Automated segmentation and classification of the atherosclerotic carotid plaque in ultrasound videos

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***Abstract*— The automated and reliable delineation of atherosclerotic carotid plaques in ultrasound (CUS) videos is of significant clinical relevance for management of the disease and the prediction of future stroke events. To facilitate stroke risk assessment, in this study, we propose an integrated software system for the automated segmentation and classification of atherosclerotic carotid plaques in longitudinal CUS videos, which was evaluated using 10 CUS videos, from 10 patients (5 Asymptomatic, AS, and 5 Symptomatic, SY). The proposed methodology involves the following steps: a) CUS video frame (VF) resolution and intensity normalization, b) speckle reduction filtering, c) Motion-mode state-based cardiac cycle (CC) identification, d) deep learning (DL)-based plaque segmentation, e) extraction and selection of plaque region of interest (ROI)-specific textural features, and f) machine learning (ML)-based plaque classification. Initially, one CC (cardiac diastole-systole-diastole) was selected per CUS video, and the CC's consecutive VFs were identified and reduced in number to exclude redundant VFs. All standardized VFs per patient were extracted, cropped and resized to mainly accommodate the ROI and were fed into a priorly trained and evaluated 2-dimensional DL plaque segmentation model. For each VF, the DL-based segmented plaque ROI was projected onto its primary resolution-normalized VF counterpart, from which textural and amplitude modulation-frequency modulation (AM-FM) plaque ROI features were extracted. Statistical analysis on the total AS and SY VFs was used for feature selection. We identified 2 plaque-originating AM-FM features, which exhibited statistically significant differences between the AS and SY standardized VFs ($p<0.05$), followed by 3 textural features ($p<0.05$). To finalize our system, in a future study, the strong AM-FM AS/SY descriptors, identified here, will be evaluated alone or in combinations with other plaque-descriptive features, in machine learning (ML)-based plaque classification, using a larger CUS video sample.**

Keywords*— *Carotid Video Ultrasound; Plaque; Deep learning; Segmentation; Instantaneous Phase; Classification.

I. INTRODUCTION

A recent study [1] estimated that in 2020 approximately 28% of the global population would have abnormal carotid intima-media thickness, while carotid plaques would be detected in 21% of the people. To focus on the examination of atherosclerotic plaques in carotid ultrasound (CUS) images and videos, as well as to extract descriptive plaque textural features, clinical experts often need to manually annotate regions of interests (ROIs). To automate this process, recent studies [2], [3] have proposed deep learning-based (DL) computational systems to segment and classify atherosclerotic plaques in CUS images and videos. Surprisingly, in the majority of these studies, comparisons among samples are drawn in the absence of a standardization process for image intensity and resolution normalization. Additionally, speckle reduction and uniform selection of a pre-specified number of cardiac cycles (CCs) per patient sample are also not performed. The aforementioned steps have been proven beneficial [4] prior to plaque-specific mainstream CUS video analysis. Apart from typical image-based families of features, previously found characteristic of either Asymptomatic (AS) or Symptomatic (SY) carotid atherosclerosis individuals [4]–[6], such as the Grayscale Median (GSM) or the Spatial Gray Level Dependence Method (SGLDM) features, new discriminatory image features have emerged for object classification in medical images, such as the multiscale Amplitude-Modulation Frequency-Modulation (AM–FM) family of features [7]–[9].

In this preliminary study, we propose and evaluate the first steps of our integrated system for automated segmentation of atherosclerotic plaques in CUS videos and images, and the image-based feature extraction for plaque classification. This proposed system aims to assist doctors in the assessment of carotid atherosclerosis, by providing an overall stroke risk score and a better understanding of the plaque image features, with a short analysis time. The rest of the paper is organized as follows. Section II provides a description of the CUS video data, the data preprocessing steps and the analytical methods, used in this study. Section III summarizes the results and Section IV discusses the experimental results and analysis.

II. MATERIALS AND METHODS

For this study, the data selection, the CUS image and video preprocessing steps, as well as the atherosclerotic plaque segmentation and image-based feature analysis steps are shown in Fig. 1 and explained further in the following subsections.

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A. Carotid Ultrasound Videos and Demographics

In this study, a total of 10 internal carotid artery longitudinal CUS videos (10 subjects, 5 AS and 5 SY) were used, captured in a Medical Centre in the United Kingdom, from 2013 to 2015. The frame per second (fps), the total number of raw frames per video, the initial image resolutions, as well as the raw video frame (VF) sizes ranged from 30 to 100, 268 to 2001 VFs, 11.3 to 17.7 pixels/millimeter (px/mm), and 432x442 pixels and 800x600 pixels, respectively. An experienced vascular surgeon (A. Nicolaides) generated manual annotations for the atherosclerotic carotid plaques, for the first VF per video. Only single-plaque videos were present.

B. Image and Video Preprocessing

In order to effectively compare the CUS VFs, in this study, we applied a predefined image and video standardization process,

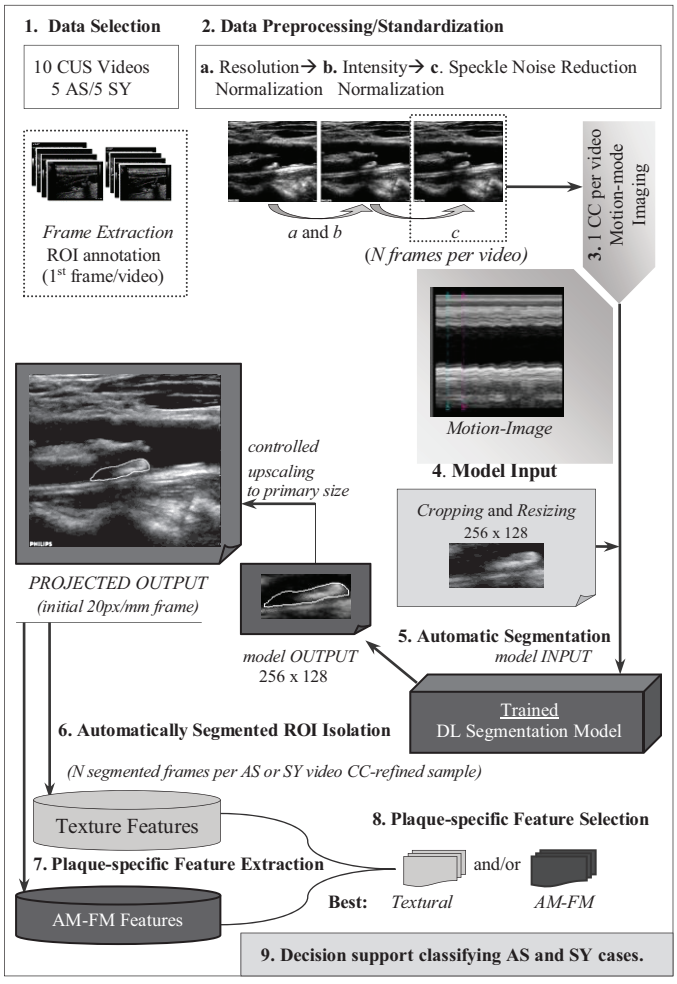


Fig. 1. Flow diagram of the following: 1) CUS video and image data selection, 2)-4) data preprocessing, 5) atherosclerotic plaque automatic segmentation, 6) plaque region isolation, 7) plaque-specific image-based feature extraction and 8) plaque-derived feature statistical analysis. AM-FM: Multiscale Amplitude-Modulation Frequency-Modulation, AS: Asymptomatic, CC: Cardiac Cycle, CUS: Carotid Ultrasound, DL: Deep Learning, N: Number, ROI: Region of Interest, SY: Symptomatic.

developed and used from our group in [10]. Specifically, from each raw CUS video we extracted all VFs (see also Fig. 1, step 1) in 'tiff' format (LZW compression), in which we applied image resolution normalization (to 20 px/mm), image intensity normalization and speckle noise reduction (see Fig. 1, steps 2a, 2b and 2c), as used in [4]. For the speckle noise reduction, we used the 'DSFhmedian' filter, with a 5x5 window running on the entire VFs, in 2 iterations; see also [11] for details.

C. Cardiac Cycle Identification and Frame Selection

In parallel, in order to be able to extract reliable statistics between the AS and SY VFs, from each CUS video, we isolated a 'diastole-systole-diastole' ('d-s-d') CC-compliant VF range, as proposed and explained in [10] (see also Fig. 1, step. 3), where a Motion-mode (M-mode) image is extracted (see Fig. 3, step. 3.1) to guide the identification of carotid artery distention and constriction occurrences. After identifying the VFs for a single CC, per video, the VF number was further reduced, by leaving out redundant VFs; we kept each 5th CC frame for fps<54, and each 10th CC frame for fps=110 or fps<100. We ended up with 88 overall CC-refined VFs (44 AS and 44 SY VFs), from the 10 AS and SY primary CUS videos. It is important to mention that, due to the different fps per video, the final number of CC-refined VFs per sample was not equal.

D. Automatic Plaque Segmentation

In a parallel study of our group, which will soon be published, we trained CFPNet-M [12], a lightweight DL model, for plaque segmentation in CUS VFs, using a dataset consisting of 3 different world populations. For the automatic plaque segmentation, in the present study (see Fig. 1, Step 5), we deployed a CFPNet-M version we previously trained, using a total of 145 CUS preprocessed (as in [10]) VFs (145 individuals, 85 AS, and 60 SY, where 125 samples were used in training, 10 in validation and 10 in evaluation). The 10 CUS videos, used in the present study, constituted the source for the 10 VFs we used to evaluate CFPNet-M. In CFPNet-M, 634,336 parameters were trained, for 120 epochs, with a batch size of 5 VFs, which we cropped and resized (256x128) to the plaque area; the plaque was kept in the center of the final model input image, having 5px included at the right and left side, and 40px at the top and the bottom of the ROI, to minimize the carotid background and boost the model training (see Fig. 1, step 4). The model was implemented using Tensorflow in Python, with the 'root mean squared propagation' as optimizer, the Dice Loss, and the Jaccard Coefficient (JC) as segmentation performance metric, during the validation and evaluation process, respectively. We started from a 0.001 learning rate and used a step decay learning rate scheduler (0.7 decay, every thirty epochs) to eliminate large loss fluctuations, noticed during training.

E. Image-based Plaque Feature Extraction

Upon automatic segmentation of the 88 plaques (see Fig.

1, step 6), we used two computational tools, previously developed by researchers in our group, to extract plaque-specific textural and AM-FM features (see Fig. 1, Step 7). The textural features extracted belong to 3 large families, namely the First Order Statistics (FOS), the SGLDM, and the GLDM (Gray Level Dependence Method) family [4]. Specifically, we examined the Correlation from the SGLDM family, the Homogeneity from the GLDM family and the FOS Mean. To assess the contribution that known AM-FM features have in the classification of the atherosclerotic plaques, we extracted 3 different features from each automatically segmented plaque in this study, namely the Instantaneous Amplitude (IA), the Instantaneous Phase (IP), and the Instantaneous Frequency (IF), each of which was examined in its own number of bins (8- bins IA, 4-bins IP and 4-bins |IF|) and in 3 scales (low, medium, and high), using the methodology developed in [8].

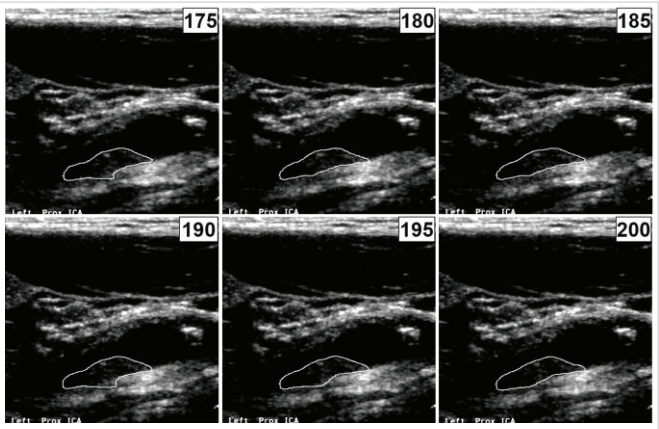
F. Plaque-specific Feature Statistical Analysis and Selection

For all extracted image-based features, from the 88 AS and SY VFs, we identified non-normal distributions, using the Kolmogorov test (from Scipy's statistics [13], in Python) (see Fig. 1, step 8). Then, we used the 'Mann-Whitney U rank' test (from Scipy) to identify features exhibiting statistically significant differences among the AS and SY segmented plaques, as well as the Spearman Correlation Coefficient (also from Scipy) to examine how the AS- and SY-specific image features are correlated, all using the median (± interquartile range, IQR) values to summarize the trend each feature follows and select the best features to distinguish between AS and SY cases.

III. Results

As explained above, we have previously trained CFPNet-M from scratch to automatically segment the atherosclerotic plaque in CUS VFs. CFPNet's segmentation performance was primarily evaluated on 10 kept out VFs (10 CUS videos; the 1st VF per video, for 10 subjects, 6 AS and 4 SY), and reached a mean 79.7±6.9% JC.

Fig. 2 illustrates the CFPNet-M-based plaque segmentation in all the CC-refined VFs of a SY subject (video) in this study, for which the extracted IP_{Medium} plaque feature is given, per VF. This example possibly depicts forces that are applied on the plaque, during the CC (see Fig. 2, 1st column, top and bottom) resulting in slightly different segmented ROIs, compared to those in the rest of the VFs, in this example. As explained earlier, none of the plaque features' distribution was normal, therefore we calculated all features summaries in the form of median (±IQR) series. TABLE I tabulates the median±IQR values for each feature, in both the AS and SY samples, as well as the results from the statistical significance and correlation testing between AS and SY cases, in this study. We identified 8 plaque features that were statistically significant between the AS and SY VFs (44 versus 44, respectively). In TABLE I, we show that the IP_{AS} and IP_{SY} returned a statistically significant difference across all scales (low, medium, high), with $p<0.05$, followed by IF_{AS} versus IF_{SY}, for the medium and high scales ($p<0.05$). As shown in Fig. 3 (Left), the IP_{Medium} and the



IP_{Medium} (median±IQR): 0.237±0.086, 0.237±0.082, 0.247±0.083, 0.246±0.087, 0.239±0.084, 0.239±0.083, for the 175, 180, 190, 195 and 200 frames, respectively.

Fig. 2. CFPNet-M-derived automatic plaque segmentations for the CC-refined VFs (6 CC frames; from 268 initial VFs, to 31 CC VFs, to 6 CC-refined VFs, see Section II-C) of a SY case of this study, given with a solid white line at 20px/mm. Below, we provide the extracted median (±IQR) (over the low, medium and high levels) of the IP_{Medium} per VF. VF: Video Frame.

TABLE I. Upon automatic segmentation of all VFs in this study, we present the stastistically significant (Mann-Whitney rank sum test on the median ±IQR values per feature), features between the AS vs SY cases, on image level. The Spearman correlation is given in the last column. 44 AS samples were compared with 44 SY samples (88 total VFs in this study). VF: Video Frame.

FF	Features	AS	SY	SS p-value	Cor. Coef. (p)
		MD (±IQR)	*MD (±IQR)*		
Multiscale AM-FM	IP_{LOW}	0.26 (±0.06)	0.345 (±0.05)	0.001	0.37 (0.013)
	IP_{MEDIUM}	0.28 (±0.01)	0.24 (±0.02)	<0.05*	-0.19 (0.223)
	IF_{MEDIUM}	0.20 (±0.04)	0.18 (±0.02)	<0.05*	-0.39 (0.01)
	IP_{HIGH}	0.15 (±0.02)	0.14 (±0.04)	0.0070	-0.12 (0.434)
	IF_{HIGH}	0.21 (±0.05)	0.20 (±0.05)	0.0318	0.47 (0.001)
Texture	$SGLDM_{COR}$	0.99 (±0.00)	0.98 (±0.01)	<0.05*	-0.26 (0.083)
	$GLDM_{HOM}$	0.29 (±0.09)	0.36 (±0.33)	0.0007	0.38 (0.00)
	FOS_{MEAN}	83.39 (±21.87)	42.72 (±63.86)	0.024	0.44 (0.010)

AM-FM: Multiscale Amplitude-Modulation Frequency-Modulation, AS, Asymptomatic, Coef: Coefficient, Cor: Correlation, FF: Feature Family, IP: Instantaneous, IF: Instantaneous Frequency, GLDM: Gray Level Dependence Method, HOM: Homogeneity, SGLDM: Spatial Gray Level Dependence Method, FOS: First Order Statistics, IQR: Interquartile Range, MD: Median, SS: Statistical Significance, SY: Symptomatic.

IF_{Medium} are very good descriptors, which may be used to differentiate between the AS and SY cases. This is depicted by the narrow IQR values they share. In Fig. 3 (Middle), we provide the correlation plot between the IP_{Medium_AS} and the IP_{Medium_SY} cases, which shows a negative linear relationship between the two classes. In Fig. 3 (Right), we show the Bland Altman plot for the IP_{Medium_AS} and the IP_{Medium_SY} cases, investigated in this study.

IV. Discussion

In this study, we deployed a DL model we had previously trained to automatically segment atherosclerotic plaques, in a CUS VF dataset (AS and SY cases), which underwent standardization, on the image and video level. We selected VFs that represent one CC per patient to facilitate reliable

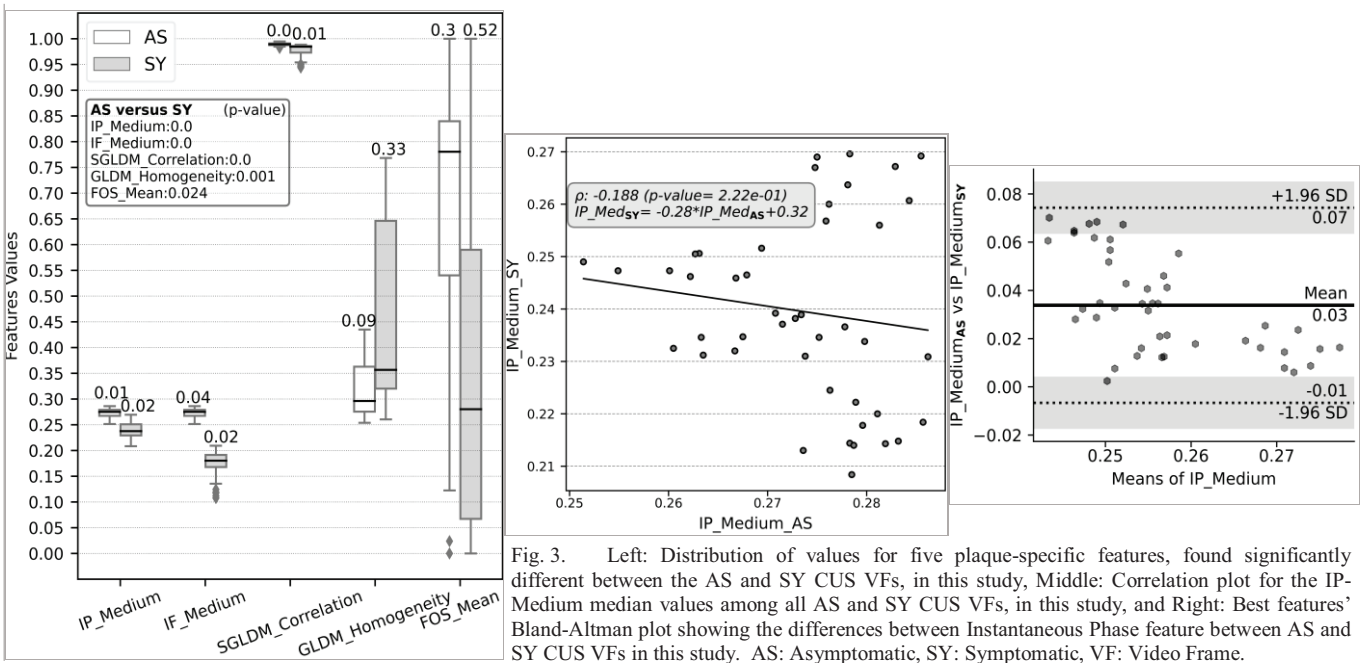


Fig. 3. Left: Distribution of values for five plaque-specific features, found significantly different between the AS and SY CUS VFs, in this study, Middle: Correlation plot for the IP-Medium median values among all AS and SY CUS VFs, in this study, and Right: Best features' Bland-Altman plot showing the differences between Instantaneous Phase feature between AS and SY CUS VFs in this study. AS: Asymptomatic, SY: Symptomatic, VF: Video Frame.

comparisons between the AS and SY samples. From all VFs, we derived CFPNet-M-based automatic plaque segmentations, from which we extracted plaque image features, with two methods of our group. All these steps are part of our new developing software system for CUS video segmentation and classification. In almost all the CUS plaque segmentation and analysis studies (except [2]), no data standardization processes are reported. In this study, we applied CUS image and video standardization, and extracted new CUS CC-representative and plaque-descriptive image features, able to distinguish between AS and SY cases. Our findings on image textural and AM-FM feature comparisons, between AS and SY, are in accordance with those in [4] and [8]. The IP_{Medium} and IF_{Medium} clearly showed a superior power, when differentiating between AS and SY cases. The AM-FM features will possibly replace the traditional plaque textural features, in our future ML-based plaque classification tasks, hosted in our systems' final version.

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REFERENCES

[1] P. Song, Z. Fang, H. Wang, Y. Cai, *et al.*, "Global and regional prevalence, burden, and risk factors for carotid atherosclerosis: a systematic review, meta-analysis, and modelling study," *Lancet Glob. Health*, vol. 8, no. 5, pp. 721–729, 2020.

[2] M. del M. Vila, B. Remeseiro, M. Grau, R. Elosua, *et al.*, "Semantic segmentation with DenseNets for carotid artery ultrasound plaque segmentation and CIMT estimation," *Artif. Intell. Med.*, vol. 103, no. 4, p. 101784, 2020.

[3] N. H. Meshram, C. C. Mitchell, S. Wilbrand, R. J. Dempsey, and T. Varghese, "Deep Learning for Carotid Plaque Segmentation using a Dilated U-Net Architecture," *Ultrason. Imaging*, vol. 42, no. 4–5, pp. 221–230, 2020.

[4] C. P. Loizou, C. S. Pattichis, M. Pantziaris, E. Kyriacou, and A. Nicolaides, "Texture features variability in ultrasound video of the atherosclerotic carotid plaque," *IEEE J. Transl. Eng. Health Med.*, vol. 5, no. 1800509, pp. 1–9, 2017.

[5] E. Kyriacou, P. Vogazianos, C. Christodoulou, C. P. Loizou, A. S. Panayides, *et al.*, "Prediction of the time period of stroke based on ultrasound image analysis of initially asymptomatic carotid plaques," in *2015 37th Ann. Int. Conf. IEEE Eng. in Med. &Biol. Society (EMBC)*, Milan: IEEE, pp. 334–337, 2015.

[6] E. C. Kyriacou, S. Petroudi, C. S. Pattichis, M. S. Pattichis, *et al.*, "Prediction of high-risk asymptomatic carotid plaques based on ultrasonic image features," *IEEE Trans. Inf. Technol. Biomed.*, vol. 16, no. 5, pp. 966–973, 2012.

[7] K. P. Constantinou, I. P. Constantinou, C. S. Pattichis, and M. S. Pattichis, "Medical image analysis using AM-FM models and methods," *IEEE Reviews in Biomedical Engineering*, vol. 14, pp. 270–289, 2021

[8] K. P. Constantinou, "AM-FM medical image analysis", PhD dissertation. Department of Computer Science, University of Cyprus, 2018.

[9] C. P. Loizou, V. Murray, M. S. Pattichis, M. Pantziaris, and C. S. Pattichis, "Multiscale Amplitude-Modulation Frequency-Modulation (AM–FM) texture analysis of ultrasound images of the intima and media layers of the carotid artery," *IEEE Trans. Inf. Technol. Biomed.*, vol. 15, no. 2, pp. 178–188, 2011.

[10] C. P. Loizou, S. Petroudi, M. Pantziaris, A. N. Nicolaides, and C. S. Pattichis, "An integrated system for the segmentation of atherosclerotic carotid plaque ultrasound video," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 61, no. 1, pp. 86–101, 2014.

[11] C. P. Loizou, C. Theofanous, M. Pantziaris, T. Kasparis, *et al.*, "Despeckle filtering toolbox for medical ultrasound video:," *Int. J. Monit. Surveill. Technol. Res.*, vol. 1, no. 4, pp. 61–79, 2013.

[12] A. Lou, S. Guan, and M. Loew, "CFPNet-M: A light-weight encoder-decoder based network for multimodal biomedical image real-time segmentation." arXiv, 2021. Available: http://arxiv.org/abs/2105.04075.

[13] P. Virtanen, R. Gommers, T. E. Oliphant, M. Haberland, *et al.*, "SciPy 1.0: Fundamental algorithms for scientific computing in Python," *Nature Methods*, vol. 17, no. 3, pp. 261–272, 2020.