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Deep-dose: a voxel dose estimationmethod using deep convolutional neural network for personalized internal dosimetry

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Internal dosimetry is becoming increasingly important owing to the growing interest in targeted radionuclide therapies, radiotheranostics, and personalized medicine[1–3]. Conventionally, internal dosimetry is conducted using the schema provided by the Medical Internal Radiation Dose (MIRD) committee of the Society of Nuclear Medicine[4–6]. Thus far, organ-based dosimetry is considered as a practical approach to internal dosimetry in nuclear medicine. The organ-based dosimetry calculates organ doses by applying organ-level S-values, which represent the absorbed doses to a target organ per unit activity in a source organ, on the generalized human mathematical phantom. However, organ-based MIRD schema assumes uniform activity distribution in each organ, which is not true. Furthermore, patient-specific body anatomy and tissue composition are not considered.

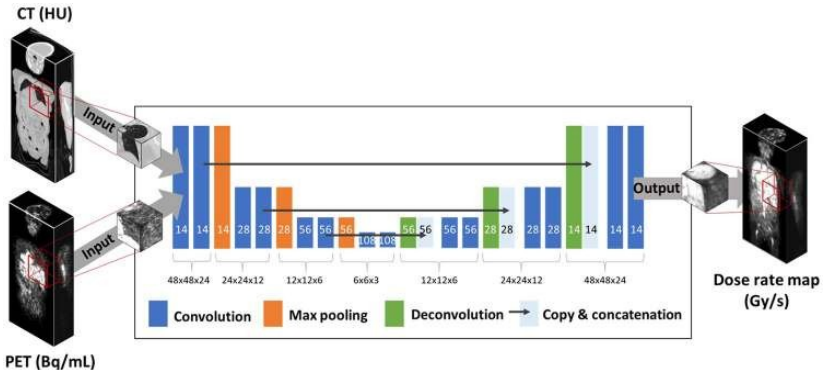
Therefore, voxel-based dosimetry techniques that consider heterogeneous activity distributions have been suggested, including the dose point kernel[7–9] and voxel S-value (VSV) approaches[10]. The dose point kernel represents a radial absorbed dose in a homogeneous water medium when an isotropic point source is located at the center[11–15]. The VSV is the voxel-level MIRD schema, in which sources and targets are defined in the voxel-level, and the voxel S-values are calculated in a 3D voxel matrix composed of the water medium. However, the application of the dose point kernel (DPK) *[Note: DPK represents the radial distribution of absorbed dose around an isotope point source of radiation in an infinite homogeneous medium]* or VSV methods is limited to lesions in homogeneous tissue media (i.e. hepatic ^{90}Y-microsphere therapy) because the medium heterogeneity is not considered in these relatively simple analytical approaches.

For more accurate personalized dosimetry, voxel-based dosimetry based on direct Monte Carlo simulation that can consider both heterogeneous activities and medium distributions has been suggested. The Monte Carlo simulation generates

and tracks particles at the voxel-level and calculates deposited energy to estimate the voxel-level absorbed doses[16,17]. Nevertheless, this approach requires extensive computational time and resources; hence, it is rarely used in a clinical routine basis. Therefore, it is necessary to develop a fast voxel-based dosimetry technique that takes accounts of heterogeneous activities and medium distribution.

Recently, deep neural networks, which is well-known as deep learning, has gained huge attention in various fields[18,19]. In particular, deep learning approaches outperforms conventional image processing approaches in many different tasks including image classifications, segmentations, and generations[20–27]. Furthermore, there have been some recent attempts to use deep learning techniques for radiation dose estimation[28–30]. However, these deep learning applications are only limited to external radiation therapy.

In this study, we suggest a new internal radiation dose calculation method, called Deep-dose, which applies a convolutional neural network (CNN) to estimate the voxel dose values from the individual nuclear medicine images. The absolute 3D radioactivity distribution given by quantitative positron emission tomography (PET) or single photon emission tomography (SPECT) and media property derived from transmission scans, such as X-ray computed tomography (CT), are fed to the CNN as an input, and the CNN is then trained to generate the dose rate map as an output, with the Monte Carlo simulation based dose rate map as the reference (ground truth). We adopted 3D patch-based network training rather than image-to-image mapping as shown in Fig. 1, considering the range of dose delivery from a source voxel to surrounding tissues. To show the feasibility of the Deep-dose method, we applied it to the PET/CT data set of 68Ga-NOTA-RGD, which is a promising diagnostic PET agent for angiogenesis assessment. We evaluated the performance of the Deep-dose by comparing its results to those of direct Monte Carlo based voxel dose estimation.



66 **Figure 1.** U-net architecture consisting of contracting and expanding path. Each box represents a
67 feature mapwith corresponding matrix dimension. The number of feature maps is denoted on the
68 bottom of the box.

1. ***What are the limitations of the organ-based MIRD schema in internal dosimetry? Which of the following limitations is not addressed in the text in lines 7 to 17?***
   a) **Assumption of uniform activity distribution**: The MIRD schema assumes uniform distribution of activity within each organ, which is often not the case in reality. Radiopharmaceuticals may accumulate in certain regions or structures within an organ, leading to heterogeneous distribution of activity. This can result in inaccurate estimation of absorbed doses to organs.
   b) **Lack of consideration for patient-specific anatomy and tissue composition**: The MIRD schema employs mathematical phantoms representing average human anatomy and tissue composition. However, individual patients can have variations in body size, shape, and tissue density, which affect the distribution and absorption of radiation. Ignoring these patient-specific factors can lead to significant discrepancies between calculated and actual absorbed doses.
   c) **Limited accuracy for personalized medicine**: With the increasing interest in personalized medicine, where treatments are tailored to individual patients, the one-size-fits-all approach of the MIRD schema becomes inadequate. Personalized dosimetry requires consideration of patient-specific factors to optimize treatment efficacy and minimize adverse effects.
   d) **Inability to account for physiological changes**: The MIRD schema does not account for physiological changes that may occur over time or in response to treatment. For example, changes in organ size or function, such as alterations in renal or hepatic clearance, can impact the distribution and elimination of radiopharmaceuticals, affecting absorbed dose estimates.

2. ***Mark the option that is in accordance with the text in lines 7 to 17.*** **The conventional method for the calculation of organ-based doses in nuclear medicine:**
   a) are calculated on a size-specific personalized human mathematical representation of an individual.
   b) are measured by using a practical approach, measuring doses in *in-vivo* on patients during procedures.
   c) are calculated on a standard mathematical representation of a human body's anatomy, or phantom.
   d) are calculated using a voxel-based dosimetric representation of a personalized individual.

3. **According to the author, why is internal dosimetry becoming increasingly important in the field of Nuclear Medicine?**
   a) Because of the shift towards personalized medicine aims to tailor treatments to individual patient characteristics, and internal dosimetry enables the customization of radiopharmaceutical doses based on patient-specific anatomy, physiology, and disease characteristics, leading to more effective and safer treatments.
   b) Because MIRD has now provided a novel organ-based schema to internal dosimetry calculations.
   c) Due to the introduction of Monte-Carlo in Nuclear Medicine as a standard method for dose calculation, which has led to a higher precision in dose calculations.
   d) Because Neural Networks are now widely available in Nuclear Medicine which enable millions of data being treated at a faster rate.

4. **What is the difference from voxel-based dosimetry techniques to the conventional MIRD schema?**
   a) In voxel-based dosimetry, the voxel S-values are calculated within the smallest distinguishable box-shaped part of a three-dimensional grid.
   b) Only the conventional MIRD schema can be tailored to individual patients by incorporating patient-specific imaging data (e.g., PET/CT or SPECT/CT scans), leading to personalized dosimetry that reflects the actual distribution of radiopharmaceuticals within a patient's body.
   c) the conventional MIRD schema requires more complex and computationally intensive calculations due to the need to process large amounts of data and accurately model the interactions of radiation within tissues.
   d) Voxel-based dosimetry is simpler and faster to implement, as it uses pre-calculated S-values and straightforward dose equations, but at the cost of reduced detail and potential accuracy.

5. **According to the author, in lines 19 to 30, referring to the current methods for calculation of VSV and the dose point kernel (DPK), the absorbed dose is simulated and calculated in which medium?**
   a) Heterogeneous tissue
   b) Homogeneous tissue
   c) Water
   d) Bone

6. **According to lines 19 to 30, what is a limitation of the DPK and VSV methods in the application of internal dosimetry?**
   a) organs and body anatomy is not considered.
   b) they use a generalized human mathematical phantom.
   c) they can only be used in external radiation beam therapy.
   d) the state of the medium being composed of many different elements is not considered in these relatively simple analytical approaches.

7. **According to the author, in lines 32 to 47, what is most needed to implement personalized medicine voxel-based dosimetry in the clinic?**
   a) Better and faster computers.
   b) Novel methods for dose calculation.
   c) Standardized phantoms of different sizes.
   d) Computational methods that are faster than Monte Carlo methods.

8. **In this work, the main objective is:**
   a) to show the feasibility of a new method to estimate the voxel dose values from the individual nuclear medicine images called the Deep-dose method.
   b) to show how Deep-dose performs in image classifications, segmentations, and generations and compare to Monte Carlo-based methods.
   c) to calculate individual patient doses in PET/CT for 68Ga-NOTA-RGD using Monte Carlo.
   d) to demonstrate 3D patch-based network training using Deep-dose.