Journal of Scientific & Industrial Research
Vol. 80, November 2021, pp. 992-1000

Effect of Pre-processing of CT Images on the Performance of Deep Neural Networks Based Diagnosis of COVID-19

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Received 01 October 2020; revised 30 April 2021; accepted 13 October 2021

COVID-19 disease is considered a new challenge around the world. Molecular testing is frequently used, aiming an early detection. However, due to its complexity in the sampling protocol and delay diagnostic, it makes critical the time to decisions on treatment or clinical interventions. In this work, the deep learning technique was adopted to evaluate the performance of 4 systems based on convolutional neural networks (VGG16, VGG19, ResNet50, and MobileNet) to support the diagnosis of COVID-19. CNN models were trained and tested using 340 CT images of patients diagnosed with COVID-19, and the same numbers of images of patients without viruses, 1700 images were obtained for each class using data-augmentation. On these images sets two types of pre-processing were performed normalization and entropy. The parameters: accuracy, recall, precision, and F1Score were used as evaluation metrics. The study found that the best performance in the classification of CT images of patients with COVID-19 was obtained by the MobileNet network with normalization pre-processing attaining 98.04% accuracy. These findings suggest that the type of pre-processing influences CNN's performance strongly. So as a guideline for future development, attention must be paid to implementing pre-processing modules dedicated to highlighting the features of CT images image of COVID-19 positives cases to improve the CNN performance.

Keywords: Convolutional neural networks, Deep learning, Entropy, Normalization, Transfer learning

Introduction

In the current, the novel COVID-19 disease is considered one of the most significant scientific challenges in all knowledge areas. To date, it is known that COVID-19 disease, according to its pathology, is associated with a severe acute respiratory syndrome, which due to massive alveolar damage and progressive respiratory failure in patients, may cause death.[1] Since the first cases of COVID-19 were detected in late 2019 in the Wuhan city, the virus has been quickly spread worldwide. This fact occurs by its relatively simple transmission mode, such as direct and indirect contact with infected people through respiratory droplets and surfaces or objects previously used by an infected person. As reported, this virus is reaching a mortality rate of up to 2%.[(2)]

In this sense, following World Health Organization guidelines that aim to mitigate the spread of the virus, some necessary measures have been taken, such as traffic control and rapid diagnostic tests. Thus, among rapid diagnostic tests is to highlight those based on the detection of viral proteins in samples taken from the respiratory tract, and those used in the detection of antibodies in the blood.[3] However, in the first case, the accurate assays may depend on factors, such as, virus concentration, since the viral loads in upper respiratory tract samples are much lower than in lower respiratory tract samples which may lead to false-positive results.

In the detection of antibodies in the blood, the clinical diagnosis may be obtained by molecular testing, such as reverse transcription-polymerase chain reaction: RT-PCR.[4] However, some studies[5–8] have reported that the developed antibody occurs days or weeks after the onset of symptoms, making decisions on treatment or clinical interventions critical. Further, this detection may be influenced by cross-react with other pathogens agents leading to false-positive results.

Other factors that may affect the results of diagnostic tests are: variations in the viral load released by patients during the different stages of infection[9]; quality of PCR reagents that may vary

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from the different provider; the manipulation-collection of high-quality specimen requires skillful by the health-workers.[8]

Despite considerable efforts for the early detection of COVID-19 disease by using molecular tests to prevent its rapid spread and reduce the mortality rate, there are still problems to solve, so it is critical to provide timely treatment to the patients.

In an attempt to reduce the false-positive results arises the necessity to found complementary methods aiming at better and optimize the results of the assays in COVID-19 patients suspicious. In this regard, the computed tomography (CT) chest may be considered an interesting alternative to the detection of COVID-19 disease due to its high sensibility, which may up to 98%.[(10)] Thus, according to the sixth official diagnosis and treatment protocol issued by the National Health Commission of the People's Republic of China[11] is suggested that diagnosis CT images-based can be included as criteria for COVID-19 detection, monitoring, and progression.

Some preliminary studies in this field have reported typical radiographic patterns for COVID-19 positive cases, such as ground-glass opacities (GGO), consolidation of patchy areas of fibrosis, airway changes, nodules presence, vascular enlargement, among other.[12] Besides, the chest CT images may provide pathologic information, but each image must be exhaustively analyzed to found anomalies, which may lead to delay diagnosis.

In recent years there has been considerable interest in computational methods for healthcare applications.[13,14] In this specific case, it is highlighted systems that involve image processing and deep learning methods, since they are considered a powerful tool for extraction, analysis, and recognition of patterns and image classification of data sets, such as chest CT images.[15–17]

Various approaches have been put forward in this area; for instance, Narin *et al.*[17] has proposed a deep learning method with a convolutional neural network (CNN) based models achieving classification performance with 98% accuracy (ResNet50 pre-trained model) to COVID-19 detection. Singh *et al.*[18] using CNN linked with multi objective differential evolution (MODE) have attained 92% accuracy. On the other hand, in a study conducted by Vaid *et al.*[19] from chest X-ray scans achieved an accuracy of 96.3% with a modification of the VGG-19 model. Ozturk *et al.*[20] on x-ray images produced a classification accuracy of 98.08% for binary classes and 87.02% for multi-class cases implemented 17 convolutional layers and introduced different filtering on each layer. Kumar *et al.*[21] introduce and evaluate the performance of a custom-made deep learning architecture SARS-Net, to classify and detect the Chest X-ray images for COVID-19 diagnosis. It was found that the model achieved an accuracy of 97.60% and a sensitivity of 92.90% on the validation set.

Such findings show that CNN based models may aid in making clinical decisions since they facilitate the screening of suspicious cases de COVID-19 with high accuracy.

In this context, the research aims to compare the effect of pre-processing CT images (normalization and entropy) on the performance of deep learning methods with convolutional neural network (CNN) based models as support to medical diagnosis COVID-19 suspicious patients. To this purpose, from public dataset were randomly selected 340 images of COVID-19 diagnoses patients and the same number of images of healthy patients. However, using data augmentation techniques this amount was increased to 1700 in each set of images. The performance of CNN was evaluated by metrics, such as Accuracy, Recall, Precision, F1 Score.

Materials and Methods

CT images dataset

Chest CT images were obtained from the public data set built and validated by Zhao *et al.*[22] It is worth noting that a senior radiologist at Tongji Hospital, Wuhan, China has validated this dataset. Dataset consists of 349 images whose patients were diagnosed as positive for COVID-19 and 463 images with a negative diagnosis. The unbalanced data problem was avoided by taking randomly selected 340 images of COVID-19 positive cases and the same number of images of healthy patients.

Image Pre-processing

As a first step, all the images were standardized by scaling pixel values to the range 0 and 1 and subsequently resized to 224 × 224 pixel size. Once had been done were employed two pre-processing steps: Normalization and Entropy, which are described below.

Image Normalization

Each image was normalized concerning statistical parameters (mean and variance) of ImageNet dataset, which is defined as:

$$N(i,j) = \frac{X(i,j)-\tilde{X}}{\sigma} \quad ...(1)$$

where, $N(i,j)$ and $X(i,j)$ represent the normalized and unnormalized pixel in the (i,j) position, respectively, and $\tilde{X}$ y σ are mean and variance of dataset ImageNet.

Image Entropy

Entropy images were computed using a circular window (5 × 5 pixel size), following the equation:

$$H = -\sum_{k=1}^{n} P_k \times log_2(P_k) \quad ...(2)$$

where, k refers to the number of gray levels and P_k the probability associated with each gray level k into a circular window (5 × 5 pixel size). Thus, the entropy aims to estimate the differences in the local distributions of gray levels in the images, seeking to maximize the characteristics that differentiate the two types of images, COVID-19 and No_COVID-19.

An increase in the diversity of available data was obtained through data augmentation techniques, such as zoom, rotation, and translation. This process increased to 1700 images, each set of images, which were labeled as COVID-19 and No-COVID-19. From these images, 80% were used for the training stage and 20% to tests and validation.

Deep Learning

Deep Learning technique was used with pre-trained CNN, such as VGG16, VGG19, ResNet50, MobileNet. VGG16 and VGG19 models present a similar structure with five convolutional blocks and three fully connected layers except that, VGG19 has a deeper architecture (19 layers). For this study, the three final layers were modified, but the depths of the networks, 16 and 19, were maintained and trained with 3.228.162 parameters. ResNet50 is a model with 50 layers deep that consists of 5 stages, each with a convolution and identity block and additionally uses residual connections. This model was adapted with three fully connected layers with a dropout of 30% and was trained with 12.861.954 parameters.

Finally, MobileNet is a network with 28 layers that includes depth wise separable convolution operations, and for this case, three fully connected layers with a dropout of 30% were added. This model was fully trained with 9.646.402 parameters. The pre-trained network architecture used in this study is shown in Fig. 1.

It is worth noting that the final layers in each model were modified to adjust these to binary classification performed in this study. Besides, all models were trained with the Adadelta optimizer being used the same training, validation, and test dataset aiming to obtain comparable results between all networks.

Performance metrics evaluated

In order to evaluate the performance of the trained convolutional neural networks, conventional metrics were used, such as Accuracy, Recall, Precision, and F1Score, which were calculated as follows:

$$Accuracy = \frac{Ntp+Ntn}{Ntp+Nfp+Ntn+Nfn} \quad ...(3)$$

$$Recall = \frac{Ntp}{Ntp+Nfn} \quad ...(4)$$

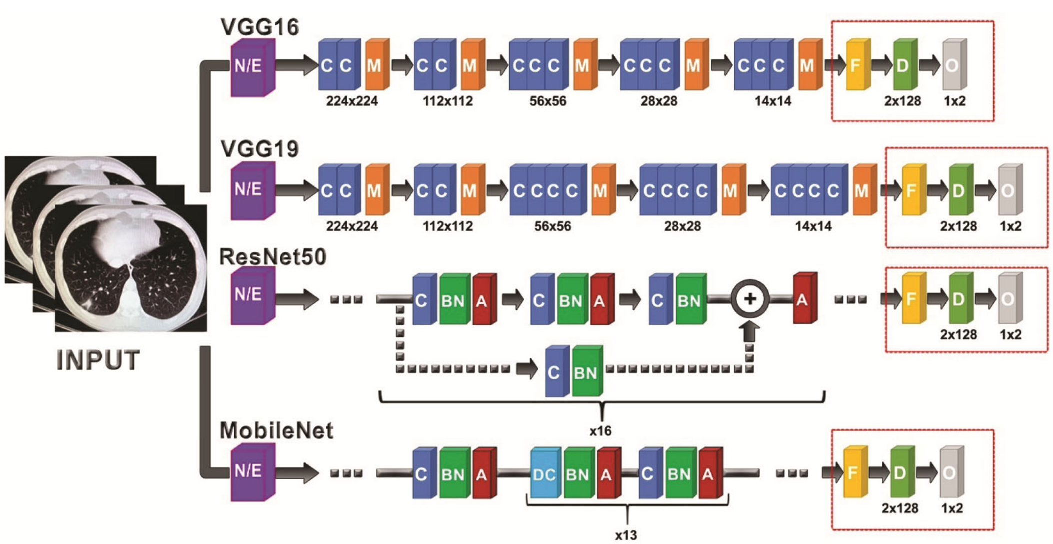

Fig. 1 — Schematic representation of the pre-trained convolutional neural networks architecture used in this study. The dotted line (red) shows the layers added in each model. Color blocks represented the operations in each model, where, N/E: Normalization or Entropy; C: Convolution; M: Maxpooling; BN: Batch Normalization; DC: Depthwise Convolution; A: Activation; F: Flatten; D: Dense; O: Output

$$Precision = \frac{Ntp}{Ntp + Nfp} \quad ...(5)$$

$$F1Score = 2\frac{precision \times recall}{precision + recall} \quad ...(6)$$

where, *Ntp* and *Ntn* represent the number of correctly diagnosed COVID-19 (true positives) and No_COVID-19 (true negatives), respectively; *Nfp* and *Nfn* are the number of incorrectly diagnosed COVID-19 (false positives) and No_COVID-19 (false negatives) respectively. Positive and negative values in these equations are associated with diagnosed COVID-19 and No_COVID-19, respectively.

Results and Discussion

Convolutional neural networks (CNN) were trained using 3400 digital tomography images to classify CT images to diagnose COVID-19. In Fig. 2 some CT images of healthy people and people diagnosed with COVID-19 arw shown. CT images were pre-processed using normalization or entropy. In Figs 2c–2d, CT images positive for COVID-19 are shown with normalization and entropy pre-processing respectively. Similarly, Figs 2a–2b correspond to CT images negative for COVID-19, with normalization and entropy pre-processing respectively. Normalization allowed to standardize the intensity of the pixels reducing the effect of outliers. Entropy describes how much randomness there is in an image, and detects unexpected intensity variations in images.

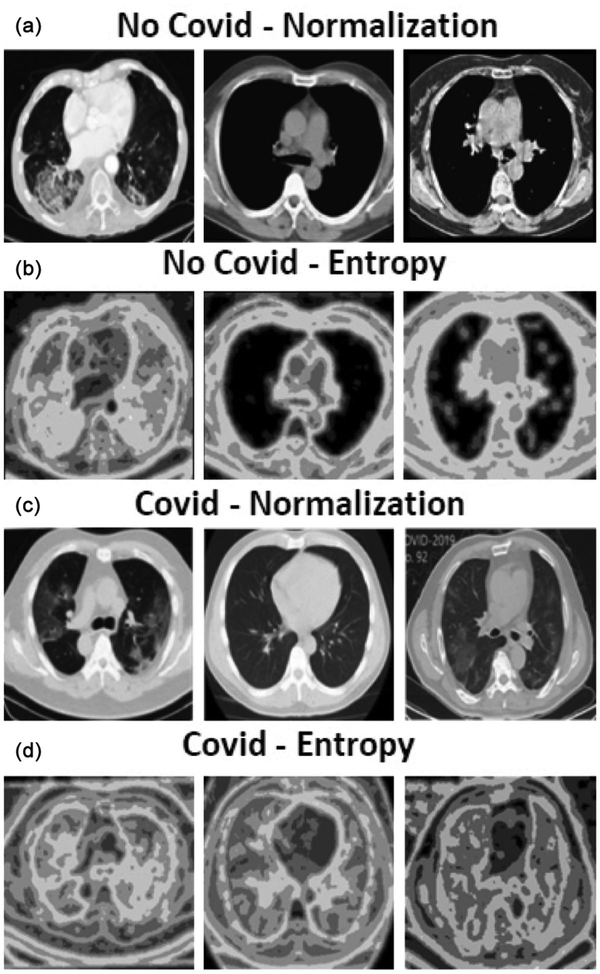

Fig. 2 — Pre-processing of CT images: a. No_Covid images with normalization; b. No_Covid images with entropy; c. COVID images with normalization; d. COVID images with entropy

For each type of pre-processing, CNN's performance was evaluated. In Table 1 the confusion matrices of the classification results are shown in the two categories (COVID-19, No_COVID-19), for CNNs trained with the two types of pre-processing. For each model in Table 1, the primary diagonal represents the correct *Ntp* and *Ntn* evaluations, and the secondary diagonal represents the wrong diagnoses *Nfp* and *Nfn.* Further, Table 2 shows the performance metrics of the trained CNNs. The performance of convolutional neural networks is evaluated with the group of test images.

The training and validation of the 4 CNNs, with normalization and entropy, used in this study are shown in Figs 3–4. Here can be observed that there was over-training in several of the CNN models. For networks with normalization pre-processing, overtraining is presented for the VGG19 and Resnet50 models. For networks with entropy pre-processing, overtraining is presented for all models except CNN MobileNet

This study showed that CNN, with the best performance in chest CT image classification for the diagnosis of COVID-19, was the MobileNet network. Besides, CNN performed better with normalization pre-processing compared to entropy calculation pre-processing. In gray-scale images, the entropy is low when the contrast between neighboring pixels is low, and the entropy increases when the contrast between neighboring pixels is higher. Entropy images show greater sensitivity to contrast variations, Fig. 2. However, this study showed that for chest CT images, the entropy calculation favored overtraining for all CNN, excluding MobileNet, decreasing the performance of the nets. This effect usually occurs when the validation error increases while the training error remains constant or decreases.[23] It is convenient to add dropout and normalization operations in the CNN architecture to mitigate over-training.

Nevertheless, as shown by Zhao *et al.*[22], pre-processing of the image is critical on CNN, since it

Table 1 — Confusion matrices of the classification systems trained in this study to Normalization and Entropy Pre-processing

Pre-processing: Normalization

CNN Model	Confusion matrix training dataset		Confusion matrix validation dataset		Confusion matrix test dataset		
	Actual Values						
	NC–19	C–19	NC–19	C–19	NC–19	C–19	Predicted Values
VGG16	1377	0	155	15	138	15	NC–19
	0	1377	7	163	15	138	C–19
VGG19	1377	0	156	14	139	14	NC–19
	0	1377	5	165	6	147	C–19
ResNet50	1237	140	144	26	130	23	NC–19
	101	1276	14	156	26	127	C–19
MobileNet	1337	40	165	5	149	4	NC–19
	37	1340	9	161	2	151	C–19

Pre-processing: Entropy

CNN Model	Confusion matrix training dataset		Confusion matrix validation dataset		Confusion matrix test dataset		
	Actual Values						
	NC–19	C–19	NC–19	C–19	NC–19	C–19	Predicted Values
VGG16	1377	0	149	21	137	16	NC–19
	0	1377	23	147	21	132	C–19
VGG19	1374	3	144	26	134	19	NC–19
	0	1377	23	147	21	132	C–19
ResNet50	1377	0	107	63	85	68	NC–19
	0	1377	15	155	13	140	C–19
MobileNet	1377	0	160	10	142	11	NC–19
	0	1377	15	155	10	143	C–19

increased the accuracy of the CNN DenseNet-169 model from 79.5% to 83.3%, adding a module that allows segmenting the regions where lung lesions caused by COVID-19 predominate. Zhang *et al.*[24] performed lesion detection with artificial intelligence methods on CT images segmented previously and were able to differentiate COVID-19 pneumonia lesions from typical pneumonia lesions with 92.49% accuracy.

Table 2 — Performance metrics of trained CNNs

Pre-processing: Normalization

CNN Model	Accuracy (%)	Recall (%)	Precision (%)	F1Score (%)
VGG16	90.20	90.20	90.20	90.20
VGG19	93.46	96.08	91.30	93.63
ResNet50	83.99	83.01	84.67	83.83
MobileNet	98.04	98.69	97.42	98.05

Pre-processing: Entropy

CNN Model	Accuracy (%)	Recall (%)	Precision (%)	F1Score (%)
VGG16	87.91	86.27	89.19	87.71
VGG19	86.93	86.27	87.42	86.84
ResNet50	73.53	91.50	67.31	77.56
MobileNet	93.14	93.46	92.86	93.16

Using RX images Ozturk *et al.*[20] obtained an accuracy of 98.08% using batch normalization as a pre-processing in a new CNN model called DarkCovidNet. Although in this study, the entropy calculation did not improve the performance of CNN, studies showed a favorable performance in diagnostic retinal images.[25]

On the other hand, the highest number of false positives was presented for the Resnet50 pre-trained model in the network with normalization and entropy pre-processing. Regarding the number of false negatives, these occurred more frequently for CNN Resnet50 with normalization pre-processing, and in the VGG16 and VGG19 networks with entropy pre-processing.

The accuracy is measured by the number of correct classifications made by the model, for the total evaluations.[26] Thus, CNN that had the highest number of correct evaluations in the test data set was

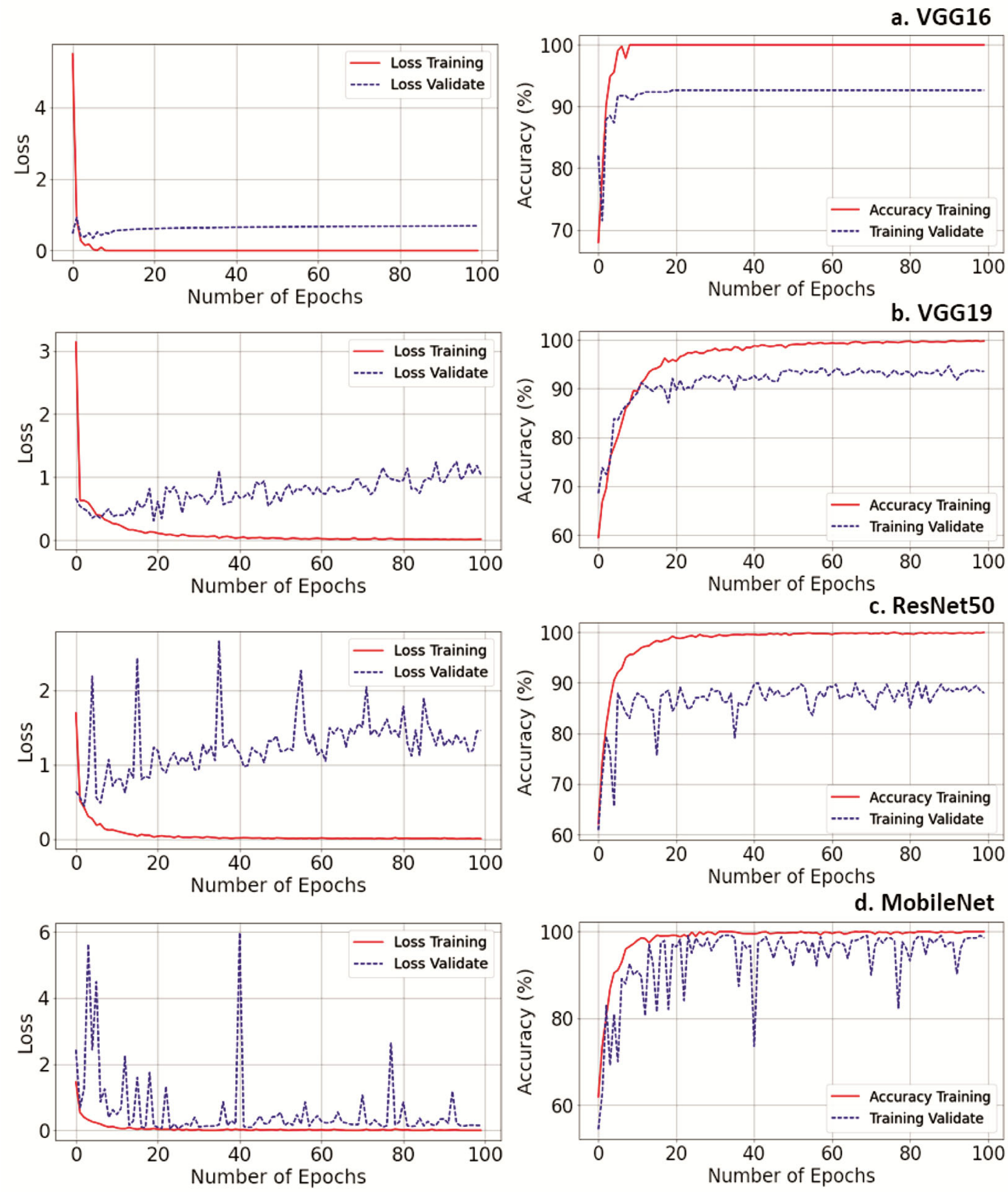

Fig. 3 —Training and validation of 4 CNN of Pre-processing normalization: a. VGG16; b. VGG19; c. ResNet50; d. MobileNet

MobileNet, with 98.04% and 93.14% for the network with normalization and entropy pre-processing, respectively. The recall and precision parameters account for the relationship between correct classifications and false positive and false negative evaluations.[26] Thus, models with false-negative evaluations are associated with the low recall, and models with false-positive evaluations are associated with low precision. The MobileNet network with normalization pre-processing showed better performance concerning these two factors. The F1 Score factor is the harmonic average between the precision and recall; in general, it can be a more representative parameter than the individual parameters.[26]

For both types of pre-processing, CNN MobileNet presented the best results. In a similar study, Ardakani *et al*.[27] compared the performance of 10 pre-trained CNNs, obtaining the best result with the Xception network with 99.51% accuracy for validation data, the author used regions of lung lesions as input images for CNN models. Other studies have evaluated the performance of other CNN models such as: Resnet with 92.49%[(24)] and 92.50%[(28)] accuracy; VGG19,

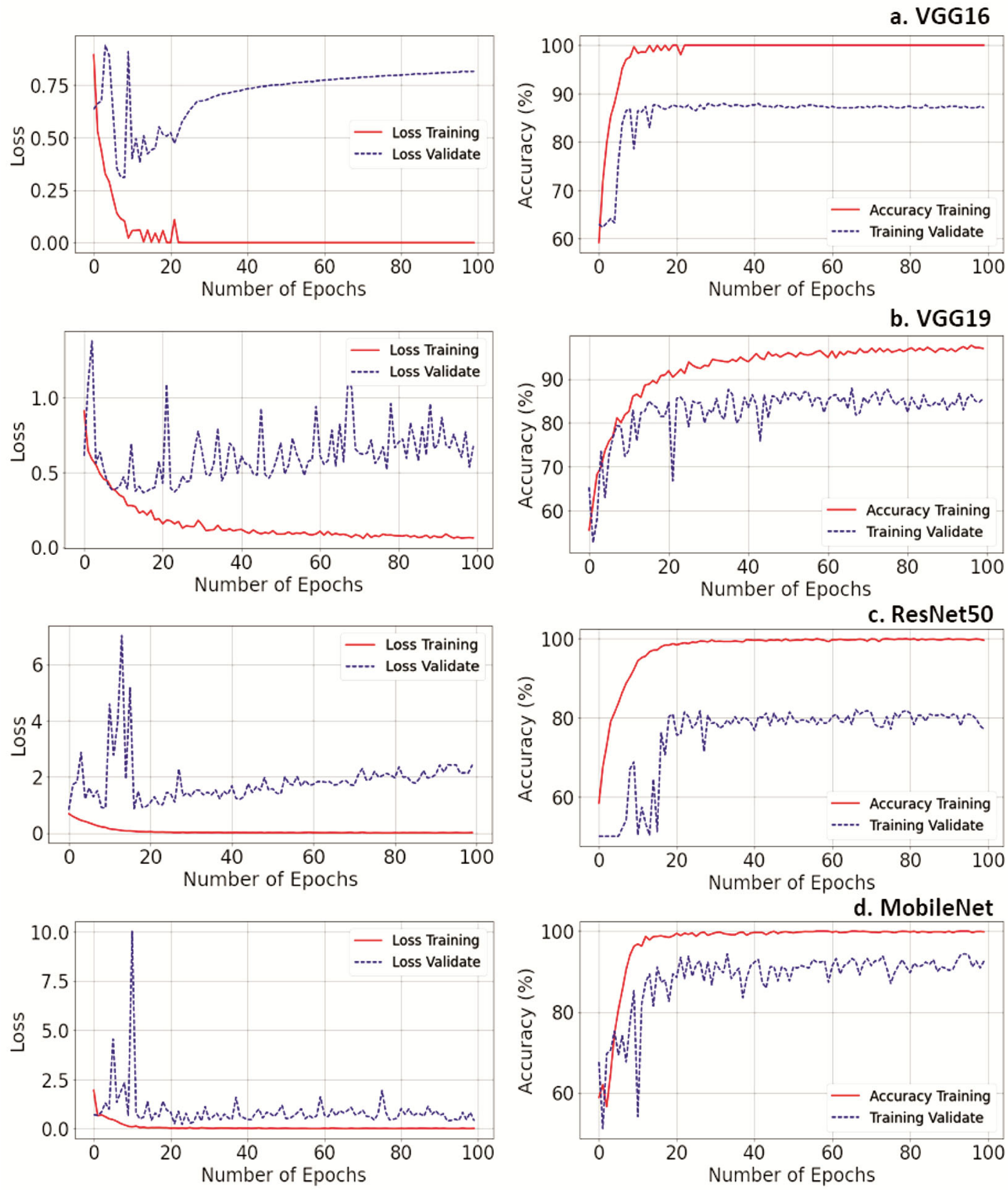

Fig. 4 — Training and validation of 4 CNN for Pre-processing entropy: a. VGG16; b. VGG19; c. ResNet50; d. MobileNet

MobileNetV2, Inception, Xception and Inception ResnetV2[(2)] accuracy 98.75%, 97.40%, 86.13%, 85.57%, and 94.38% respectively.

Entropy allows contrast enhancement in images by performing localized preprocessing, which could have favored the detection of features of interest to the classification system. Lin *et al*.[25] found a modest improvement in diabetic retinopathy detection (with a 4.3% increase in accuracy) using entropy as preprocessing. However, in this work, the results showed that there was slightly better performance using a global preprocessing technique such as normalization. Tsiknakis *et al*.[29] showed that global pre-processing can contribute to avoid bias in classification systems, and remove potential noise in images, but also degrade important details. While, Lin *et al*.[25] showed that entropy improved neural network performance, Chen *et al*.[30] found that for iris detection a pre-processing without normalization improved the classification system. Although it has been shown that deep learning techniques perform feature extraction hierarchically, and obtain good performances with raw data, it has also been found that certain preprocessing techniques can improve the performance of the models.[29]

The results of this study suggest that deep learning techniques applied to pre-trained CNN models may be used as support to diagnostic COVID-19 disease. However, aiming better, the performance in chest CT image classification attention must be paid to image pre-processing.

Conclusions

In summary, among the 4 CNN models evaluated, the MobileNet model obtained the best performance in the classification of CT images of patients with COVID-19, attaining 98.04% accuracy, 98.69% recall, 97.42% precision and 98.05% F1score. These findings suggest that the CNN performance is dependent on the pre-processing type performed on the image.

In general, images with normalization pre-processing favored CNN behavior compared to entropy calculation. Thus, it is recommended that future studies should develop pre-processing modules dedicated to highlighting the features of CT images of COVID-19 positives to improve CNN performance

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