of computer algorithms (figure 1) to perform tasks that are generally associated with human intelligence (e.g. learning or problem solving) (*4,5*). A significant factor driving the emergence of AI in radiology has been that, since 2015, visual recognition using AI had a lower error rate than the human error rate for the first time (*5,6*). An interesting application given the heightened capabilities of AI is visual recognition is in incidental findings. The classic "gorillas in our midst" experiment on inattentional blindness (*7*) highlighted that humans focussing on a specific task (counting the number of times a ball was passed) in a complex scene could render the observer blind to a person in a gorilla suit walking through the middle of the scene. This was later examined in chest computed tomography (CT) interpretation with an artifactual gorilla inserted into multiple CT slices (*8*). The artifact was overlooked by 83% of expert radiologists and 60% of those were shown to have looked directly at the artifact using eye tracking. While incidental findings in general nuclear medicine studies are readily identifiable, inattentional blindness may decrease detection in more complex data sets associated with single photon emission computed tomography (SPECT), positron emission tomography (PET) and co-registered images; a role perhaps for AI.

Machine learning (ML) is a subtype of AI (figure 1) that employs ML algorithms through data analysis without being explicitly programmed (*4,9*). ML tends to be associated with solving problems of logic after learning from human-defined teaching cases. ML has been used widely more recently because of the emergence of improved hardware, availability of big data or at least large datasets for training, and because ML is a valuable tool for analysis of extracted features in radiomics (*10*). Radiomics interprets an image as data and extracts / analyses features and groups of features to predict outcomes. Some features may be apparent to visual interpretation (semantic) while others may only be revealed through computational extraction. Radiomics has traditionally been associated with radiological imaging (e.g. texture, shape amongst many features) but includes molecular imaging (the various standard uptake values, ejection fraction, and many more). The importance of radiomic feature extraction is identifying those image features that individually or in combination with other -omic features, predicts an outcome. This includes identifying redundancy in the data; features that have high correlation with one another. Indeed, ML can aid in determining which of many extracted radiomic features should be used alone or in combination (figure 2). Specific capabilities of ML include (*2,5,11,12*):

- disease or lesion detection and classification,
- automated image segmentation, pre-analysis and quantitation,
- extraction of radiomic features from image data,
- image reconstruction,
- case triage and reporting prioritisation,
- research and data mining, and
- natural language processing.

Representation learning (RL) is then a sub-type of ML (figure 1) where the algorithm is not fed human-interpreted images to learn from (*4*). RL requires larger sets of training data to learn the features required to then accurately classify the images and extracted features. In many cases, if adequate training data is available, RL will perform better than ML (*4*). Deep learning (DL) is then a sub-type of RL (figure 3) that adds a number of processing layers (deep or depth) to detect complex features in an image (*4*). The vehicle typically used by ML, RL and DL is the artificial neural network (ANN). A convolutional neural network (CNN) is a type of ANN used for DL that employs a convolutional process to extract features from the image itself (figure 3) while an ANN typically has feature data as the input (figure 2).

Application of AI in Nuclear Medicine

The emphasis on precision nuclear medicine, emergence of radiomics, and the establishment of large patient data bases (big data) demands implementation of DL processes to optimise outcomes (figure 4). Largely, these applications depend on a CNN, however, there are numerous important applications of an ANN without the need for convolution. An ANN for some data, is an excellent adjunct to traditional statistical analysis in research or clinical practice. An ANN could also be used to build theranostic decision trees, business analysis and quality assurance. While a CNN is required for automated segmentation and extraction of data from images in radiation dosimetry, an ANN may be useful in modelling radiation dosimetry in therapy patients.

The use of ANNs in nuclear medicine is not new. In 1993 a single hidden layer of 15 nodes was used with 28 input features trained on 100 ventilation perfusion lung scans and validated against 28 new cases with the ANN superior to experienced physicians (P=0.039) (*13*). More recently, an ANN was trained with 5685 regions with grounded truth provided by 6 expert nuclear cardiologists and was shown to be superior to 17 segment defect scoring in myocardial perfusion scans (*14*). In all cases (stress, rest and defect regions), the ANN had better area under the curve on receiver operator characteristic (ROC) analysis than the 17-segment defect score. A multi-centre trial (*15*) recently reported the use of a deep CNN trained on 1160 patients across 4 centres and reported a marginal, but statistically significant, improvement for DL over total perfusion defect scores with area under the curve (AUC) superior in all 4 sites for both per-patient and per-vessel data, and cumulatively for per-patient (3.8%, P<0.03) and per-vessel (4.5%, P<0.02). The highlight of the report was the integration of CNN outcomes seamlessly into a radiomic polar map display typical of standard practice; signposting the future software integration of AI (figure 5). In an earlier report, Betancur et al (*16*), evaluated ML in predicting major cardiac events (MACE) in 2619 myocardial perfusion SPECT patients with ML providing superiority in predicting MACE compared to expert readers and automated quantitative software but was less reliable in providing a timeline to MACE.

Choi et al (*17*) reported the use of unsupervised DL for fluorodeoxyglucose (FDG) PET to identify Alzheimer's disease with an AUC) for ROC of 0.9 for differentiating Alzheimer's disease and identified abnormal patterns in 60% of studies classified as normal by expert visualisation. DL has also been used to identify high risk patients most likely to benefit from induction chemotherapy in nasopharyngeal carcinoma using 18 radiomic features extracted from PET and CT, although disease free survival rates at 5 years (50.1% high risk and 87.6% low risk; P<0.001) is not a measure of CNN accuracy (*18*). Quantitative SPECT/CT has also been combined with DL for automated volume of interest segmentation on CT and application to SPECT data for calculation of glomeruli filtration rate (*19*). The manual versus automated regions differed by 2.8% with a correlation of 0.96 highlighting the value of AI in automating otherwise time consuming and potentially prohibitive manual functions (i.e. allowing SPECT to be employed over planar). CNN based automatic renal segmentation on non-contrast CT was applied to post 177Lu PSMA (prostate specific membrane antigen) SPECT to estimate radiation dosimetry (*20*). Trained against 89 manually drawn regions, the CNN was demonstrated to be fast with comparable accuracy to humans (mean dice scores of 0.91 for right and 0.86 for left), although the CNN had some difficulties with cystic kidneys.

An important area of development in AI is pseudo-CT attenuation maps (figure 6). The premise is that CT-based attenuation maps in SPECT and PET, are not only associated with increased patient radiation dose but also position mismatch between the emission and transmission scans

(*21*). Magnetic resonance imaging (MRI) suffers significant limitations in estimating an attenuation map for SPECT/MRI or PET/MRI hybrid system (*21*). The maximum likelihood reconstruction of activity and attenuation (MLAA) method has been previously published but suffers issues associated with crosstalk and noise (*21*). A combination of advances in time-of-flight and DL has seen a number of investigators explore the use of CNNs to overcome the limitations of MLAA and provide accurate attenuation maps without transmission studies. Hwang et al (*21*) evaluated 3 architectures of deep CNNs that combined the MLAA produced attenuation map with emission data and the CNN to produce an attenuation map that more closely modelled the CT based grounded truth (lower error). The results reported reduced noise, less cross talk, and elimination of artifact but relied on some trial and error. Later work (*22*) confirmed these observations in PET/MRI using a deep neural network in 100 cancer patients. In PET/MRI, Torrado-Carvajal et al (*23*) integrated the Dixon method with a CNN to generate pseudo-CT for pelvic PET scans and reported less than 2% variation from the CT based attenuation map and nearly 7 times better error than the standard Dixon method. Similarly, Leynes et al (*24*), used a deep CNN combined with zero-echo-time Dixon pseudo-CT to produce more accurate attenuation maps than traditional MRI pseudo-CT methods. Both the Dixon method and the zero-echo-time method for pseudo-CT have a number of limitations (*25*) that have been overcome with the application of deep CNN MRI based pseudo-CT generation that is rapid and has a reconstruction error less than 1% (*25*). More recently, DL approaches have been reported to produce pseudo-CT attenuation maps from the 18F FDG brain PET sinogram with a mean error against CT corrected PET of less than 1% (*26*).

Discussion

ANNs are effective in evaluating the potentially large number of extracted radiomic features and identifying those that should be used alone or in combination in decision making (*2*). ANNs have the capability to demonstrate relationships amongst features and outcomes that may not be apparent in the standard combination of semantic reporting (*2*). While ANNs are unlikely to make physicians and radiologists redundant, there is an opportunity to enhance patient outcomes, reporting accuracy and efficiency using ANNs (figure 7).

There has been significant angst amongst radiologists around the prospect of AI encroaching on their work function (*1-3*). A fire fuelled by regular social media, blogs and other forms of discussion proposing the end is near for the radiologist. Any serious endeavour to integrate AI in radiology or nuclear medicine must maintain human authority and the proposed "radiologist-in-the-loop" model provides some re-assurance (*2*). For nuclear medicine, physician expertise relates to tasks that cannot be readily automated while lower order tasks that are easily automated not only free up valuable time for higher order tasks but also increase the value of the physician. The same argument could be made for other nuclear medicine professionals. AI stands to create efficiencies and increase the perceived value of human resources. In consideration of the tasks that are more suitable to AI automation, the bulk of discussion centres on the impact AI will have on radiologists. It is important in nuclear medicine to look more broadly at the influence of transformative technology on the roles and responsibilities of the medical physicist and nuclear medicine technologist. Consequently, understanding the principles and applications of AI equip nuclear medicine professionals with the capacity to assimilate AI technologies into the workplace; in a similar manner to the many advances in technology that have reshaped roles and responsibilities.

Conclusion

AI has penetrated the daily practice of nuclear medicine over recent decades with little disruption. The emergence of ANNs and CNN applications has seen a significant shift in the landscape whose opportunity outweighs the threat. Nonetheless, understanding of the potential applications and the principles of AI, ANNs and DL will equip nuclear medicine professionals for ready assimilation; averting the 'doomsday' fears permeating radiology. A deeper understanding of the ML and DL anatomy will be explored in a future JNMT article.

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List of figures

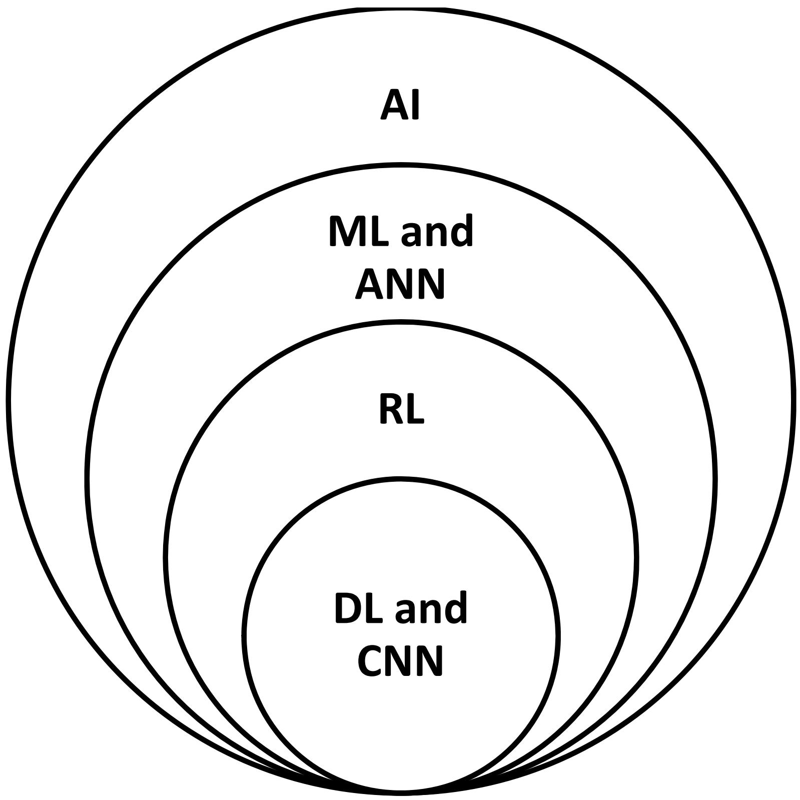

Figure 1: Hierarchy of AI. AI; artificial intelligence, ML; machine learning, ANN; artificial neural network, RL; representation learning, DL; deep learning, CNN; convolutional neural network.

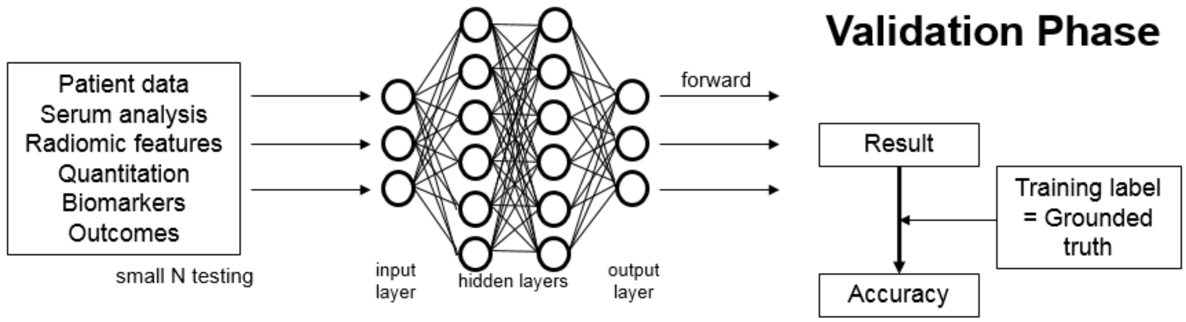

Figure 2: The validation phase of an ANN demonstrates the basic structure of an ML based ANN.

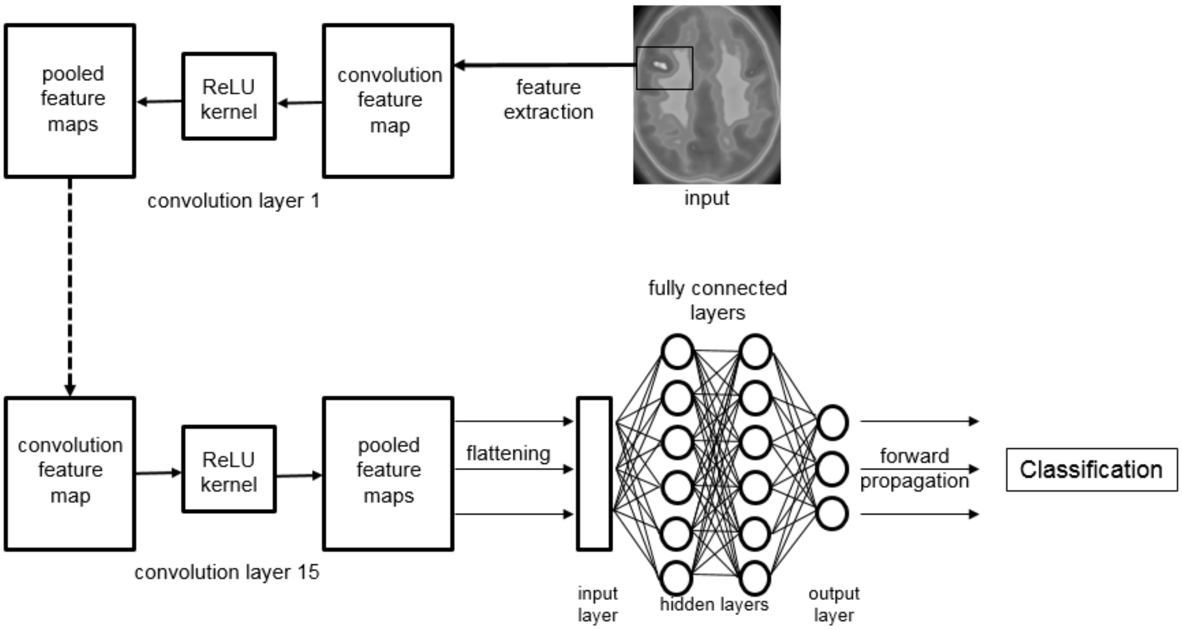

Figure 3: Basic structure of a CNN where the network extracts the radiomic features, produces a convolution function, pools the data through a kernel and flattens the pooled feature map for input into the fully connected hidden layers of the neural network. ReLU = rectified linear unit.

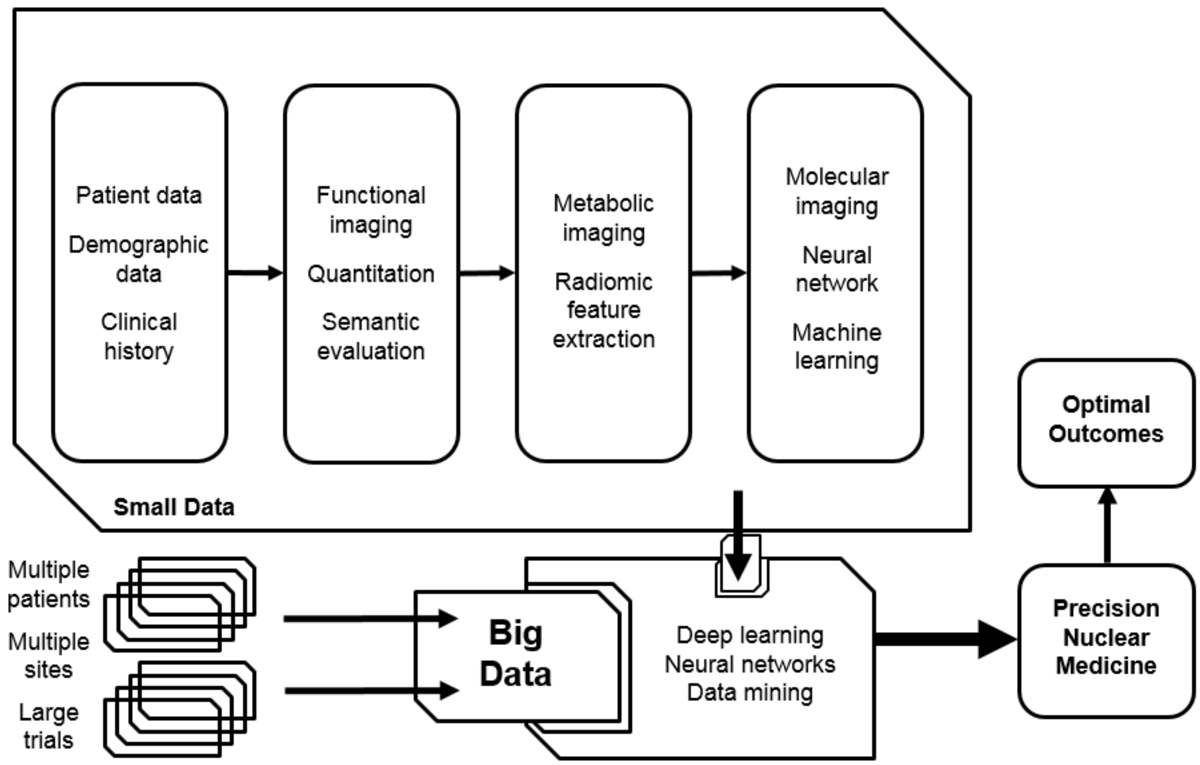

Figure 4: Schematic representation of the semantic evaluation of imaging data, addition of radiomic feature extraction and ANN analysis to produce small data and the potential to integrate with big data to enhance outcomes and drive precision nuclear medicine.

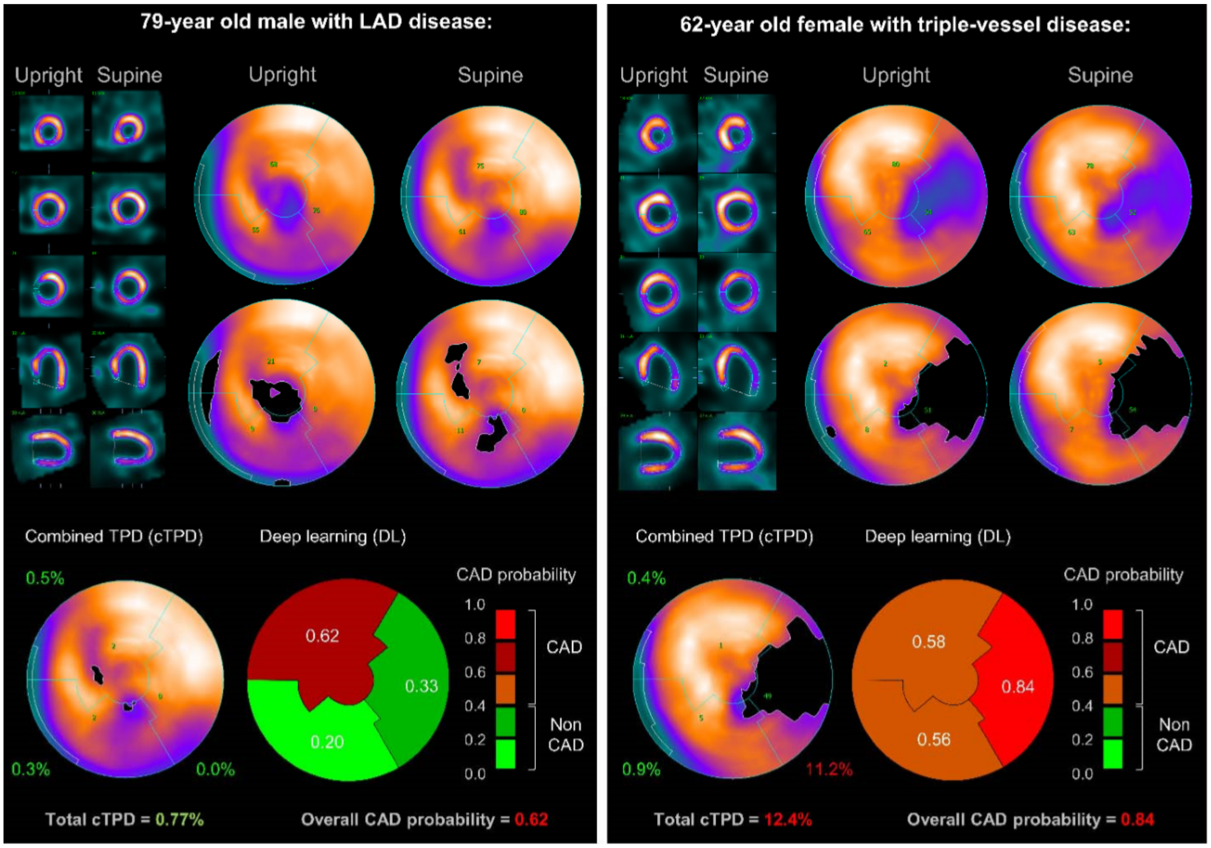

Figure 5: Prediction of obstructive CAD with integration of DL outputs into polar maps. The image provides an example of how the outputs of AI might be integrated into traditional image display, in this case in the form of polar maps with the AI predictive data displayed in the same mode. Reprinted with permission; figure 6 (*15*).

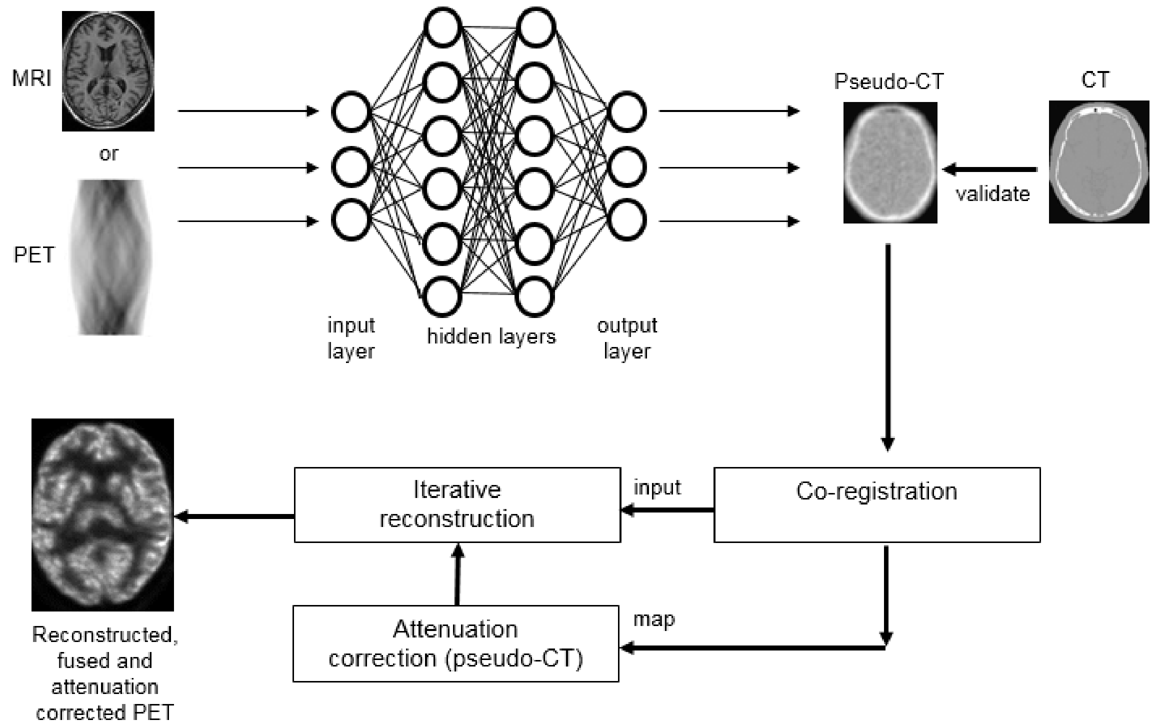

Figure 6: Model for potentially using CNN for improved pseudo-CT attenuation correction in PET/MRI (*25*) or for attenuation correction of PET without CT (or MRI) (*26*).

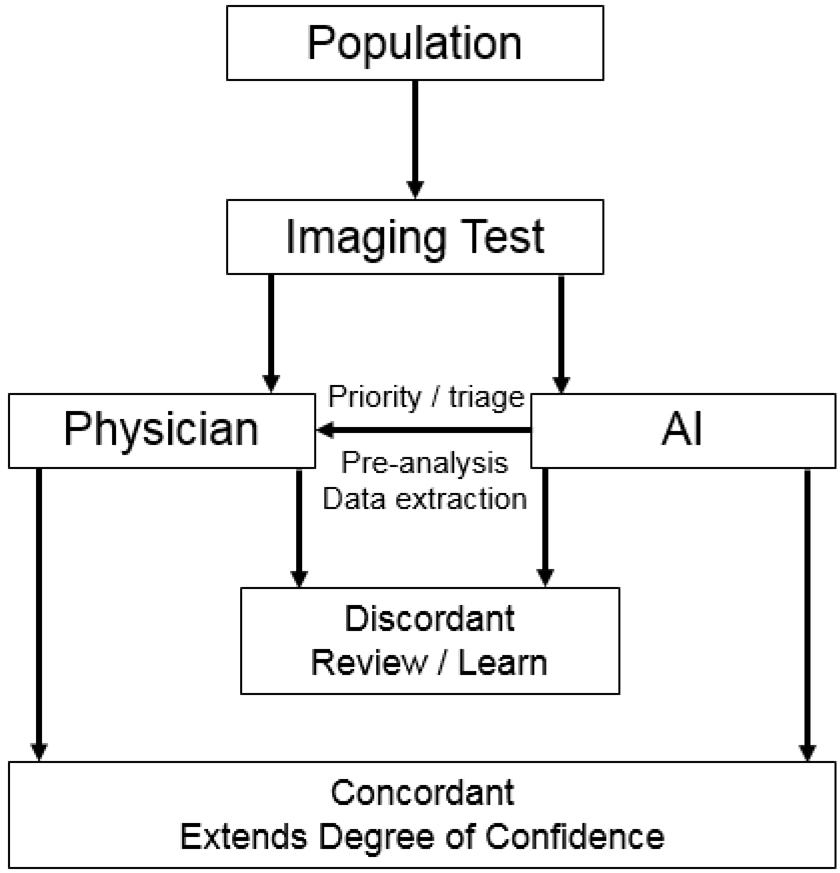

Figure 7: A number of models for integration of AI into radiology have bene proposed (*4*) but in nuclear medicine, perhaps the most appropriate model captures the best of each domain.