Investigating the Performance of Generative Adversarial Networks for Prostate Tissue Detection and Segmentation

No names

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Abstract

The manual delineation of region of interest (RoI) in 3D MRI prostate image is time-consuming and subjective. Correct identification of prostate tissue is helpful in defining a precise RoI to be used in CAD systems in clinical practice during diagnostic imaging, radiotherapy and monitoring the progress of disease. Taking into account, along with the popularity of generative adversarial networks (GANs), we used conditional GAN (cGAN) and cycleGAN and studied their performances for the detection and segmentation of prostate tissue in 3D magnetic resonance images (MRI). In addition, we investigated the effect of using different augmentation schemes during the training process. We trained and evaluated these models on the MR Data from 40 patients with biopsy-proven prostate cancer. We concluded that the cGAN model was more appropriate as a robust detection and segmentation model owing to its paired image supervision.

Keywords: Prostate MRI, Computer Aided Diagnosis, Segmentation, Detection, Generative Adversarial Network (GAN)

1. Introduction

Prostate cancer is the most common type of cancer in men, annually with nearly 47,700 and 11,500 new cases worldwide and in the UK, respectively (Cancer-Research-UK, 2018). Prostate segmentation and accurately localising prostate tissue boundaries is a challenging task and a fundamental problem in medical image-based diagnosis due to (1) the lack of a clear edge between the prostate and the surrounding anatomical structures (e.g. urinary system), (2) heterogeneous background texture, (3) large size and shape variations of the prostate itself and (4) the tissue intensity distribution (Grall et al., 2019). Many automatic prostate segmentation methodologies have been developed in ultrasound, magnetic resonance and computed tomography images (Ghose et al., 2012) to reduce the possibility of subjectivity in delineating tissue boundaries. Among the deep learning-based methods for prostate segmentation, Zhu et al. (2017b) used a deeply-supervised convolutional neural network (CNN) to pass the features extracted from early layers to later layers. Yu et al. (2017) proposed residual connections into a volumetric CNN for 3D MR images. Guo et al. (2015) proposed a deformable prostate segmentation method to unify deep feature learning with sparse patch matching instead of hand-crafted features. Liao et al. (2013) used a different learning-base method, namely representation learning. In this method, they introduced a stacked independent subspace analysis (ISA) network to learn the effective features in a hierarchical and unsupervised way. Kohl et al. (2017) used a simple generative model where there is only one discriminator and one generator and Grall et al. (2019) adopted the conditional GAN architecture for prostate segmentation.
Computer Aided Diagnosis (CAD) systems have been used to assist doctors in the analysis of medical images. Generative Adversarial Networks (GANs) have shown success in generating different kinds of visual content and achieved state-of-the-art performances in many traditional and novel medical image applications such as medical image reconstruction, segmentation, detection, synthesis and classification (Xue et al., 2018; Lahiri et al., 2017; Grall et al., 2019; Kohl et al., 2017).

The goal of this research is to propose a pipeline to improve the detection and segmentation of prostate tissue boundaries on 3D MR images (on ADC, DWI and T2W modalities) in order to help identify subtle abnormalities within the prostate gland. This tool can be utilised as an alternative to double reading by clinicians, while reducing the time burden and increasing accuracy and patient outcomes. To develop this model, we propose three data augmentation schemes (super-pixel, noise addition and moving mean) and investigate and compare the robustness of U-Net (Ronneberger et al., 2015), cGAN (Isola et al., 2017) and cycleGAN (Zhu et al., 2017a) models using this augmented training data.

2. Methodology

The aim of this work was to develop a fully automatic segmentation system for detection and segmentation of prostate using cGAN and cycleGAN on different MR image modalities. In addition, we proposed three different data augmentation methods (super-pixel, Gaussian noise addition and moving mean approaches) and observed whether the performance improved. As far as we know, this work is the first use of cycleGAN model on the prostate MR analysis in terms of segmentation and detection.

2.1. Datasets

The MR Data from 40 patients with biopsy-proven prostate cancer was collected from a university hospital. This dataset includes ADC (Apparent Diffusion Coefficient), DWI (Diffusion Weighted Imaging) and T2W (T2-Weighted) MRIs for each case. All images were obtained with a 3 Tesla magnet GE Medical Systems, using a phased array pelvic coil, with a field of view equal to $100 \times 100 mm^2$, 6mm slice thickness, acquiring $512 \times 512$ images, while covering the whole prostate and seminal vesicles in both transverse and coronal planes. There were between 16 to 32 axial images for each case, in each modality in the dataset. All images were manually annotated by an expert radiologist to indicate the precise location of the prostate on a slice-by-slice basis. We divided the dataset into training and testing sets as 75% and 25% of the all database, guaranteed that there was no overlap between testing and training sets. For the training process, we generated different combinations of training samples by using augmented samples (covered in Section 2.2). This augmentation was done separately for each modality. To obtain objective results, the test set included only raw images. Examples of super-pixel, noisy and moving mean images are shown in Figure 1.

2.2. Augmentation Schemes

Super-pixel (SP) Approach A super-pixel is a group of pixels sharing similar visual features such as pixel intensity, location or texture. Super-pixel based methods reduce the risk of assigning pixels to the wrong labels and also reduce the computational cost due to
Figure 1: Examples of generated images for training. From top to bottom: raw image, super-pixel image, noise affected image and moving mean image.

its strong adhesion to the object’s boundary. It has been used in several computer vision applications (Ren and Malik, 2003; Zhang et al., 2019). (Tian et al., 2015) used a super-pixel based 3D graph cut algorithm to obtain the prostate surface. In their method, they considered super-pixels as the basic processing units to construct the graph, which was reported to provide an effective and robust segmentation of the prostate. Inspired by this approach, we propose to generate super-pixels to group similar pixels in prostate MR images and use them in the training dataset. We use the Simple Linear Iterative Clustering (SLIC) algorithm (Achanta et al., 2012) to cluster the relevant pixels in prostate MR images in the combined three-dimensional gray and image plane space and efficiently generate compact super-pixels. We define a super-pixel as an image patch that is better aligned with intensity edges. These super-pixels can produce highly irregular super-pixels on MR images, with widely varying sizes and shapes. Therefore, it is of critical importance to define a suitable number of clusters. The number of segments (clusters) is tested in the range [200] to [1500] and chosen to be 1200 per image. This value is selected based on the empirical evaluation in order to achieve a uniform number of segments.

Gaussian Noise Addition (GNA) Approach MR images are generally affected by Rician noise (He and Greenshields, 2008). For low signal intensities (SNR < 2), the noise follows a Rice distribution, while for larger signal intensities (SNR > 2) the noise distribution can be modeled as Gaussian distribution (Chen et al., 2016). Inspired by (Grall et al., 2019), Gaussian noise with ($\sigma = 0.5$) is added to images from all three modalities (ADC, T2W and DWI) and the resulting noisy images are used along with the raw training samples in the training step of model development.

Moving Mean (MM) Approach Moving average or moving mean (MM) is a common finite filtering method in image processing (Cadzow et al., 1993; Eom, 1999). Using this
approach, the raw image is divided into $5 \times 5$ non-overlapping grids and the average pixel value of each grid is calculated independently to create a series of averages of different subsets of the whole MR image. Then the average pixel value is assigned to all pixels of the specified grid. This procedure smooths the image and removes the sharp features in it.

### 2.3. The Deep Learning Frameworks

The first GAN architecture that was introduced by (Goodfellow et al., 2014) has a generator and a discriminator. The generator’s training objective is to produce realistic images from a latent space or random noise to the targeted data distribution. The images generated by the generator are evaluated by the discriminator and the aim of the discriminator is to classify whether the generated image is accepted or not. The generator tries to fool the discriminator while the discriminator tries to detect the generator’s falsely created images as much as possible. The key idea of GANs is to generate images that are indistinguishable from original images (desired output) using an adversarial loss. In this work, we use two recent extended versions of GAN called cGAN and cycleGAN. 3D Prostate tissue detection and segmentation using MRI scans is implemented as finding the prostate tissue on each 2D MR scan in terms of its semantic label map representing the desired tissue in the image.

#### Conditional GAN (cGAN) (Isola et al., 2017)

This model uses paired data during the training and is regarded as a supervised methodology. It learns a mapping from conditional image $x$ and $z$ to output $y$, which can be demonstrated as $G: x, z \rightarrow y$. The goal of the generator is to minimise the overall loss function by generating similar images to the target mask images, where the discriminator $D$ tries to classify the generator’s created images as truly generated or not and to maximize the defined loss function stated as:

$$G^* = \arg \min_G \max_D \mathcal{L}_{\text{cGAN}}(G, D) + \lambda \mathcal{L}_{L1}(G).$$

(1)

where $\mathcal{L}_{\text{cGAN}}$ can be expressed as:

$$\mathcal{L}_{\text{cGAN}}(G, D) = E_{x,y}[\log D(x,y)] + E_{x,z}[\log(1 - D(x,G(x,z))].$$

(2)

and the generator learns to produce output images similar to ground truth $(x)$ under the $L1$ condition:

$$\mathcal{L}_{L1}(G) = E_{x,y,z}[||y - G(x,z)||_1].$$

(3)

With regard to the network architecture, a U-Net based structure (Ronneberger et al., 2015; Isola et al., 2017) is used for the generator and a convolutional PatchGAN classifier (Isola et al., 2017) is used for the discriminator. The PatchGAN determines if $70 \times 70$ overlapping image patches are correctly generated.

#### CycleGAN (Zhu et al., 2017a)

This model aims to learn mapping between domains without using paired data. Its architecture consists of two mapping functions $G: X \rightarrow Y$ and $F: Y \rightarrow X$. The model aims to learn mapping functions between domains $X$ and $Y$ given training images $\{x_i\}_{i=1}^N$, where $x_i \in X$ and $\{y_j\}_{j=1}^M$, where $y_j \in Y$. The goal of the mapping function $G$ is to generate images $G(x)$ indistinguishable from images in domain $Y$ and minimise the loss function in Equation (4), where the discriminator $D_Y$ is trying to distinguish the generator’s generated images and maximise the overall loss.

$$\mathcal{L}_{\text{GAN}}(G, D_Y, X, Y) = E_{y \sim p_{\text{data}}(y)}[\log D_Y(y)] + E_{x \sim p_{\text{data}}(x)}[\log(1 - D_Y(G(x))].$$

(4)
There is also a similar adversarial loss function for the mapping function \( F : Y \rightarrow X \) and the discriminator \( D_X \):

\[
\min_F \max_{D_X} \mathcal{L}_{GAN}(F, D_X, Y, X)
\]  

(5)

The mapping functions need to be cycle-consistent. When we map each image \( x \) from domain \( X \) to domain \( Y \), it is brought back to the original image i.e. \( x \rightarrow G(x) \rightarrow F(G(x)) \approx x \), which is called forward cycle consistency. A similar idea holds for the generator \( F \) and every image in domain \( Y \), which is called backward cycle consistency i.e. \( y \rightarrow F(y) \rightarrow G(F(y)) \approx y \). These constitute cycle consistency loss as stated in Equation (6):

\[
\mathcal{L}_{cyc}(G, F) = E_{x \sim \mathcal{P}_{data}}(x)[||F(G(x)) - x||] + E_{y \sim \mathcal{P}_{data}}(y)[||G(F(y)) - y||].
\]

(6)

Therefore, the final loss function of the cycleGAN is:

\[
\mathcal{L}(G, F, D_X, D_Y) = \mathcal{L}_{GAN}(G, D_Y, X, Y) + \mathcal{L}_{GAN}(F, D_X, Y, X) + \lambda \mathcal{L}_{cyc}(G, F).
\]

(7)

where \( \lambda \) indicates the importance of cycle consistency loss. With regards to the network architecture, the ResNet architecture (He et al., 2016) with 6 blocks is used for the generator and the 70 \( \times \) 70 PatchGANs is used for discriminator.

3. Training and Post-processing

For each MR modality used in this study (DWI, T2W and ADC), raw images were combined with the augmented images (described in Section 2.2) to create different types of datasets. Using each created dataset, cycleGAN and cGAN models were trained. The detection and segmentation performance of each trained model for the prostate tissue was evaluated only on the raw test images. All networks were trained with 70 iterations for the batch size=1 as reported by Zhu et al. (2017a). We tried a variable range of learning rates for both models. We tested in the range [0.00001] to [0.001] and empirically found that the learning rate of 0.00004 and 0.0002 worked well for the cGAN and the cycleGAN, respectively. The other parameters were kept as default (Isola et al., 2017; Zhu et al., 2017a). All the network training was performed within the Torch framework using unpaired image-to-image translation software\(^1\) and pix2pix software\(^2\) with a NVIDIA GeForce GTX 1080 GPU on Intel Core i7-4790 Processor with an Ubuntu 16.04 operating system.

Based on our observations of the data, we understood that the prostate tissues were located in the images, away from borders. Therefore, in order to eliminate false positive predictions, we put a constraint in the post-processing step. So, detected segmentation masks which are close to the image boundary are removed and only the masks that are located between 1/4 and 3/4 of the height, and 1/4 and 3/4 of the width were maintained and the rest are discarded. Moreover, the top and bottom slices of the prostate are disregarded as they are always empty of targeted tissue. Finally, using connected component analysis, the largest object is extracted as the output.

\(^1\) [https://github.com/junyanz/CycleGAN](https://github.com/junyanz/CycleGAN)

\(^2\) [https://github.com/phillipi/pix2pix](https://github.com/phillipi/pix2pix)
4. Results and Discussion

We evaluated the detection and segmentation performances using common metrics (Litjens et al., 2014): (1) the Dice Similarity Coefficient (DSC), (2) the 95% Hausdorff distance (HD) and (3) F.Score for the 10 unseen images in the testing set. We evaluate the segmentation performances of U-Net, cGAN and cycleGAN models in terms of DSC and HD on the base-model (the model that was trained only on the raw images); while the detection performance of these models is reported in terms of F.Score and shown in Figure 2. Based on our evaluation metrics, we conclude that the best segmentation performance in all modalities is achieved by the cGAN model, followed by the U-Net model. This outperforming of the cGAN model can be justified by comparing its structure with the U-Net architecture. The generator of the cGAN model is built on a U-Net model architecture; while its performance is adjusted by an additional discriminator. Using the adversarial loss, the discriminator forces the generator to produce more robust and realistic output images in every iteration in contrast to the U-Net. On the other hand, comparing the performance of the U-Net and the cycleGAN model, we observe that the U-Net has better performance. Although the cycleGAN model has two discriminators, without the supervision of paired input-output data it was not able to learn robustly and segmentation performance got the lowest values for the evaluation metrics compared to the other two models.

Table 1 shows the quantitative results in terms of mean and standard deviation of the evaluation metrics for each created dataset (see Section 2.2) and each modality. Based on our quantitative results, for the ADC modality, the best results were obtained when the model was trained on the dataset combining raw and GNA images. Training the networks with the combination of SP, MM and raw images could also improve the learning performance for this modality compared to using only the raw data. However, the nature of raw and noisy images was slightly different and more adaptive for the ADC modality in both cGAN and cycleGAN models. This outcome was consistent among the three evaluation metrics.

In terms of the T2W modality, similar outcome was achieved with regards to the training samples used during learning procedure for the cGAN model. The combination of raw and GNA was the best in the cGAN model; while the combination of raw and SP obtained the best output results in the cycleGAN model. To justify this by investigating the T2W modality images, we observed that the images in this modality show parts of the body especially surrounding the structures of prostate more visibly than other modalities. Superpixelizing
Table 1: Quantitative results of the segmentation/detection for each modality using cGAN and cycleGAN models.

<table>
<thead>
<tr>
<th>Modality</th>
<th>Training Dataset</th>
<th>cGAN Model</th>
<th>cycleGAN Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DSC</td>
<td>$HD_{95}$</td>
</tr>
<tr>
<td>ADC</td>
<td>Raw</td>
<td>0.665 ± 0.187</td>
<td>12.327 ± 6.393</td>
</tr>
<tr>
<td></td>
<td>Raw + GNA</td>
<td>0.732 ± 0.153</td>
<td>11.550 ± 5.437</td>
</tr>
<tr>
<td></td>
<td>Raw + SP</td>
<td>0.716 ± 0.184</td>
<td>12.796 ± 8.117</td>
</tr>
<tr>
<td></td>
<td>Raw + MM</td>
<td>0.703 ± 0.199</td>
<td>12.105 ± 5.401</td>
</tr>
<tr>
<td></td>
<td>Raw + SP + MM + GNA</td>
<td>0.641 ± 0.232</td>
<td>12.633 ± 5.510</td>
</tr>
<tr>
<td>T2W</td>
<td>Raw</td>
<td>0.668 ± 0.160</td>
<td>11.819 ± 7.036</td>
</tr>
<tr>
<td></td>
<td>Raw + GNA</td>
<td>0.729 ± 0.144</td>
<td>11.200 ± 5.293</td>
</tr>
<tr>
<td></td>
<td>Raw + SP</td>
<td>0.698 ± 0.132</td>
<td>12.160 ± 7.881</td>
</tr>
<tr>
<td></td>
<td>Raw + MM</td>
<td>0.685 ± 0.201</td>
<td>11.281 ± 5.504</td>
</tr>
<tr>
<td></td>
<td>Raw + SP + MM + GNA</td>
<td>0.626 ± 0.101</td>
<td>14.545 ± 8.801</td>
</tr>
<tr>
<td>DWI</td>
<td>Raw</td>
<td>0.744 ± 0.254</td>
<td>9.821 ± 9.895</td>
</tr>
<tr>
<td></td>
<td>Raw + GNA</td>
<td>0.787 ± 0.146</td>
<td>11.744 ± 5.223</td>
</tr>
<tr>
<td></td>
<td>Raw + SP</td>
<td>0.765 ± 0.129</td>
<td>11.789 ± 8.271</td>
</tr>
<tr>
<td></td>
<td>Raw + MM</td>
<td>0.795 ± 0.173</td>
<td>9.738 ± 9.745</td>
</tr>
<tr>
<td></td>
<td>Raw + SP + MM + GNA</td>
<td>0.766 ± 0.171</td>
<td>11.933 ± 4.032</td>
</tr>
</tbody>
</table>

The T2W images group the pixels better and makes the surrounding parts more visible for the cycleGAN network. In addition, in cycleGAN model there are two different domains and there is no paired input-output relation between them. The generators are penalized by the adversarial loss with the cycle consistency loss, which forces the generators to not only do the segmentation but also synthesize the original MR image from the created mask back again. As a result, the network learns a mapping between the training images and their masks and vice versa. Therefore, by the SP approach, the learning is more optimised. Comparing the results of the raw plus SP images on the three modalities in cycleGAN model, we realised that training using the T2W modality images got the best results (with DSC values of 0.651) while the DSC outcomes for DWI and ADC modalities were 0.622 and 0.630, respectively.

For the DWI modality, the best results for the cGAN and cycleGAN models were achieved by using the raw plus MM images as the training set. The MM approach removes the unnecessary details of an image helping the network to focus on prostate tissue as the target part of the image during the training process. It shows consistent results with regards to the three evaluation metrics.

According to our quantitative results, combining the SP, GNA and MM images individually with the raw images could increase the segmentation accuracy for both cGAN and cycleGAN models. However, combining the samples all together, we concluded that not necessarily the number of training images affects the learning performance but discriminative samples are more important and these discriminative samples in each modality can be generated differently based on the nature of the images and their contents. So with the combination of all samples, the learning does not become robust for unseen cases but also starts to memorize the training data, which is known as over-fitting (Lawrence and Giles, 2000).

For the detection performances, based on the numerical values provided in Table 1, the best results for the ADC, T2W and DWI modalities were obtained using the raw plus GNA
images in the training with the cGAN model, achieving the F.Score of 0.70, 0.77 and 0.73, respectively.

Comparing the cGAN and cycleGAN models, based on our results, we conclude that the cGAN model achieve better results than the cycleGAN model. Unlike the cycleGAN model, the cGAN has paired input-output images and both the generator and discriminator could see the ground-truth data; while the cycleGAN model learns to transfer images from one domain to another with lack of the supervision of paired images.

Table 2 compares the evaluation results of different prostate tissue segmentation methods, developed based on the recent deep learning approaches. Among various deep learning approaches, the aim of this work was to investigate the performance of generative adversarial networks for prostate tissue detection and segmentation on 2D MR images. Our model achieved better results than (Kohl et al., 2017) which used a simple generative model with one generator and one discriminator. Unlike (Grall et al., 2019), we used Gaussian noise with \( \sigma = 0.5 \) on T2 weighted prostate images and achieved comparable state-of-the-art results.

5. Conclusion

In recent years, generative adversarial networks have received significant attention from machine learning and computer vision communities because of their ability to generate highly realistic images with the adversarial loss created by the discriminator. This has been also used in many medical imaging problems such as classification, image reconstruction, synthesis, detection or segmentation. In this paper, our contribution was to detect and correctly segment prostate tissue in different MR modality scans using cGAN and cycleGAN models. We observed the robustness and generalization performances of such simple but effective GAN models in detection and segmentation tasks by using various data-augmentation methods including Super-pixel, Gaussian Noise Addition and Moving Mean approaches. The proposed segmentation methods can be useful in medical imaging of prostate since prostate-based diseases are becoming more common and more efforts are put into understanding this.

References

Radhakrishna Achanta, Appu Shaji, Kevin Smith, Aurelien Lucchi, Pascal Fua, and Sabine S"usstrunk. Slic superpixels compared to state-of-the-art superpixel methods. IEEE Trans-

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Table 2: The state-of-the-art prostate segmentation approaches for the MRI-T2W modality.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Deep learning base methodology</th>
<th>Dataset</th>
<th>HD</th>
<th>DSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhu et al. (2017b)</td>
<td>deeply-supervised CNN</td>
<td>National Cancer Institute, NIH, USA</td>
<td>5.41</td>
<td>0.864</td>
</tr>
<tr>
<td>Yu et al. (2017)</td>
<td>Volumetric ConvNets</td>
<td>MICCAI PROMISE12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Guo et al. (2015)</td>
<td>deep feature learning &amp; sparse patch matching</td>
<td>University of Chicago Hospital</td>
<td>7.43±2.82</td>
<td>87.8±4.0</td>
</tr>
<tr>
<td>Liao et al. (2013)</td>
<td>stacked independent subspace analysis network</td>
<td>University of Chicago Hospital</td>
<td>8.2±2.5</td>
<td>86.7±2.2</td>
</tr>
<tr>
<td>Kohl et al. (2017)</td>
<td>a simple generative model</td>
<td>National Center for Tumor Diseases, Germany</td>
<td>-</td>
<td>0.41±0.28</td>
</tr>
<tr>
<td>Grall et al. (2019)</td>
<td>conditional generative adversarial model</td>
<td>Norfolk &amp; Norwich University Hospital</td>
<td>9.59±4.37</td>
<td>0.73±0.16</td>
</tr>
<tr>
<td>U-Net model used in this work</td>
<td>U-Net model</td>
<td>our private dataset (Section 2.1)</td>
<td>12.10±5.17</td>
<td>0.65±0.10</td>
</tr>
<tr>
<td>cycleGAN model used in this work</td>
<td>conditional GAN model</td>
<td>our private dataset (Section 2.1)</td>
<td>12.61±5.80</td>
<td>0.65±0.16</td>
</tr>
<tr>
<td>U-Net model used in this work</td>
<td>paired img-to-image translation(cycleGAN)</td>
<td>our private dataset (Section 2.1)</td>
<td>11.28±5.23</td>
<td>0.72±0.14</td>
</tr>
</tbody>
</table>

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