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Synthetic Positron Emission Tomography Using Conditional-Generative Adversarial Networks for Healthy Bone Marrow Baseline Image Generation

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Abstract

A Conditional-Generative Adversarial Network has been used for a supervised image-to-image translation task which outputs a synthetic PET scan based on real patient CT data. The network is trained using only data of patients with healthy bone marrow metabolism. This allows for a patient specific synthetic healthy baseline scan to be produced. This can be used by a clinician for comparison to real PET data in the absence of a baseline scan or to aid in the diagnosis of conditions such as Multiple Myeloma which manifest as changes in bone marrow metabolism.

Keywords: Medical Imaging, Conditional-Generative Adversarial Networks, Deep Learning, PET-CT, Bone Marrow.

1 Introduction

1.1 Multiple Myeloma

Multiple myeloma (MM) is a malignant haematologic disorder characterized by bone marrow (BM) infiltration with neoplastic plasma cells. Approximately 10% of all haematologic cancers are related to MM, with an incidence of approximately 4/100,000 per year [Bredella et al., 2005]. Bone lesions are present in approximately 80% of symptomatic patients. The extent of bone lesions will impact later choices of therapy and it is therefore vital to diagnose myelomatous lesions accurately and as non-invasively as possible. In order to standardize treatment approaches it is essential that the disease be clearly characterised at the time of diagnosis, this is achieved through the Durie-Salmon staging system for MM which was introduced in 1975 [Durie and Salmon, 1975]. Advances in diagnostic imaging techniques led to the introduction of the Durie-Salmon PLUS staging system in 2003 [Fechtner et al., 2010]. The Durie-Salmon PLUS system highlights the benefits of 18F-FDG PETCT in accurate staging of MM [Durie, 2006] which can show regions of the bone and BM that demonstrate signs of elevated metabolism.

1.2 PETCT

Positron Emission Tomography Computed Tomography (PETCT) imaging utilizes 18F-fluorodeoxyglucose (18F-FDG), which is an analogue of glucose that has positron-emitting radionuclide 18F attached to the molecule. Metabolically active cells take up the 18F-FDG which remains trapped within the cell and is then imaged using PET [Bredella et al., 2005]. The Standard Uptake Value (SUV) is used as a diagnostic tool to semi-quantitatively differentiate between benign and malignant anatomic regions, such as the lesions caused by MM [Hallett et al., 2001]. The semi-quantitative nature of SUV measurements allows for a more objective assessment of PET images. At present, there is an ever growing body of evidence to suggest PETCT’s increasing importance in the future of MM diagnosis [Touzeau and Moreau, 2013].
1.3 Conditional-Generative Adversarial Networks (C-GANs)

The framework first proposed by [Goodfellow et al., 2014] simultaneously trains a generative model $G$ that captures the data distribution, and a discriminative model $D$ that determines whether a sample came from the training data or was artificially generated by $G$. At each training step the goal for $G$ is to maximize the probability of $D$ making a mistake. In the original GAN framework there is no control over the output sample, it is initialized using a random noise distribution. By adding in a conditional component, in this case the CT image, the output, in this case the PET, must relate to the conditional component. The task is a supervised image-to-image translation where a CT image is translated to a PET image [Huang et al., 2018].

2 Methods

The work presented trains a C-GAN which uses the CT component of the scan to infer a corresponding synthetic PET component. Images have been filtered and masks applied to retain only regions relating to the bone marrow. The network is trained using datasets of patients considered to have normal/healthy bone marrow metabolism and so produce corresponding healthy artificial PET component which can then be compared to the real patient PET scan. Differences may indicate signs of malignancy. Qualitative comparison is presented in the form of visual comparison of the outputs from the trained network when given a dataset of both a healthy BM patient and a patient with MM.

2.1 Training Data

After receiving ethical approval by the institution, PET-CT scans of 10 patients were compiled. The data was anonymised prior to analysis to ensure compliance with data protection procedures. All scans performed on the same Siemens Biograph 16 PETCT scanner. All scans used in the study were oncology related, with patient referrals indicating a history of cancer. The scan reports were reviewed to ensure the PET component of the patient scan was considered to show normal levels of BM metabolism and had not received recent therapy or intervention which could impact normal BM metabolism.

2.2 Preprocessing

All data processing and C-GAN development was carried out using a combination of Matlab software (for image processing steps) and Python via Spyder interface (for C-GAN and Tensorflow steps). PETCT data were loaded and images calibrated using the dicom metadata to convert to medical image standards of Hounsfield Units (HU) and Standard Uptake Value (SUV) and resampled from $(1 \times 1 \times 3)$ mm$^3$ to $(1 \times 1 \times 1)$ mm$^3$. The software first segments cortical bone from the CT component of the PETCT data. Segmentation was based upon thresholding of pixel values followed by a series of region filling and region growing steps, to ensure both the cortical bone and red marrow bone are part of the segmentation [Puri et al., 2012] [Martínez-Martínez et al., 2016]. This results in a bone marrow binary mask that can be applied to the already mechanically co-registered PET data through a pixel-wise matrix multiplication operation [Sambuceti et al., 2012]. The various stages in the creation of a bone marrow binary mask are shown in figure above.

2.3 Training the Network

The network applied here is a modified version of the Tensorflow (GPU version 2.0) implementation of the PIX2PIX network described by Isola et al, for more details of the hyperparameters set, additional image processing and overall architecture see [Isola et al., 2017]. Training data consisted of approximately 6,000 PETCT
axial slices from the 10 patient dataset. This was split into 15 batches which ran for 160 epochs. Training took approximately 13 hours to complete using a 6 GB Nvidia Geforce 1060 graphics card.

3 Results

Once the network was trained it could then be used to create synthetic PET images based on the CT component alone. An entire series of axial CT slices were fed into the network to produce the corresponding synthetic PET volume. This was done for both a healthy bone marrow patient not used in training and a patient with a diagnosis of MM. In order to further assess differences between between the real PET and the synthetic PET the 3D volumes were first filtered using a mean filter of size 21 x 21 x 21 to reduce impact of noise and then a pixel-wise subtraction between the real and synthetic data was performed to highlight regions where the real data had a greater pixel value, and hence metabolism, than predicted. The results are presented in the figures below as Maximum Intensity Projection images in the coronal plane.

![Figure 1](image1.png)

Figure 1: The main differences in BM metabolism relate to a lack of diffuse activity in the sacrum as well in the left acetabulum of the synthetic PET and are not suggestive of malignancy.

![Figure 2](image2.png)

Figure 2: The main differences in BM metabolism relate to numerous focal regions of activity consistent with a diagnosis of MM.

4 Conclusions

The synthetic PET is based on a network which has been trained only on data of patients with healthy BM metabolism. This is a bias of the network which means when given CT data of a patient with unhealthy BM metabolism it will predict the healthy corresponding synthetic PET scan. The results show differences are present in both the healthy and myeloma test data. This is to be expected as, despite the large number of images used, only 10 patients were used in training, and this will not be enough to capture normal variances in
metabolism seen between healthy patients. The differences between the MM patient do highlight several regions of focal uptake which is consistent with a diagnosis of MM. Further refinement of the proposed technique will involve more training data, quantitative analysis of the network’s performance and fine tuning of network hyper-parameters.

References


