Synthesis of Gadolinium-enhanced MRI for Multiple Sclerosis patients using Generative Adversarial Network

Sumana Basu SUMANA.BASU@MAIL.MCGILL.CA
School of Computer Science
McGill University
260727568

Abstract

Multile Sclerosis is detected by MRI using contrast agent Gadolinium (GAD). But this chemical agent has side effects on patients and many people are allergic to it. As a broader goal of this project, we aim to use Generative Adversarial Network to generate multiple possible gadolinium enhancements for the same patient. This will associate a measure of uncertainty to GAD activity. Actual GAD MRI would then only be used on patients with high level of uncertainty. As a first step towards this goal, in this project we have tried to generate 64 x 64 MRI images from low-resolution MRI images of same size.

1. Introduction & Problem Description

Multiple Sclerosis (MS) is a progressive autoimmune disease of the Central Nervous System. Immune System defends our body from foreign objects like virus and bacteria. Autoimmune diseases are developed when immune system considers healthy tissue as foreign and fights them back. Affected cells differ based on the disease. For Multiple Sclerosis, affected tissue is myelin sheath of nerve. Due to damage of the sheath transmission of nerve impulses get disrupted (Compston).

Cause of MS is still unknown, and the disease currently has no cure. Moreover, there is no single test to diagnose MS. But the revised guidelines of MS detection recommend using MRI with gadolinium enhancement to diagnose and track disease progression (A. Traboulsee and Li). Unfortunately, according to recent studies, contrast agents containing Gadolinium have side effects ranging from nausea and urticaria to cardiovascular collapse and seizure(Hunt CH). Hence, the use of such agents should be avoided.

We plan to propose to use machine learning methods in order to generate GAD enhanced images out of ordinary MRIs in order to detect and track the progression of MS without using gadolinium enhancement on patients. This project is a first step towards that goal. Here, we generated 64 x 64 brain MRI images from down-sampled images of contrast enhanced MRI. Generative Adversarial Networks (GAN) (Goodfellow et al. (2014)) have emerged as a very useful tool for generating complex data such as images or text. For this project, we have access to 2759 pairs of regular MRI and GAD-enhanced MRIs for MS patients, which we will use to train GAN models. Evaluation is performed quantitatively by monitoring scores of generator and discriminator network and qualitatively by visual appearance of generated images.

2. Data Description

We conducted our experiments on MRI images of MS-LAQ dataset received from NeuroRx. MS-LAQ has MRI for different modalities such as T1, T2, flair. For each modality, pre-contrast, post-contrast images and masks corresponding to lesions are available. For this project we have restricted ourselves to contrast enhanced images of T1 modality. Available images are data cubes of 256 x 256 x 60 dimension. The 2D image changes, with each depth dimension. However, for the sake of simplicity we have only considered 2D MRI image corresponding to depth 125. We further down-sampled the 2D MRI to 64 x 64 images. We only considered T1C images having a corresponding GAD mask. There were 2759 such images. It is noteworthy that not all the GAD masks have lesion labels. Some of the masks are all zeros indicating that patient is not affected by MS. Sample images from the input dataset is shown in figure 1.

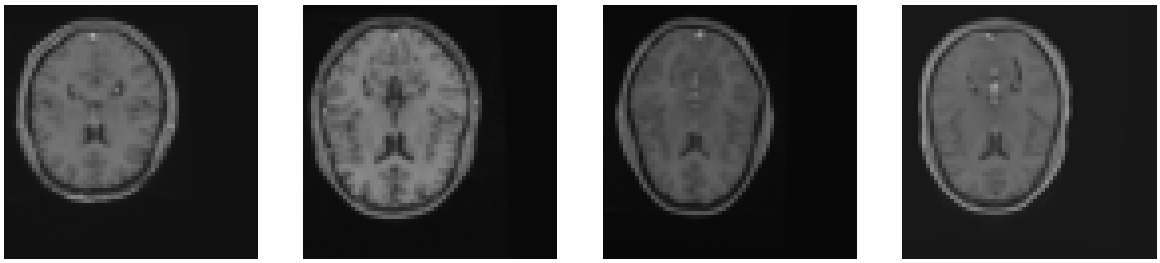


Figure 1: Images from Dataset (Single Layer 2D image, resized to 64 x 64)

3. Background

Generative Adversarial Network(GAN)(Goodfellow et al. (2014)) is a concept introduced by Ian Goodfellow et al. in 2014 and has extensively been used since then on various application. Deep Convolutional Generative Adversarial Network (DCGAN)(Radford et al.) has successfully been applied to different datasets like MNIST, CIFAR10, LSUN etc. But it is not known to be applied on MRI images. We selected GAN for our experiment since of all the available generative models, GANs are known to perform best.

GAN is a minimax game between generator and discriminator which are trained as adversaries. The generative network is taught to map from a latent space to a data distribution of interest, and the discriminator network is simultaneously taught to discriminate between instances from the true data distribution and synthetic instances produced by the generator. Loss for both generator ($G(z)$) and discriminator ($D(x)$) function is given by Equation 1 and equilibrium is a saddle point of the discriminator loss.

$$\begin{aligned} J^{(D)} &= -\frac{1}{2}\mathbb{E}_{x\sim p_data}\log D(x) - \frac{1}{2}\mathbb{E}_z \log(1 - D(G(z))) \\ J^{(G)} &= -J^{(D)} \end{aligned} \tag{1}$$

4. Training

The discriminator and generator have been trained in parallel with learning rates of 0.00005 and 0.0001. Also for each training of generator, discriminator has been trained 5 times to ensure that the generator does not learn to fool discriminator with sub-optimal images. Apart from down-sampling the images, no pre-processing has been done on them. But to ensure faster training, all the images have been normalized prior to training the discriminator. Model is trained with mini-batch stochastic gradient descent with mini batch size of 64. We initialized our biases as 0 and weights as per normalized initialization (Xavier Glorot (2016)):

$$W \sim U\left[-\frac{\sqrt{6}}{\sqrt{n_{in}+n_{out}}}, \frac{\sqrt{6}}{\sqrt{n_{in}+n_{out}}}\right] \tag{2}$$

where $U[-a, a]$ is the uniform distribution in the interval $(-a, a)$ and n_{in} and n_{out} are the size of the input and output layer respectively.

As suggested in DCGAN paper (Radford et al.), convolutions (discriminator) and fractionally strided convolutions (generators) are used instead of pooling layers. ReLU (Nair and Hinton (2010)) activation function has been chosen for all layers of both discriminator and generator. We have used Rmsprop optimizer for faster convergence.
Input to the generator is a 64 bit vector of Gaussian noise and 8 x 8 filters have been chosen for each of the convolution and transpose convolution steps.

5. Results

We trained DCGAN for 50 epochs on 2759 contrast enhanced MRI images of 64 x 64 dimension captured using T1 modality. We calculated score as described in Wasserstein GAN (Arjovsky). As depicted in Fig 2, both generator and discriminator score increases upto epoch 30, beyond which they converge. Fig 3 shows generated images over epochs. Generated images don't make any noticeable progress beyond epoch 20, though generator score constantly increases during this period.
We generated 16 images per epoch. Though the generated images are still of poor quality as compared to actual images, they are considerably consistent and don't generate noise. Tuning the hyper parameters further is expected to improve the results.

6. Discussion

The generator is learning the shape of brain, but it is yet to learn the details of it even though score converges. Poor resolution input data might be responsible for this. Sub-optimal learning rate was assumed to be a factor. To verify that we tried a learning rate of 0.0001 for both the generator and discriminator, but that did not improve the results.

Right hand part of the image consistently constitutes as a section of the dark background. This does not add any value towards feature learning. Instead it increases the overall mean and standard deviation of the image, making the normalized values of central

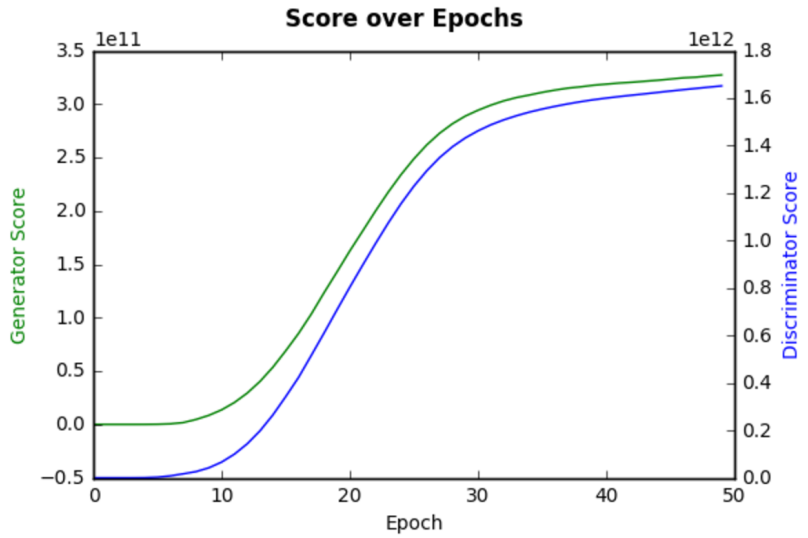
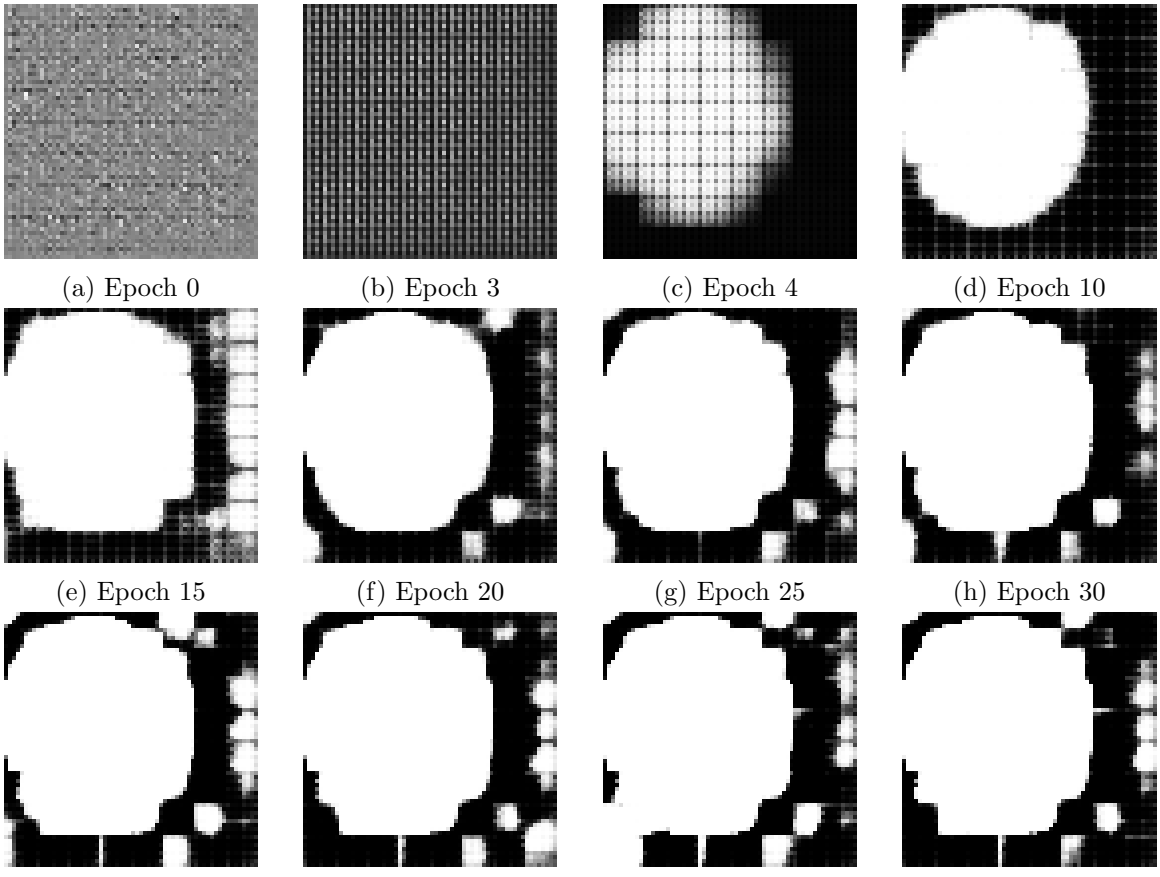


Figure 2: Generator and Discriminator Score



(a) Epoch 0 (b) Epoch 3 (c) Epoch 4 (d) Epoch 10

(e) Epoch 15 (f) Epoch 20 (g) Epoch 25 (h) Epoch 30

(i) Epoch 35 (j) Epoch 40 (k) Epoch 45 (l) Epoch 49

Figure 3: Evolution of Generated Images over Epochs

part of brain so small that the generator fails to learn it. Since it is not part of the original normalized image, discriminator erroneously recognizes only the contours of brain as real brain images. Getting rid of this section of background might be beneficial for learning features of actual brain.

7. Future Work

Though this experiment synthesizes sub-optimal images, it proves that GAN can be applied to small sized datasets of MRI images. Till date the model has successfully been applied to only large scale datasets. So the fact that it is learning features of MRI from relatively smaller dataset is promising. As a next step, we plan to extract patches of 64 x 64 x 60 containing GAD lesions from the original MRI. We will get rid of the dark background and also will be able to feed the networks with images of higher resolution enhancing the scope to learn detailed features.

If GAD enhancements could be generated for MRIs, the clinical procedure would not need to be used anymore on all patients. Instead, the GAN model could be used to generate multiple possible enhancement for the same patient, which would result in a measure of uncertainty of GAD activity. Actual GAD MRI would then only be used on patients with high level of uncertainty. This would put patients at lower risk of adverse effects and minimize health care costs without compromising quality. We could also get multiple and more frequent data on patient evolution, which may open avenues to select patient to test new drugs and therapies without putting them in a perpetual loop of MRI.

8. Acknowledgement

For this project, I have used DCGAN code written by Emmanuel Bengio of McGill Reasoning and Learning Lab. I would like to thank him not only for the code, but more for his constant support and mentorship during and beyond the course of this project.
I would also like to thank NeuroRx for sharing their internal MRI data with us.

References

L. Stone E. Fisher D.E. Jones A. Malhotra S.D. Newsome J. Oh D.S. Reich N. Richert K. Rammohan O. Khan E.-W. Radue C. Ford J. Halper A. Traboulsee, J.H. Simon and D. Li. Revised recommendations of the consortium of ms centers task force for a standardized mri protocol and clinical guidelines for the diagnosis and follow-up of multiple sclerosis.

Soumith; Bottou Lon Arjovsky, Martin; Chintala. Wasserstein gan.

Alastair et al. Compston. Multiple sclerosis.

I.J. Goodfellow, J. Pouget-Abadie, M. Mirza, B. Xu, D. Warde-Farley, S. Ozair, A. Courville, and Y. Bengio. Generative adversarial networks. In *ArXiv e-prints*, 2014.

Hesley GK. Hunt CH, Hartman RP. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses.

Vinod Nair and Geoffrey E Hinton. Rectified linear units improve restricted boltzmann machines. page 807814, 2010.

Alec Radford, Luke Metz, and Soumith Chintala. Unsupervised representation learning with deep convolutional generative adversarial networks. volume abs/1511.06434.

Yoshua Bengio Xavier Glorot. Understanding the difficulty of training deep feedforward neural networks. In *AISTATS 2010*, pages 249–256, 2016.