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3D Brain MRI GAN-based synthesis conditioned on Partial Volume Maps

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Abstract. In this paper, we propose a framework for synthesising 3D brain T1-weighted (T1-w) MRI images from Partial Volume (PV) maps for the purpose of generating synthetic MRI volumes with more accurate tissue borders. Synthetic MRIs are required to enlarge and enrich very limited data sets available for training of brain segmentation and related models. In comparison to current state-of-the-art methods, our framework exploits PV-map properties in order to guide a Generative Adversarial Network (GAN) towards the generation of more accurate and realistic synthetic MRI volumes. We demonstrate that conditioning a GAN on PV-maps instead of Binary-maps results in 58.96\% more accurate tissue borders in synthetic MRIs. Furthermore, our results indicate an improvement in the representation of the Deep Gray Matter region in synthetic MRI volumes. Finally, we show that fine changes introduced into PV-maps are reflected in the synthetic images, while preserving accurate tissue borders, thus enabling better control during the data synthesis of novel synthetic MRI volumes.

Keywords: Generative Adversarial Network · Partial Volume Maps · Synthetic MRIs · 3D Image Synthesis.

1 Introduction

Deep Neural Networks, particularly Convolutional Neural Networks (CNNs), have demonstrated tremendous capability to perform accurate segmentation tasks when trained on large datasets [19, 20]. In medical imaging, these methods are limited by the scarcity of available data. Labelling medical data is time consuming and requires a high level of expertise which is expensive. Many different CNN-based methods attempted to overcome this hurdle by mitigating the amount of data needed for their training, such as using unsupervised [3, 15], weakly-supervised [8, 27], semi-supervised [2, 17] and self-supervised [14, 21] methods. The drawback of these methods is that they are typically less accurate than supervised methods [13]. Furthermore, since the ground truth label is missing, it is more difficult to evaluate the performance of these methods [12].

In contrast to aforementioned methods, data augmentation methods [5, 22, 23] aim to increase the number of available labelled samples needed for training of
supervised methods. Data augmentation methods fall into two major trends: geometric transformation-based and GAN-based. Most geometric transformation-based augmentation methods provide limited improvement in terms of samples variety as their output highly relies on the input data.

A GAN is a data synthesis approach capable of injecting more variety into synthesised data and generating outputs less dependant of the input data, while aiming to follow the training data distribution [6]. MRI synthesis using GANs can be classified into two prominent approaches: unconditional [6, 7, 11] and conditional [16, 22]. The main drawback of unconditional MRI synthesis approaches, in the context of supervised segmentation, is the missing segmentation labels of the newly synthesised MRIs. Another drawback of such approaches is the lack of synthesis control [16]. On the other hand, MRI synthesis approaches based on conditioning a GAN with segmentation labels, as presented in [22], keeps the brain anatomical structures intact, while segmentation labels give the ability to control the synthetic results. Nevertheless, the segmentation labels only provide an estimate of brain tissue types. Their accuracy is limited by the image resolution and consequently the segmentation accuracy may suffer from partial volume (PV) effects at the border between two tissues where a single voxel may contain multiple classes. More accurate segmentation can be represented with PV-maps as they define accurate border between two tissue classes [4], which makes them a suitable choice for conditioning GANs in the context of MRI synthesis. Conditioning GANs on PV-maps opens a pathway to generate MRIs of different appearances while retaining the same anatomical structure with fine boundary details. Having control over MRI synthesis by defining tissues with PV-maps as well as the ability to change them may be used as a powerful data synthesis approach.

In this paper, we propose a framework for synthesising 3D brain T1-weighted MRI images from PV-maps. Our proposed framework is inspired by well-known Image-to-Image conditional GAN approach described in [9]. We use PV-maps of Gray Matter (GM), White Matter (WM) and Cerebrospinal Fluid (CSF) as inputs to assist the training of the model and the generation of realistic 3D brain MRIs. We report the first attempt to synthesise realistic 3D brain MRI images from PV-maps using GANs. Furthermore, we demonstrate that changes in PV-maps reflect changes in newly generated synthetic images and show how the framework can increase the number of synthetic training images. The contributions of this paper are the following:

1) We proposed a GAN-based framework that exploits PV-map properties to obtain synthetic MRI volumes with accurate borders between tissue classes as well as more accurate and realistic Deep Gray Matter (DGM) regions.

2) In the context of 3D T1-w brain MRI generation using GANs, we demonstrated that conditioning GANs on PV-maps produces better results than binary-maps. The difference is most evident in the regions of tissue borders, which is an important feature for applications such as cortical thickness estimation and segmentation.
2 Methods

Hypothesis Formulation. When it comes to T1-w brain MRI synthesis, a desirable synthetic MRI image \(sI_{MRI}\) is expected to respect relations between brain anatomical structures of the original MRI images \(I_{MRI}\). A possible method to generate such images is to condition a GAN on a particular class label to obtain results that meet the imposed condition [16]. The same mechanism may be applied to the problem of generating \(sI_{MRI}\) generation with intact anatomy is to use Binary Maps \(M_b\) of different tissues. A \(M_b\), in the context of 3D images, is a volume \(M_b \in \{0,1\}^{w \times h \times d}\), where the value of each voxel denotes affiliation to a single class (1 indicates class affiliation). In the case of brain synthesis, a GAN can be conditioned on three classes: WM, GM and CSF; where each class is represented as a \(M_b\). The limitation of such a class labelling method is the indivisible nature of voxel affiliation. In certain regions of an MRI, especially in the region around a tissue border, the voxel may not be of an adequate size. This limitation can be overcome by using PV-maps \(M_{pv}\) which, in the context of 3D images, is defined as a volume \(M_{pv} \in [0,1]^{w \times h \times d}\), where the value of each voxel represents the proportion of affiliation to a single class (1 indicates 100% class affiliation). The main advantage of \(M_{pv}\) is the ability to represent partial affiliation to a certain class, which allows tissue labelling with higher precision when compared to single-class voxels.

We hypothesise that conditioning a GAN with \(M_{pv}\) instead of \(M_b\) results with better \(sI_{MRI}\), especially at tissue interfaces. The hypothesis was evaluated by the experimental method presented in Fig. 1. The Fig. 1 shows the generation of \(M_{pv}\) from \(I_{MRI}\) by performing brain segmentation, implemented with the Expectation-maximisation (EM) algorithm [25], followed by PV-estimation implemented as in [1]. Three \(M_{pv}\) are derived from \(I_{MRI}\), one for each tissue-type (WM, GM and CSF). We binarise \(M_{pv}\) by assigning each voxel to the \(M_{pv}\) with the highest partial affiliation for a particular voxel and obtain the corresponding \(M_b\) for each class. Two models were trained, \(GAN_{pv}\) on \(M_{pv}\) and \(GAN_b\) on \(M_b\) and used to generate synthetic images, \(sI^{Gpv}_{MRI}\) and \(sI^{Gb}_{MRI}\) respectively. Once the \(sI_{MRI}\) were synthesised, the reverse process was performed, where \(sI^{Gpv}_{MRI}\) and \(sI^{Gb}_{MRI}\) were segmented followed by PV-estimation in order to obtain the synthetic \(M_{pv}\) \((sM_{pv})\). \(sM_{pv}\) derived from \(sI^{Gb}_{MRI}\) are denoted as \(sM^{Gb}_{pv}\), while
sMpv derived from sI MRI are denoted as sMpvGpv. We generated sMpv in order to evaluate to what extent are the imposed conditions preserved in sI MRI.

Model Architecture. The architecture of our model was inspired by Pix2Pix [9] and adapted to facilitate the needs of 3D MRI images. Pix2Pix is a conditional GAN capable of translating labels into images that follow a certain distribution, which makes it suitable for many image-to-image translation problems. The network is composed of a U-net-based generator [18] and a PatchGAN-based discriminator that compares image patches instead of whole images [9]. The modified architecture and its hyper-parameters are presented in Fig. 2.

We denote data of a certain distribution $d_x$ with $x$, generator with $G$, its output $G(c_{1-3}, z)$ and discriminator with $D$. Moreover, we denote three condition variables with $c_{1-3} (M_b$ or $M_{pv}$ for three tissue-types) and a noise variable with $z$. The objective function is defined as follows,

$$\min_G \max_D \mathbb{E}_{c_{1-3}, x} \left[ \log \left( D \left( c_{1-3}, x \right) \right) \right] + \mathbb{E}_{c_{1-3}, z} \left[ \log \left( 1 - D \left( c_{1-3}, G \left( c_{1-3}, z \right) \right) \right) \right] + \mathbb{E}_{c_{1-3}, x, z} \left[ \| x - G \left( c_{1-3}, z \right) \|_1 \right],$$

(1)

where $G$ has a goal to minimise the probability of $D$ performing a correct binary classification task, while $D$ aims to maximise the same. Referring to [9], we also added the L1 distance clause to the objective function as L1 tends to mitigate blurriness in the resulting images, which is needed for generation of images with accurate tissue borders. We also used the noise $z$ in the form of dropout (activated at training and inference) across a number of layers instead of providing it as an input.

Data. For the evaluation of our training method we used a subset of 3T scans (181x218x181 voxels) from the ADNI [10, 26] dataset. The subset contained 700 baseline subjects where only 3D T1-w volumes were used. Subjects were split into train and test sets. The train set included 500 subjects, while the 200 remaining subjects were used for the test set. All volumes were pre-processed by applying: (i) bias field correction in the brain region [24], (ii) rigid registration to the MNI-space and (iii) zero-mean normalisation with the mean value computed from the voxels in brain region of interest (ROI) only.

Training. We trained our models for 200 epochs. For the training of both models we used Adam optimiser, batch size of 1 and initial learning rate of 0.0002. After 100 epochs, we reduced the learning rate by $2 \times 10^{-6}$ every epoch.

3 Data used in the preparation of this article were obtained from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). The ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer’s disease (AD). For up-to-date information, see www.adni-info.org.
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3 Experiments

Our experiments were constructed to assess the benefit of using $M_{pv}$ over $M_b$ for the purpose of synthesising T1-w brain MRI volumes with accurate tissue-borders. Moreover, as a proof of concept for MRI synthesis, we assessed the reflection of fine changes, introduced on the $M_{pv}$, in $sI_{MRI}$ and $sM_{pv}$. In the

![Model architecture with supplementary hyper-parameter details.](image)

**Fig. 2.** Model architecture with supplementary hyper-parameter details.

**Fig. 3.** Qualitative results of our framework trained on $M_{pv}$. Presented results show that changes introduced in the $M_{pv}$ are reflected in the $sI_{MRI}$. The ground truth (a,f), two sets of $M_{pv}$ from the same subject as well as corresponding $sI_{MRI}$ (e,j) are presented respectively, where the region of DGM in the first case (b,c,d) is weakly defined, in comparison to the second case (g,h,i).
The following experiments we evaluated the quality of \( sI_{\text{MRI}} \) and \( sM_{\text{pv}} \) on the level of the brain volume, three tissue ROIs, tissue borders and the region of DGM.

**Image Synthesis Quality.** We evaluated our models by generating \( sI_{\text{MRI}} \) from both, \( M_b \) and \( M_{\text{pv}} \), and comparing them with the corresponding \( I_{\text{MRI}} \). Images were compared by employing the following metrics: Peak Signal-to-Noise Ratio (PSNR), Mean Absolute Error (MAE), Mean Squared Error (MSE) and Structural Similarity (SSIM) (see quantitative results in Table 1). PSNR, MSE and MAE were computed in the brain ROI. The dynamic range measured in the brain ROI of \( I_{\text{MRI}} \) spans between \([-0.56, 9.88]\), and was used to compute PSNR. SSIM was calculated on the whole volume, with background values set to zero as our generator generates brain \( sI_{\text{MRI}} \) without a background. Table 1 shows that \( GAN_{\text{pv}} \) produced \( sI_{\text{MRI}} \) more similar to \( I_{\text{MRI}} \) than \( GAN_b \).

**Evaluation at tissue level.** We took a closer look and evaluated the quality of \( sI_{\text{MRI}} \) as well as the corresponding \( sM_{\text{pv}} \) in the ROI for every tissue-class (WM, GM and CSF). The \( GAN \), segmentation and PV estimation may introduce errors in either \( sI_{\text{MRI}} \) or \( sM_{\text{pv}} \). Therefore, we computed MAE and MSE between \( I_{\text{MRI}} \) and \( sI_{\text{MRI}} \) in order to evaluate the error introduced by \( GAN \). We also used the Dice similarity metric (DSM) to evaluate the overlap with the ground truth and MAE as well as MSE to evaluate the error in \( sM_{\text{pv}} \) introduced by \( GAN \), segmentation and PV estimation. Quantitative results of the error metrics for each tissue type, calculated on \( sI_{\text{MRI}} \), are presented in Table 2. Quantitative measurements of shape and intensity error for each tissue-type computed on \( sM_{\text{pv}} \) are presented in Table 3. We concluded that less error was introduced in case of \( GAN_{\text{pv}} \), for all three tissues. Further, \( sM_{\text{pv}} \) are more similar to the ground truth in case of \( GAN_{\text{pv}} \) where smaller shape and intensity errors were introduced. According to Table 3, CSF has a lower DSM than WM and GM for both \( GANs \). The rational behind it is the nature of T1-w images where CSF is difficult to distinguish from the other non-brain tissues.

**Evaluation of multi-class voxels.** In this experiment, we quantitatively evaluated multi-class voxels, their position and intensity values. Quantitative evaluation was performed by computing DSM between \( M_{\text{pv}} \) and \( sM_{\text{pv}} \) for evaluation

Table 1. Metrics computed between \( I_{\text{MRI}} \) and \( sI_{\text{MRI}} \) created by \( GAN_b \) and \( GAN_{\text{pv}} \).

|       | PSNR     | MAE       | MSE       | SSIM       |
|-------|----------|-----------|-----------|------------|
| \( GAN_b \) | 32.777 ± 1.041 | 0.166 ± 0.024 | 0.054 ± 0.014 | 0.955 ± 0.01 |
| \( GAN_{\text{pv}} \) | 33.449 ± 1.103 | 0.144 ± 0.023 | 0.047 ± 0.013 | 0.96 ± 0.01 |

Table 2. Tissue-wise validation of \( sI_{\text{MRI}} \). MAE and MSE are computed between \( I_{\text{MRI}} \) and \( sI_{\text{MRI}} \) inside each tissue class.

|       | MAE       | MSE       |
|-------|-----------|-----------|
| WM    | 0.03 ± 0.003 | 0.009 ± 0.001 |
| GM    | 0.056 ± 0.006 | 0.016 ± 0.002 |
| CSF   | 0.046 ± 0.007 | 0.006 ± 0.001 |

|       | MAE       | MSE       |
|-------|-----------|-----------|
| WM    | 0.014 ± 0.003 | 0.003 ± 0.001 |
| GM    | 0.027 ± 0.004 | 0.006 ± 0.001 |
| CSF   | 0.032 ± 0.007 | 0.022 ± 0.007 |
Table 3. Tissue-wise shape validation of $sI_{MRI}$ and measurements of errors injected into $sI_{MRI}$ by a GAN segmentation and PV estimation.

|        | MAE |        |       | MAE |        |       |
|--------|-----|--------|-------|-----|--------|-------|
|        | WM  | GM    | CSF   | WM  | GM    | CSF   |
| GANb  | 0.959| 0.947 | 0.922 | 0.007| 0.007 | 0.007 |
| GANpv | 0.985| 0.981 | 0.954 | 0.035| 0.007 | 0.017 |

DSM measured in $sI_{MRI}$ generated from both GANs equals the value of one, which implies the location of multi-class voxels is fully preserved in $sM_{pv}$ for both GANs. We measured MAE of $0.134 \pm 0.017$ and MSE of $0.03 \pm 0.008$ in the multi-class voxels of $sI_{MRI}$. In the case of $sI_{MRI}^{pv}$, we measured MAE of $0.079 \pm 0.024$ and MSE of $0.01 \pm 0.007$. We also overlaid $I_{MRI}$ with absolute errors, computed voxel-wise, between $M_{pv}$ and $sM_{pv}$, to provide more information about the localisation and severity of the errors introduced by a GAN, segmentation and PV estimation (see Fig. 4). We found that most of the errors happen at tissue boundaries and observed errors of higher value in case of GANb. This result illustrates the benefit of using $M_{pv}$ over $M_b$ for the purpose of preserving well defined tissue borders in $sI_{MRI}$.

According to the presented quantitative results, we obtained 58.96% smaller MAE and 33.33% smaller MSE in multi-class voxels of $sI_{MRI}^{pv}$ comparing to $sI_{MRI}^{b}$. The presented results support the illustration of absolute errors and strongly suggest that tissue-borders are preserved with higher accurately in $sI_{MRI}$ generated by $GAN_{pv}$ opposed to $GAN_{b}$.

**Evaluation of Deep Gray Matter.** The region of DGM contains voxels that belong to WM, GM or to both classes. The border between WM and DGM is vaguely defined and hard to segment. Furthermore, in the context of MRI synthesis, a loosely defined or flawed border between WM and DGM makes it easy to distinguish between $I_{MRI}$ and $sI_{MRI}$. We evaluated the performance of both models in the region of DGM. Quantitative analysis was performed on $sI_{MRI}$ by computing MAE and MSE to measure the error injected by a GAN. In

![Fig. 4](image.png) Location and severity of errors injected into $M_{pv}$ by GAN, segmentation and PV estimation. Absolute errors between $M_{pv}$ and $sM_{pv}^{Gpv}$ as well as $M_{pv}$ and $sM_{pv}^{Gpv}$ are shown in (a) and (b), respectively.
the DGM region of $sI_{MRI}^{b}$ we measured MAE of $0.129 \pm 0.021$ and MSE of $0.029 \pm 0.01$. Yet, in the same ROI of $sI_{MRI}^{pv}$ we measured MAE of $0.108 \pm 0.024$ and MSE of $0.022 \pm 0.008$. This indicates that the DGM region is more accurately represented in $sI_{MRI}$ generated by the $GAN_{pv}$ when compared to $GAN_{b}$.

**Introduction of fine changes on PV-map level.** The outcomes of this experiment stand for a proof of concept that brain MRI synthesis may be controlled by changing $M_{pv}$, as the changes are reflected in the $sI_{MRI}$, while the model still preserves accurate tissue borders. To validate stability, we assessed the ability of the model to preserve fine changes (in this case seven voxels only) in $M_{pv}$ by verifying if the changes are reflected in $sI_{MRI}$. Both the changed and unchanged $M_{pv}$ were used to generate $sI_{MRI}$, which were further used to derive $sM_{pv}$. We obtained the introduced changes in $sI_{MRI}$ and $sM_{pv}$ as shown in Fig. 5.

4 Conclusion

In this work, we tackle the problem of synthesising 3D brain T1-w MRIs with accurate borders between tissues. This is an important feature in the context of medical image applications related to cortical thickness estimation and segmentation. We propose a framework that exploits PV-map properties and demonstrate that it performs better when it comes to synthetic MRI generation with accurate tissue borders compared to binary-map-based alternative. Moreover, we show that even fine changes introduced on PV-maps are reflected in synthetic images. This implies the possibility of using the framework as a data augmentation mechanism and it will be further explored in our future work.
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