Using temporal GAN to translate the current CTP scan to follow-up MRI, for predicting final acute ischemic stroke lesions

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Abstract:

Over 795,000 Americans suffer a stroke every year, leading to a death every 3.5 minutes. Approximately 87% of all strokes are Acute Ischemic Strokes (AIS), i.e., an abrupt interruption in cerebral circulation due to a blocked artery. Early prediction of AIS final outcomes (AIS lesions) is crucial to effective treatment planning for AIS patients. Due to its speed, availability, and lack of contraindications, Computed Tomography Perfusion (CTP) is preferred over other imaging modalities with higher resolution (e.g., MRI), for AIS lesion prediction. However, the low contrast of baseline CTP images makes it difficult to determine AIS lesions precisely, while follow-up MRI images do. Therefore, this paper proposes a method of synthesizing follow-up MRI images from baseline CTP scans by a Temporal Generative Adversarial Network (TGAN) — which encodes baseline CTP frames with a series of encoders, followed by a decoder that forecasts the high-resolution follow-up MRIs. It also uses a discriminator that competes with the generator to identify whether its input MRI is real or fake. Furthermore, our TGAN includes a segmentor that can identify AIS lesions in those synthesized MRI images. The generator, discriminator, and segmentor in TGAN each use MultiRes U-Nets, an extension of the original U-Net architecture, which can robustly segment objects of various scales and shapes. Our experiments with Leave-One-person-Out Cross-Validation (LOOCV) obtained an average dice coefficient of 56.73%, with a significant $p<0.05$. In comparison to traditional methods using CTP perfusion parameters, we found that our novel method was more accurate in predicting AIS lesions.

Summary:

Recently, GAN models have been successfully applied to image-to-image synthesis and translation. Our study confirms that the temporal GAN model can effectively be used to translate the baseline CTP scan to the follow-up MRI, for predicting final acute ischemic stroke lesions. This model shows that using MultiRes U-Net we can extract multi-resolution features and temporarily correlate them to produce the follow-up MRI. By using the high-resolution produced MRI images we could predict the follow-up ischemic stroke lesion. In addition, our proposed model could eliminate some manual error-prone steps in ischemic stroke prediction resulting in a more accurate and quick stroke assessment.

Description of purpose:

An Acute Ischemic Stroke (AIS), accounting for almost 87% of all strokes, is a sudden interruption of cerebral circulation due to a blocked artery in the brain [1]. More than 6.2 million people die each year from AIS, which is more than the deaths from AIDS, tuberculosis, and malaria [2]. The treatment of AIS is a very time-sensitive task since failure to restore blood flow can lead to irreversible brain damage [3]. Predicting final AIS outcomes (AIS lesions) using baseline images is a crucial step leading to the most effective AIS treatment decision [4]. Due to its speed, availability, and lack of contraindications, Computed Tomography Perfusion (CTP) is preferred over other higher resolution imaging techniques, such as MRI, for AIS assessment. CTP involves injecting a contrast bolus into the bloodstream of a patient and taking a CT scan every second as the bolus passes through their arteries.

AIS lesion prediction is a challenge because of four main reasons: (1) we are only given baseline information; (2) CTP images do not show much difference between the appearance of the lesion and the rest of the brain tissues; (3) AIS lesions have heterogeneous sizes, shapes, and loci, and (4) there is a limited number of brain images that are labeled (actual AIS lesions). Current standard approaches to predict AIS lesions rely on thresholding CTP parameter maps — i.e., predefined perfusion parameters extracted from CTP time series to quantify brain cerebral circulation [5]. This simple thresholding method, however, might lead to poor treatment decisions because it does not accurately predict AIS lesion volumes. magnetic resonance imaging (MRI) images are much more sensitive to AIS lesions than CTP scans, according to clinical experiences. In addition, the MRI images at follow-up time clearly show the AIS lesions. Hence, in this paper, we propose to use an end-to-end AIS lesion predictor named TGAN that consists of a Temporal image-to-image translator which uses a Generative Adversarial Network (GAN) to generate follow-up MRI images and a segmentor to identify AIS lesions.

Method:

Our proposed AIS prediction method, consists of three main sections, preprocessing, temporal image translation, and AIS lesion segmentation. First, we used some common techniques to augment our image dataset in order to prevent overfitting and improve the model's ability to generalize to unseen images. To

augment the training images dataset, the images were rotated to an angle that was randomly chosen from a normal distribution of N(≺0, ≺20). Then a Gaussian noise N(0, 0.03) was added to the already normalized (zero mean and unit std) original images. Both the normal distribution and Gaussian noise parameters were determined empirically.

The next step is baseline CTP to follow-up MRI image translation. As with the original GAN structure, our proposed image translator consists of two main sections, a generator, and a discriminator. As Figure 1 shows, the generator section consists of 10 encoders to encode 10 selected frames of the CTP image time series and one decoder to generate their corresponding follow-up MRI image. Our methodology reduces unnecessary computations and avoids the inefficient large size of neural networks by just using 10 frames of CTP images rather than the entire sequences, which typically contain 40 to 60 frames. According to Figure 1, we found the frame with the highest contrast agent volume out of a sequence of CTP images. We then select three and four frames before and after the selected frame, respectively. We also added the first and last frames that do not contain any contrast agents. The purpose of including these two images is to provide some information on the structure of brain tissue without highlighting blood flow or arteries.

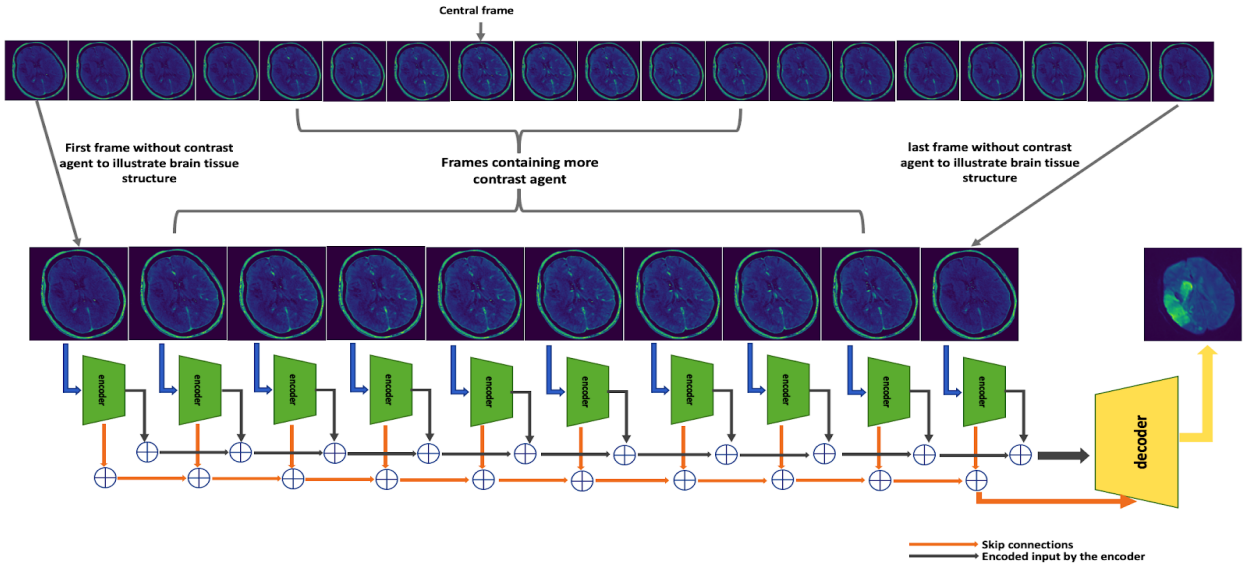


Figure 1. 10 frames selection for the temporal generator

Figure 2 shows that both encoders and decoders of the generator are based on an extension of the original U-Net architecture, called MultiRes U-Net [9]. In this modified U-Net, figure 3(a), the original CNN layers are replaced with MultiRes layers to be robust in detecting objects of various scales and irregular shapes [10][9].

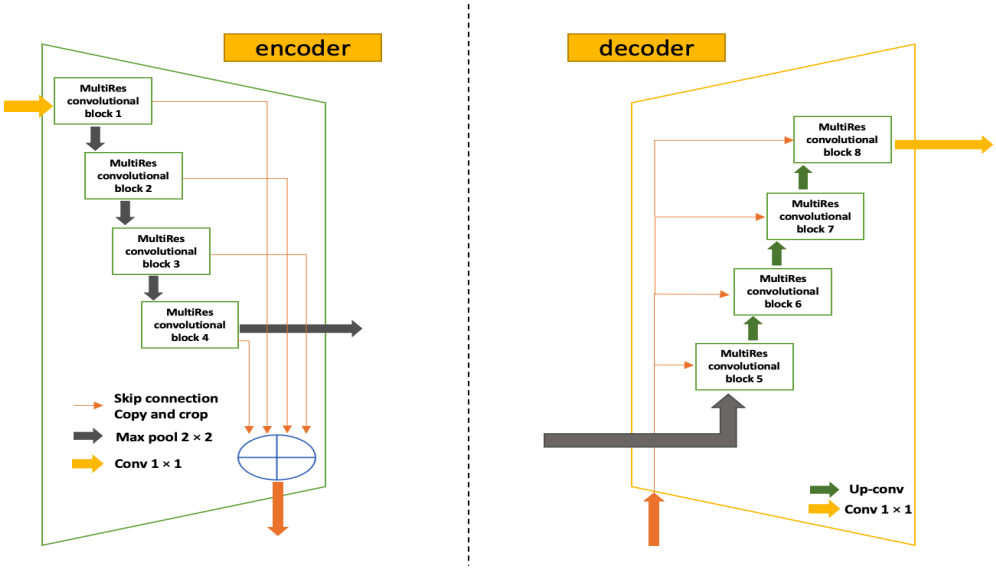
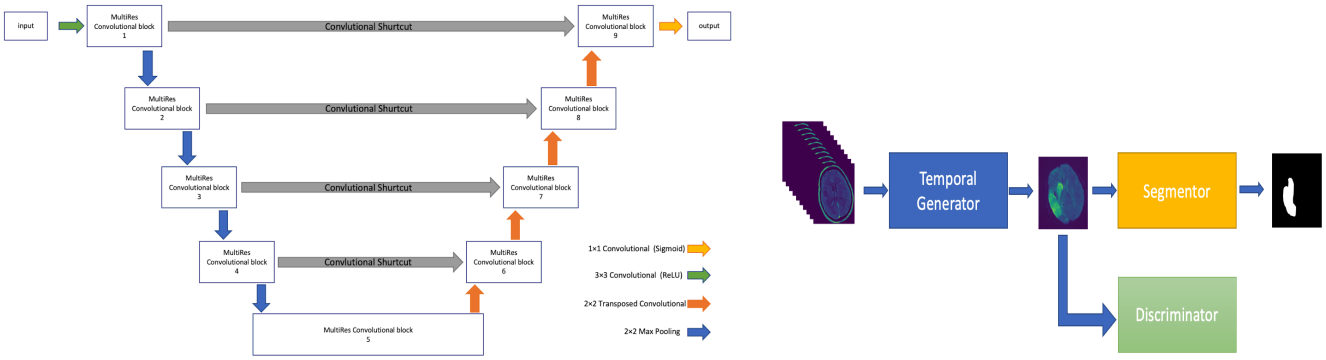


Figure 2. MultiRes encoder and decoder

In contrast to original CNN layers, which have only one unique kernel size, MultiRes layers have three kernels sizes allowing them to extract features at different scales and resolutions. In addition, in MultiRes U-Net the simple skip connections are replaced by CNN shortcuts from the encoder to the decoder. With CNN shortcuts in MultiRes, U-Net was able to overcome one of its weaknesses, which was combining features from different levels that might cause a semantic gap between them leading to no convergence in the training process.



(a) (b)

Figure 3. (a) MultiRes U-Net architecture; (b) the TGAN AIS lesion predictor pipeline.

Figure 3(b) shows the proposed segmentor model's complete pipeline. The TGAN consists of a generator constructed from a series of encoders to encode CTP frames and one decoder that can synthesize their corresponding high-resolution follow-up MRI. As one can see, we trained a TGAN that learns to translate a sequence of 2D CTP

frames to their corresponding follow-up MRI. The discriminator in the TGAN is also a MultiRes U-Net. Then we also used MultiRes U-Net as a segmentor that identifies AIS lesions by using the generated follow-up MRI.

Results:

To evaluate our proposed AIS lesion predictor we have used our local dataset including 55 patients. We had to exclude 12 patients because they did not have follow-up scans or had CT scans as the follow-up image. In our experiments, an average dice coefficient of 57.73%, with a significant $p<0.05$, is achieved with Leave-one-person-out cross-validation (LOOCV). Figure 4 shows some randomly selected images. The first row shows the CTP images, and the second and third rows show the generated and actual MRI images, respectively. On the generated MRI images, the red line indicates the predicted lesion by our model, and on the actual MRI, the red line indicates the actual lesions. Moreover, table 1 shows a comparison between our proposed method and some previous methods for predicting AIS lesions. They were selected for comparison due to their similarity in approach because they also used generated MRI rather than baseline CTP to predict AIS lesions. According to Table 1, our proposed TGAN can improve the accuracy of AIS lesion prediction by synthesizing MRI data more efficiently.

Table 1. Evaluation results were obtained by using our proposed method and some previously proposed ones.

Model	Dice Score (%)	Jaccard (%)	Precision (%)	Recall (%)
C²MA-Net [6]	53.35 ±19	54.81 ±16	49.18 ±13	**57.61 ± 15**
Pengbo Liu [7]	49.14 ±23	50.87 ±12	48.19 ±21	51.88 ±20
Mobarakol Islam et al. [8]	54.05 ± 22	**55.73 ± 17**	50.73 ± 18	54.42 ± 21
TGAN (original U-Net)	51.35 ±21	50.59 ±21	47.14 ±13	53.16 ±23
TGAN (MultiRes U-Net)	**56.73 ± 17**	52.94± 16	**53.38 ± 20**	51.91 ±24

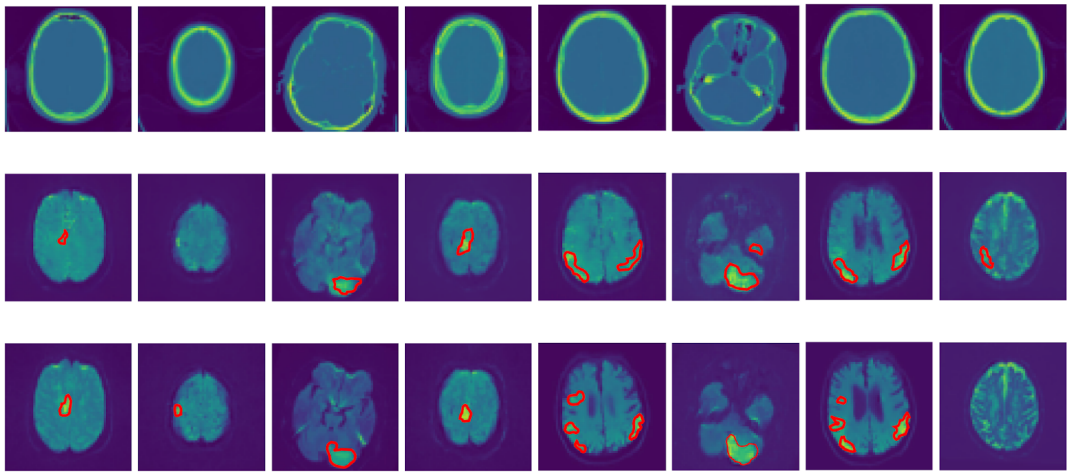


Figure 4. CTP images are shown in the first row and generated and actual MRI images are shown in the second and third rows. In the second and third rows, the red lines are predicted and actual AIS lesions, respectively.

Conclusions:

This paper presents TGAN, a novel prediction model for AIS lesions using 4D CTP time series. TGAN used MultiRes U-Net to translate baseline CTP images into high-resolution follow-up MRI images, then to predict AIS lesions from the generated MRI images. Instead of using pre-defined CTP maps that have already lost much information and are error-prone, our TGAN can utilize the temporal information of the CTP time series to predict follow-up MRI images as well as predict AIS lesions. Additionally, by applying MultiRes U-Net, the lesions can be identified from various shapes and scales. Our TGAN achieves superior performance to other state-of-the-art AIS lesion predictors by using our local dataset of 55 patients. We anticipate that the TGAN prediction model will have strong practical applications in different time series analyses — such as temporal modeling of localized brain activity.

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