PET/CT or PET/MRI scan image processing techniques

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Abstract

Medical imaging technique is particularly significant in today's medical profession since it allows radiologists and doctors to examine various diseases and understand therapy effects on patients. Medical imaging techniques such as PET/CT and PET/MRI scans are one of the most widely utilised methods for diagnosis. However, owing to technicality or other factors, there will be noise in the image during the imaging process. Because of the noise and lack of clarity in the image, radiologist analysis is challenging, which can lead to false positive and false negative disease reports. Apart from this noise, there is a lot of medical image data created day to day life, which makes analysis tough. Medical image processing is necessary which help overcome from this issue. To improve the quality and reliability of these medical images, a range of computational algorithms have been proposed, developed, and tested. In this review study, a few thought methods like as threshold-based segmentation, its drawbacks, CNN, and its applications which are applied on PET/CT and PET/MRI images will be discussed.

Keywords: *Image pre-processing, Segmentation, Threshold, Deep learning, Convolution neural network*

Introduction

Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), computed tomography scan is the few of the oldest methods used for medical diagnosis [25]. PET (positron emission tomography) is a type of imaging technique that is used to diagnose cancer. This method used to detect pathophysiological changes in tissues of cancer patient. Here cancer tissues functional changes are detected before anatomical changes detected by convention radio diagnostic technique. Currently hybrid techniques like PET/CT or PET/MRI provide combined functional and morphological information of cancerous tissues. Fluorine-18 fluor deoxy-glucose (^{18}F-FDG) is the most used glucose-based radiotracer in oncology, this detects glycolytic activity, by detecting the photons emitted from ^{18}F-FDG which are more in tumour cells than that of normal cell. Advancement in digital MRI image processing have aided in everything from simple tumour detection to assessing tumour response and therapy [10]. Due to complementary advantage of hybrid technique (PET/CT or PET/MRI) it has gained attention but there is still room for improvement regarding image quality [26]. A variety of computing techniques have been proposed, developed, and tested to increase the image quality, accuracy and reliability of this medical images. Stages in image processing can be classified in pre-processing, segmentation, feature extraction.

Image pre-processing

Image pre-processing is an important step done prior to image segmentation, feature extraction which can increase the algorithm's efficiency as well as the accuracy of the segmentation outcomes [27]. Image enhancement and noise reduction can improve the image viewing quality [9] and better understanding. The noise caused from low frequency signals emitted from MRI machine can be reduced and artifact on MRI or CT image can be removed using different methods, few of them prospective, retrospective methods which explained in detail in ([10],[27]), few other are temporal filter, medial filter, spatial filter, gaussian filter etc.

Standardized uptake value

Metabolic tumour volume (MTV) and Standardized uptake value (SUV) are two features of PET images that are traditionally considered to be the most important in clinical settings. SUV – a semiquantitative normalised parameter derived from the intensity of PET photographs.

$$\text{SUV} = \frac{R}{A/W}$$

where R is the radioactivity concentration [kBq/ml] measured by the PET scanner at a specific time inside a region of interest (ROI), A is the decay-corrected amount of administered radiolabelled FDG [kBq], and W is the patient's weight [g] at a specific time. (Paul E. Kinahan et.al [6]). Because of its simplicity and efficiency, the SUV-based threshold is frequently employed for segmentation. MTV is characterized by volume with similar SUV. Maximum SUV (SUV_{max}) which often used in segmentation, which normally makes uses a single-voxel value, which might lead to uncertainty due to the presence of high level of PET image noise. While Peak (SUV_{peak}) or mean SUV (SUV_{mean}) are proposed as noise-resistant alternatives to SUV_{max} [1].

Segmentation

Image segmentation is a method that splits the image into many layers which make it easy to analyse and interpret images [7]. There are many types of PET image segmentation methods few of them are Thresholding Segmentation, learning methods, stochastic modelling-based techniques, variational approaches [3], Watershed Segmentation, K-means Clustering Segmentation, Graph cut segmentation, Performance Evaluation of Segmentation, Mean shift Clustering Segmentation, FCM clustering segmentation [5].

Threshold based segmentation

Thresholding is an image segmentation approach that turns a grey-level image into a binary image by classifying all voxels with a value greater than a certain value as foreground and all other voxels as background [2]. Several studies have shown that threshold-based segmentation is more resistant to noise and resolution, than image gradient-based segmentation. However, there is considerable uncertainty that cannot be prevented when using thresholding-based techniques. That is, there is no universal agreement on a thresholding level because of the wide variety of diseases, low resolution, intrinsic noise, low

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signal-to-noise ratio (SNR), and substantial uncertainties in fuzzy object boundaries. As a result, determining the best threshold remains a difficult issue. In order to improve the segmentation mechanism and get the best boundary extraction, thresholding-based methods are still being developed. Threshold based PET image segmentation classified into several groups – Fixed threshold method, adaptive threshold method [1] and apart from this there are many other threshold-based methods they are Iterative Thresholding Method, Maximum Likelihood Thresholding etc.

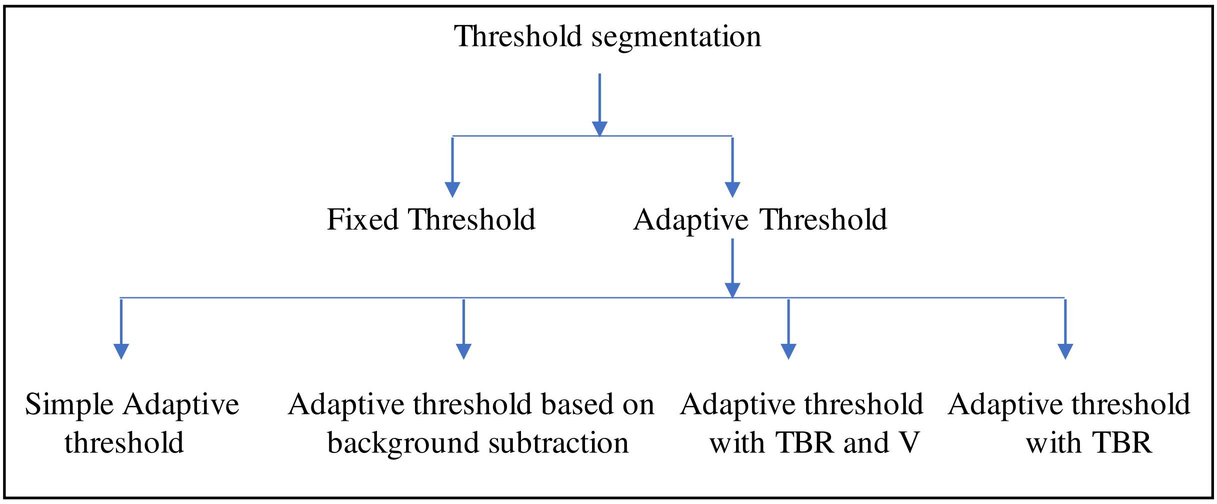

Fig 1: Threshold segmentation classification

Fixed threshold (T_{Fixed})

In Fixed threshold, everything above a certain intensity level is assigned to a group, while the rest is considered background. This intensity level can be given by an expert, learned from a training set of images of same type, or calculated using realistic phantoms using analytic expression. In many clinical studies, a pre-defined threshold level, such as an SUV of 2.5, is used to distinguish malignant lesions from benign lesions [2]. SUV_{max} can be used to distinguish an object from its surroundings by applying a specific percentage of SUV_{max} to the object. Commonly thresholding (T_{Fixed}) value 40 – 43% of the SUVmax is chosen but it's value could change as per few of the characteristics of PET image.

In a fixed threshold-based PET image segmentation method, a fixed percentage T_{Fixed} of the SUV_{max} of the tumour SUV_{maxT} is used to determine the SUV_{Fixed} value and can be given as

$$SUV_{Fixed} = T_{Fixed} \text{ X } SUV_{maxT}$$

Theoretically, for noise free image T_{Fixed} value 50% can give a good estimated volume [1]. T_{Fixed} is affected by a variety of factors, including volume and tumour to background ratio (TBR), as well as scanner specifications, reconstruction and data acquisition procedures, noise level, and so on. TFixed can be stated as

$$T_{Fixed} = F\ (V, TBR, SNR, FWHM)$$

since all of these factors are used in SNR and FWHM as a measure of image resolution [1].

The many disadvantage of this fixed thresholding method is 1) that it has a tendency to exaggerate lesion margins, especially for small lesions, 2) if a patient is treated for tumour and his/her tumour volume reduced results to reduce in uptake value, TBR, SNR, it may not provide similar accuracy for tracer with lower uptake value because of this Fixed method is not suitable for diagnosis. As a result, in order to give a clinically sound demarcation, an adaption of thresholding with additional information or user instruction is frequently required.

Adaptive threshold ($T_{Adaptive}$)

To address the shortcomings of the fixed threshold method, a number of adaptive threshold-based PET image segmentation approaches have been developed. They are a) simple adaptive threshold, b) adaptive threshold based on background subtraction, c) adaptive threshold with TBR and V and d) adaptive threshold with TBR, whose complete detail available in [1].

The difficulty of reproducing the similar segmentation results in multiple scanners or patients is a fundamental drawback of analytical expression-based thresholding approaches. Another disadvantage is that these expressions usually fail for lesions with a complex shape since the analytic model for those circumstances is incorrect [2]. Adaptive method is not optimum for smaller volumes with lower TBR and SNR and there is need of a robust technique which is not sensitive to TBR, SNR and SUV_{maxT}.

Even though threshold-based segmentation is simple and effective it has its own limitations. The threshold does not normally take into account an image's spatial features and by using threshold it may not able to separate all tissue [9].

Later for segmentation, fuzzy c-means (FCM) and machine learning methods were introduced. However, in order to obtain accurate outcomes, intensity and spatial characteristics is required. The use of convolutional neural networks (CNNs) could eliminate need of spatial and intensity features [9].

Deep learning

It's a neural network with numerous layers of nonlinear processing units. The output from the preceding layer is used as input for each subsequent layer. Using these layers, the network can extract complicated hierarchical characteristics from a massive amount of input. One can utilise simple feedforward neural networks while implementing neural networks to image. Some of the deep learning algorithms are Boltzmann machines, deep stacked auto-encoders and convolutional neural networks [18]. Since connecting all nodes in one layer to all nodes in the next layer is inefficient which can overcome from CNN, it become popular in image segmentation.

Deep Learning Applications in Medical Image Processing

Deep learning is used in various fields like analysis of digital pathology images, cytology diagnoses diseases, Ophthalmology, Radiology. A variety of radiology techniques such as computed tomography, X-rays, magnetic resonance imaging, ultrasound and positron emission tomography are used to diagnose or treat diseases. These methods frequently necessitate massive amounts of data. The CNN is a method that is based on data. As a result, CNN techniques are widely used in radiology imaging and analysis [11].

Convolution neural network

A CNN is a type of artificial neural network that is designed to preserve spatial correlations in data by using only a few connections between the layers. Among many neural network techniques, the most successful model for image analysis is the CNN. K. Fukushima, [15] pioneered the CNN in 1980.

LeCun et. al. [13] learned convolution kernel coefficients from photographs of handwritten digits using backpropagation in 1989. The learning process was completely automated, and it produced excellent results. This approach became the foundation of modern computer vision technology [11].

Various CNN architectures have been developed over the previous decade. LeNet-5 and shift-invariant models, have been introduced. A network of neurons in 2012, Krizhevsky [14] made a significant contribution to the ImageNet Challenge. They proposed a 7-layer CNN called Alex Net that used a variety of useful approaches like ReLU, dropout, and data augmentation. Alex Net outperformed the previous state-of-the-art system by a significant margin. Now CNN used not only in picture recognition, but also in saliency [11] object detection, recognition, classification, regression, segmentation.

CNN learns by controlling the change in weights according to the target using the backpropagation technique, optimization of backpropagation works same as human brain [16]. A Convolution neural network usually have numerous convolutional layers, often interleaved with pooling layers, and is taught via backpropagation and gradient descent in the same way that ordinary artificial neural networks. Furthermore, CNNs features a fully connected layers at the end that compute the final outputs [12]. Along with basic CNN component different mapping functions, regulatory units like batch normalization and dropout are used to enhance CNN performance.

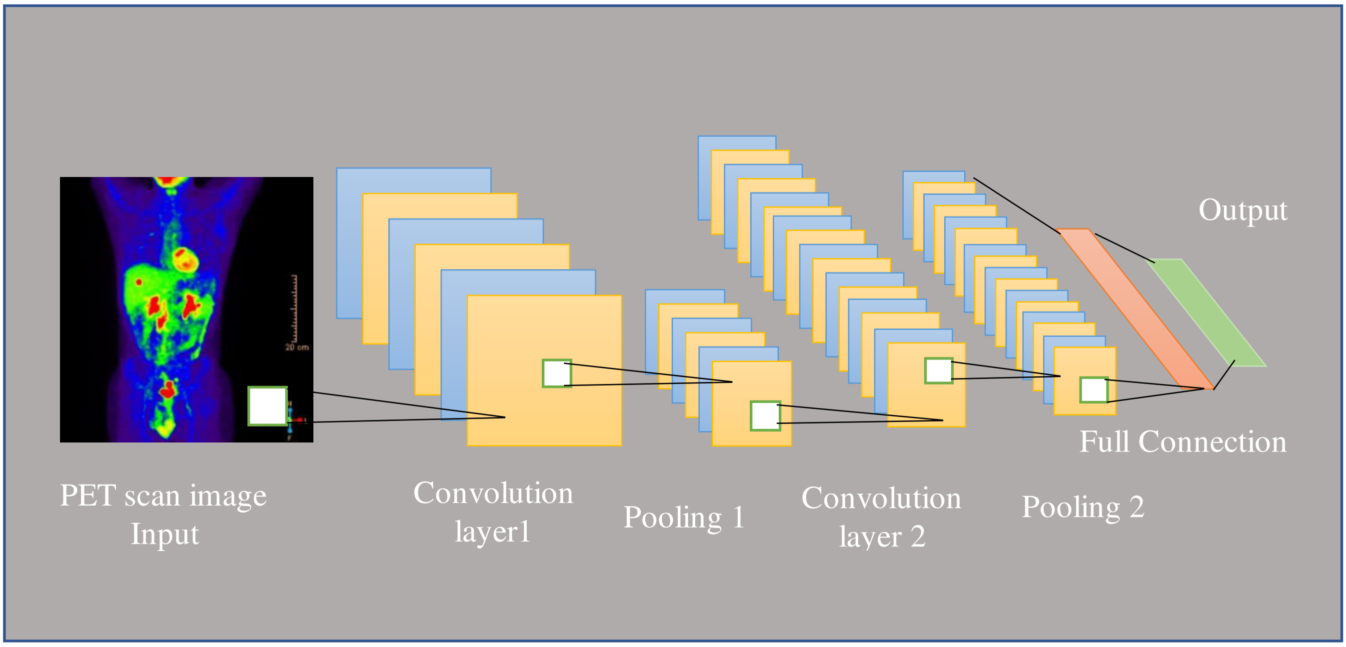

Fig 2: Basic components of a Convolution neural network

Convolution layers

Convolution layers one of the important parts of the CNN which contain multiple convolution filters. In image processing, a convolution filter is often used to modify or improve an image by highlighting or deleting particular elements. A matrix of numbers representing the intensity of pixels can be created from a digital image. Gray scale values range from 0 (black) to 255 (white). Image filtering alters an image's pixel values. In an image, neighbour pixels are more closely correlated than distant pixels, which is an important characteristic of an image [11].

Pooling Layer / Down sampling

Pooling layer, a type of nonlinear down sampling, is one of the data compression methods used in the CNN. Max and mean operations are the most common type of pooling operators. Pooling is done solely for the aim of shrinking the image's spatial size. Because medical images have a lot of local and global redundancy of pixels, it's fair to compress image characteristics in the CNN. Since pooling is operated independently for each depth dimension, the image's depth stays unchanged. The max pooling layer is the most common type of pooling layer used. The pooling layer controls overfitting and enhances adversarial robustness by reducing the spatial size of features, the amount of processing in the network, and the number of parameters [11].

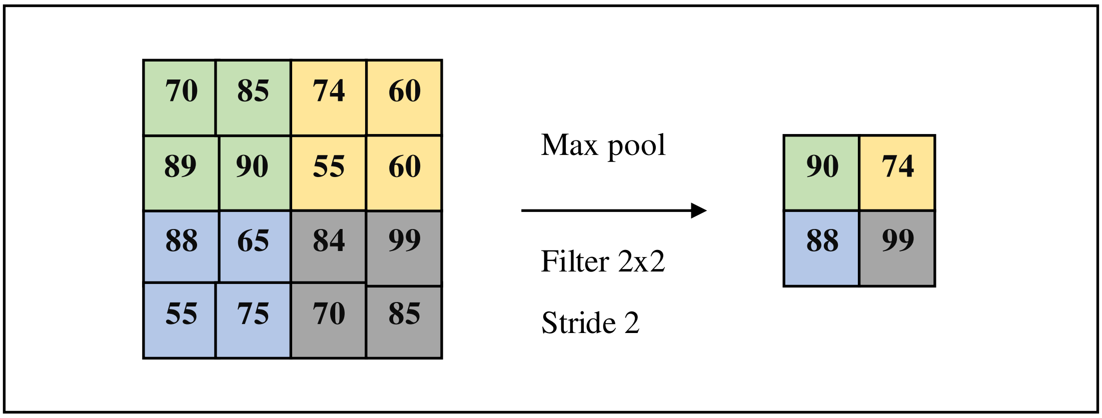

Figure 2 : A pixels matrix of size 4×4 is reduced to half of it's size 2×2 by applying max pool operator, with Stride 2

Fully Connected Layer

Fully connected layers are frequently introduced after a number of convolution and pooling layers in a CNN in some case it will be replaced by global average pooling layer [16]. They will categorize incoming pixel values using high-level features provided by convolution or pooling layers. Each neuron in a fully connected layer is connected to every output of preceding layers. Fully connected layers provide a vector of values, each expressing the likelihood that a given feature belongs to a certain class.

Activation function

The activation function is a decision-making function that aids in the learning of complex patterns. The use of the right activation function can speed up the learning process. The activation function calculates a weighted total and then adds bias to it to determine whether a neuron should be activated or not. Its goal is to induce non-linearity into a neuron's output. There are many different activation functions such as sigmoid, maxout, tanh, SWISH, ReLU and its type like leaky ReLU, ELU, and PReLU are used [16]. Relu is the most commonly used activation function [17].

Batch normalization

Batch normalization is often inserted after activation layers, this method follows unit Gaussian distribution. Here output at each layer will be normalised by subtracting the mean and dividing by the standard deviation ([12], [17]). Some of the batch normalization advantages are, reduces chances of over-fitting, reduces the time required for network convergence, to decrease training dependency across hyper-parameters.

Dropout

Dropout is a commonly used generalisation technique which acquired by introducing regularization. In this technique neurons are lost at random throughout each training session. As a result, the feature selection power is divided evenly over the whole group of neurons, and the model is forced to learn several independent features. Multiple connections learning a non-linear relation in neural network are occasionally co-adapted, resulting in overfitting to overcome from overfitting dropout is used ([12], [16], [17]).

Image processing application

Keisuke et.al. [19] used CNN to overcome patient misidentification in imaging examination. In this experiment they collected FDG PET/CT whole body scanned images of over 6462 patients (3623 men, 2839 women), body weight and age. Usually, to avoid patient misidentification wristband were used but cannot be applied during emergency. So, using CNN could be an efficient way of preventing patient misidentification. Here patients were fasted for ≥6 hr before FDG injection and emission scan was done after 60 min post-injection. CNN used was had a 4-layer convolution layer, ReLU function, local response normalization, SoftMax function and have used dropout and early stopping to prevent overfitting. A regression model to predict age, bodyweight, sex by CNN was trained. And it found out that using CNN they were able to predict sex of a patient approx. of 99.6%, the model trained using 50 epochs could predict age by 83.2% at absolute error being smaller than 5years and body weight at 96.1% at absolute error being smaller than 5 kg.

Zhenglun Kong et. al. [9] Due to indistinct borders, it's difficult to differentiate between grey matter, white matter and cerebrospinal fluid especially in cross-sectional image that don't show the brain's centre. As a result, doctors have a difficult time analysing them separately and pinpointing the disease's site. Here author collected 5 patients brain MRI images, for each patient’s 160images total of 800 images of image size 256x256 pixel. Pre-processing of this image is done by histogram equalization method. In the end CNN was implemented for segmenting grey matter, white matter and cerebrospinal fluid. The result that got from CNN is compared with Visible Chinese Human (VCH) (It is one of the most realistic head models that contains precise cerebral cortex folding geometry), it showed that author found an accuracy of 95% of clear segmentation of grey matter, white matter and cerebrospinal fluid.

Margarita Kirienko et.al. [20] here the author tried to classify a lung cancer lesion as T1-T2 or T3-T4. FDG PET/CT scan image of 472 patient were collected who were within 60days before biopsy or surgery. In CNN weights of neuron were randomly chosen, they were adjusted at each iteration, used loss function, SoftMax function was applied. Here data were divided in training (n = 303), test (n= 94), and validation (n= 75). The overall result is in below table. It shows that the author was able to apply CNN efficiently to classify a lung cancer lesion as T1-T2 or T3-T4.

	Training	**Validation**	**Test sets**

Accuracy and AUC	87%	86%	90%
Recall	69%	77%	47%
Specificity	69%	70%	67%
Area under the curve (AUC)	0.83	0.73	0.68

Noam Tau et.al. [21] here by assessing characteristics of the primary tumour using PET, finding out CNNs could be used to predict the existence of lymph node metastases and the systemic metastatic potential of newly diagnosed Non–Small Cell Lung Cancer (NSCLC). PET scan images of 264 patients were collected and analysed using CNN, it found that the sensitivity, accuracy and specificity of CNN for predicting node positivity were 0.74 ± 0.32, 0.80 ± 0.17 and 0.84 ± 0.16. The corresponding values for predicting distant metastases were 0.45 ± 0.08, 0.63 ± 0.05 and 0.79 ± 0.06. This shows that CNN's sensitivity in predicting distant metastases is fairly low.

Similarly, there are many applications of CNN, Amy J. et.al. [22] used CNN to automatically detect lymph nodes involved in lymphoma the CNN achieved a 90% true-positive rate (TPR) at 3.7 false-positive (FP) findings per patient. Keisuke et.al. [23] used CNN on FDG PET/ CT images to classify benign, equivocal and malignant, with 99.4, 87.5, and 99.4% accuracy, respectively. Weiming et.al. [24] Alzheimer's Disease Prediction from Mild Cognitive Impairment and many more.

Image processing advantages

1. Image processing can improve both the efficiency and the reliability.
2. Image noise reduction and enhancement can make the image more conforming for viewing.
3. Medicine: - In medicine, many techniques such as segmentation and texture analysis, is used for cancer and other disorder identifications. Cerebrospinal fluid, grey matter, and white matter boundaries differentiated during cross section. In the field of bioinformatics, it helps analyse large imaging data faster without any need of expertise.
4. Forensics: - In forensics image processing techniques can help in edge detection, pattern matching, security, denoising and biometric purposes such as identity, face, and fingerprint documentation.

Conclusion

We studied the basic fundamental of a medical image processing technique, need of image pre-processing, few of segmentation method. From this review we can conclude that fixed threshold has the tendency to exaggerate lesion margins, especially for small lesions, their threshold value needs to change when there is change in TBR, SNR value which is quite inefficient. Adaptive method is not optimum for smaller volumes with lower TBR and SNR and there is need of a robust technique which is not sensitive to TBR, SNR and SUV_{maxT}. And threshold does not normally take into account an image's spatial features and by using threshold it may not able to separate all tissue. The use of convolutional neural networks (CNNs) could eliminate need of spatial and intensity features so could be a better choice but there is need to large data for efficient result.

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