Review Article

Artificial intelligence in radiotherapy: Where do we stand?

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Abstract
Artificial intelligence (AI) has been a topic of great curiosity in the medical field. This paper reviews the use of AI in radiotherapy especially in patient imaging, treatment planning, quality assurance and radiation dose delivery. The review highly anticipates the future use for AI in various areas of radiotherapy. However, in view of certain limitations in terms of availability and security of using big data, we may not be ready to use AI primarily in radiotherapy at the moment.

Keywords
Artificial intelligence, Radiotherapy, Treatment planning

Introduction

Artificial intelligence

AI is capability of a machine of mimicking human intelligence. AI can be classified into two branches based on its application: virtual and physical. Physical component can be represented in medical devices and sophisticated robots (care bots). The virtual component can be represented in machine learning.

Machine learning is a mathematical algorithm that learns through experience [1]. Humans are limited in terms of learning by gathering large amount of data primarily due to time constraints. A radiologist will look at approximately 225,000 MRI/CT exams in 40 years, while AI can start with 225,000 scans to train itself and reach millions of scans within a very short period of time. Massive amount of data is now available to train algorithms and modern computational hardware. These algorithms are being applied in many fields, such as drug discovery, medical diagnostics and imaging, remote patient care, risk management, hospital assistants and virtual assistance. [2].

Radiotherapy

Radiotherapy can be divided into; imaging, treatment planning (TP), radiation delivery, radiotherapy verification, and patient monitoring. The TP (3DCRT, IMRT, VMAT, SBRT) can be classified into many categories, such as knowledge based, expert based or artificial intelligence (AI) based.[3]

Methods

Machine learning is the idea of computer learning to perform a task from studying a set of training examples. Machine learning is generally classified into two different categories: supervised learning and unsupervised learning.

In supervised learning, the training set contains the data and the correct output, where computer uses both the data and the output (label data) to predict the output of the future data. The goal of supervised learning is to come up with a functional relationship from training data that generalizes testing data [4].

In unsupervised learning, training set does not contain the solution, so the computer must find the solution on its own and use both the data and the derived solution to predict the outcome of the future data [5]. The goal of unsupervised learning is to come up with the unknown variable behind the observation or find the relationship between samples.

Indepth, various machine learning algorithms are: Linear dicriminant analysis (LDA), Quadratic discriminant analysis (QDA), Artificial neural network (ANN), Kernels, Probalisitic models, Cluster analysis, K mean algorithm, DBSCAN algorithm, Gaussian mixture models, Reinforcement learning, Graph matching, Deep neural networks (DNN) and Convolutional neural networks(CNN).

Implementation of machine learning algorithms in radiotherapy

1. **Medical imaging**

AI-based algorithms are primarily implemented in three aspects of medical imaging as shown below:

a) **Image segmentation**

There are a lot of segmentation methods available but none is universal. Some commonly used image segmentation methods are the snake model introduced by Kass et al. and the level set method (LMS). LMS can further be divided into two categories: region-based models and edge-based models. Edge-based model utilizes edge information, where region-based model utilizes region information to control the motion of the active contour. [6] Segmentation can be applied to many structures, such as bones, organs, muscles and fractures. Deep learning methods can automatically segment MRI brain images.[7]

Ultrasound is normally used to diagnose breast cancer and improvement in segmentation of breast ultrasound images into functional tissues provides a better tumour localization, assessment of treatment response, and breast density measurement. Segmentation of ultrasound is very time consuming for radiologist and it is skill andexperience dependent. Automated segmentation of ultrasound image will help mitigate those problems.

Recent study shows convolutional neural networks (CNN) based segmentation can segment the 3D image into four major tissues: skin, mass, fibro glandular tissue, and fatty tissue with high accuracy. This shows potential to provide segmentation in the future in clinical diagnosis of breast cancer.[8] A fully automated whole-body segmentation for diagnostic CT has already been proposed. The segmentation method used random forest algorithms and explored its accuracy and limitation. Tissue segmentation of CT scans was done by training various data sets and applying them to neck, chest, pelvis and abdomen CT scans.[9]

b) **Medical image registration**

Image registration is an application of machine learning. The goal of this process is to find the optimal transformation that best aligns the structures of interest in the input images. Few examples of commonly used image fusion modalities are CT or MRI with PET or SPECT. In the intensity-based registration method, the algorithm searches for geometric transformation iteratively so that when applied to the moving image it optimizes (maximizes or minimizes the similarity measure or cost function). Cost function is related to voxel intensity and computed in the overlapped region of the input image. In the feature-based registration method, the algorithm searches for optimal transformation after the features are established. Criterion based on geometrical, physical or statistical properties is used to match among features.[10]

c) Computer-aided detection (CAD) and diagnosis system

Automated image recognition has improved significantly in the recent years primarily due the availability of large scale datasets. CT lung node identification is an improved example in CAD. Image Net consists of more than 1.2 million categorized natural images of over 1,000 classes, which play a big role in training this complex CNN. CAD-based CNN trained from Image Net on thoraco-abdominal lymph node and interstitial lung disease shows promising results for clinical use.[11] CAD also shows a potential in detection of metastases, and colonic polyps.[12] Computer-aided detection and diagnosis (CADe and CADx) for colonoscopy use deep learning algorithms that are currently being studied. This AI has two principal roles in diagnosis: Polyp detection (CADe) and polypcharacterization (CADx).

2. **Treatment Planning**

Recent radiotherapy modalities such as photon-based VMAT require a lot of planning before dose delivery. The dose deposition in VMAT is very complex and an accurate prediction of the plan outcome allows radiation oncologists to make a better and more informed decision for therapy and saves a lot of time. New proposed machine learning algorithm can predict dose distribution for organs-at-risk and planning target volume. The algorithm's accuracy was validated on 69 plans for lung SBRT and 121 head-and-neck plans; this resulted in a mean error below 2.5 Gy. This shows a potential to be used as automated treatment plan in SBRT for lung and head-and-neck therapy.[13] In Cho et al, Artificial neural network (ANN) shows outcome prediction capabilities for head-and-neck cancer. ANN combines relevant variables into a predictive model during train-ing and analyses all possible correlation of variables. Out of 73 test subjects, 51 patients were used for the training set, 11 patients were used for the test set and the remaining 11 patients were used for the validation set. The result shows that for focal target control the accuracy for all combined sets is 90.4% and distant metastasis outcome accuracy is 91.8%, proving its viability as a prediction tool.[14] ANN also allows the prediction of survival of radiotherapy alone from uterine cervical cancer by evaluating important prognostic factors.

3. Radiotherapy delivery

In microbeam radiotherapy (MRT), the treatment field is fractionated into arrays of a few tens of a micrometre wide planar beam with high peak doses that are separated by a low dose region. MRT has proven to spare normal tissue more efficiently than general radiotherapy. The dose calculation in MRT is based on MC simulations, which are time consuming. So, Debus et al. provided a kernel-based dose calculation algorithm which separates the pho-ton and electron mediated energy transport and can calculate the valley and peak dose of MRT field within a few minutes. The peak dose value matched the MC simulation within 4% deviation and valley dose within 8%, except for the region close to the material interfaces.[15]

Kernel method provides an inexpensive computational solution to markerless tracking of respiration induced tumour motion in kilovoltage fluoroscopy image sequence in image-guided radio-therapy. The method first enhances the contrast of kilovoltage fluoroscopic image using histogram equalization, then the target tracking is formulated by maximizing the Bhattacharyya coefficient using the mean shift algorithm. The obtained result was compared with four clinical kilovoltage fluoroscopic image sequences and four conventional template matching methods. The kernel method proved superior to the conventional template matching method, showing comparable result to the fluoroscopic image sequence.[16]

Markerless prostate localization strategy using DNNs to interpret projection x-ray images in image-guided radiotherapy has been investigated and the experimental result shows high accuracy and can be used for patient positioning and real-time target tracking.[17] In IMRT the optimized beam angle typically clusters around in a distinct orientation, so a K-means algorithm is used to identify cluster centroids as irradiation angle of an IMRT treatment plan. The optimized beam angles provide better sparing of organs-at-risk in the case of pancreas and intracranial cancer.

4. Radiotherapy verification and patient monitoring

IMRT is heavily dependent on the accuracy and position of each radiation beam. Gamma analysis is the standard method for analysing the fidelity of IMRT. The gamma statistic is used to compare the measured dose distribution to the planned dose distribution. Gamma analysis does not correlate with many clinically relevant deviations in delivered dose and is insensitive to small errors in multi-leaf collimator positioning. A method was developed to detect specific errors using image features in gamma image. It treats the gamma distributions as an image and uses feature evaluation on the patient image to predict prognoses, response to therapy and other outcomes.

Carrara et al. showed that ANN can be used to predict any selected acute or late toxicity endpoint after prostate radiotherapy.[18] LDA is used in various radiotherapy studies and applications such as identifying predictive genes using whole genome microarray data from prostate cancer patients to study cancer related fatigue115; and linking the connection between gut microorganism and chemotherapy induced diarrhoea from CapeOXregimen in resected stage III colorectal cancer patients.[19]

Conclusion

AI has unlimited potential in radiotherapy; however, it is not completely tuned yet to be used widely by itself in clinical use. It is already being implemented in some diagnostic cases; however, more works need to be done. In the future, with more research and development, AI is expected to take massive workload away from the radiation staff including radiotherapists, medical physicists and radiation oncologists in radiotherapy.

Conflict of interest

None declared.

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