Lung infection region quantification, recognition, and virtual reality rendering of CT scan of COVID-19

Benbelkacem, Samir, Oulefki, Adel, Agaian, Sos, Trongtirakul, Thaweesak, Aouam, Djamel, et al.

Samir Benbelkacem, Adel Oulefki, Sos Agaian, Thaweesak Trongtirakul, Djamel Aouam, Nadia Zenati-Henda, Kahina Amara, "Lung infection region quantification, recognition, and virtual reality rendering of CT scan of COVID-19," Proc. SPIE 11734, Multimodal Image Exploitation and Learning 2021, 117340I (12 April 2021); doi: 10.1117/12.2587757

SPIE.

Event: SPIE Defense + Commercial Sensing, 2021, Online Only

Lung infection region quantification, recognition, and virtual reality rendering of CT scan of COVID-19

Samir BENBELKACEM[a], Adel OULEFKI[a], Sos AGAIAN[b], Thaweesak TRONGTIRAKUL[c], Djamel AOUAM[a], Nadia ZENATI-HENDA[a] and Kahina AMARA[a]

[a]Centre de Développement des Technologies Avancées | CDTA, PO. Box 17 Baba Hassen, Algiers 16081, Algeria
[b]Dept. of Computer Science, College of Staten Island, New York, 2800 Victory Blvd Staten Island, New York 10314, USA
[c]Faculty of Industrial Education Rajamangala University of Technology Phra Nakhon, 399 Samsen Rd. Vachira Phayaban Dusit Bangkok 10300, Thailand

ABSTRACT

In recent years, virtual reality has experienced steady growth in the medical field, such as surgery, rehabilitation, disease diagnostic, and learning. The 3D representation of radiological images plays a significant role in disease diagnostic and treatment planning compared to standard 2D medical images. Since March 2019, almost all laboratories and medical centers have improved their patients' management methods with confirmed coronavirus (COVID-19) disease. Providing appropriate treatment in the well moment may contribute to save lives. Our study aims to develop an advanced COVID-19 CT scan image segmentation and 3D visualization using an unsupervised thresholding procedure and virtual reality technology to better plan and monitor affected patients. Our proposed system provides three-dimensional COVID-19 lesion visualization, which clearly shows segmented infected region (in 3D) rather than traditional two-dimensional images. Radiologists and doctors on actual patients tested the developed system. The experimenters noticed that VR rendering of CT scan of COVID-19 improves the disease diagnostic and drug prescription.

Keywords: Virtual Reality, 3D reconstruction, Segmentation, CT Scan, COVID-19.

1. INTRODUCTION

COVID-19 pandemic caused a significant health crisis and declared a Public Health Emergency of International Concern (PHEIC), raising the urgent need for specific and efficient vaccine development. The magnitude and extent of this pandemic have prompted scientists to think about sensitive and rapid diagnostic technologies. While COVID-19 continues to spread, efficient diagnostic methods are requested to prevent further transmission, reduce the outbreak's impacts, and apply effective and appropriate control measures[1]. Currently, reverse-transcriptase-polymerase-chain-reaction (RT-PCR) is considered as the reference standard in the diagnostic of COVID-19[2]. However, RT-PCR may likely provide both false-negative and false-positive results[2]. For instance, a negative result does not necessarily mean that COVID-19 infection is excluded. Thus, RT-PCR should not be considered as a unique parameter for the disease diagnostic. Since COVID-19 is a pneumonia disease, the chest computed tomography (CT) scan seems to be a useful tool in the diagnostic process of viral pneumonia situations related to COVID-19[3]. Chest CT recognizes 100% pulmonary parenchymal abnormalities in the advanced stage of COVID-19 patients. Furthermore, a CT scan provides the results almost immediately after scanning. In Algeria, Public and Private hospitals used CT scans as an alternative diagnostic tool to detect COVID-19 for patients due to the lack of diagnostic kits and RT-PCR's false prediction. CT scan takes many images, called slices, of the lungs and lesions and inside the chest. A computer processes these images and displays them to the radiologists. The segmentation stage is necessary to identify the boundaries of lesions inside the lung where we can extract quantitative information such as volumetric data of the infected area[4,5,6]. The proposed segmentation techniques for COVID-19 applications from the literature are categorized into lung-region-oriented and lung-lesion-oriented methods[7].

Multimodal Image Exploitation and Learning 2021, edited by Sos S. Agaian, Vijayan K. Asari, Stephen P. DelMarco, Sabah A. Jassim, Proc. of SPIE Vol. 11734, 117340I
© 2021 SPIE · CCC code: 0277-786X/21/$21 · doi: 10.1117/12.2587757

For instance, the 8 implemented Inception Recurrent Residual Neural Network (IRRCNN) approach for COVID-19 detection and NABLA-N model was for the segmentation task. In [9] ShuffleNet V2 model[10] was applied to classify COVID-19 images from normal healthy images. A system was proposed in [11] for lung segmentation, and COVID-19 detection in CT slices using a predetermined threshold based on the counted COVID-19 positive slices. In [12] a pre-trained DenseNet201 model was implemented to classify 2,492 CT-scans. Singh et al.[13] implemented multi-objective differential evolution-based convolutional neural networks to detect COVID-19 in chest CT images. In [14] an approach was developed for image segmentation, reconstruction, and classification tasks, using the encoder and convolutional layer. Segmentation proposed approaches for COVID-19 detection and recognition have the potential to help improve diagnostic efficiency and accuracy. The current challenges to generate 3D models could be used to develop an advanced COVID-19 lesion display using Virtual Reality (VR) technology.

In the last decade, researchers in the medical field expressed their interest in VR as a new technology to implement innovative treatments in motor and cognitive rehabilitation, mental health disorders (e.g., anxiety disorders and depression), pain management[15], stroke[16], and anatomy courses training[17, 18]. VR could be an alternative solution for 3D visualization of medical images compared to standard technologies and may serve as non-destructive diagnostic techniques for measuring the volume of infected regions[19,20]. VR allows doctors and radiologists to interact with and become immersed in computer-generated 3D models naturally. Recent technological developments in camera technology and computer hardware's processing power make VR one of the effective technologies to improve CT scan-based diagnostic.

In the ongoing pandemic COVID-19, the theories and techniques developed in virtual reality could help healthcare-related applications[21, 22,] and particularly in COVID-19 diagnostic. The work presented in[23,24] sets the listed VR applications for the COVID-19 pandemic (some of the proposed systems are described in Table 1). Thus, virtual reality's proposed concept could also provide valuable learnings to the COVID-19 medical staff. Finally, with VR, it becomes possible to analyze and locate areas of COVID-19 lesion within the patients' lungs.

Table 1: Some VR-based applications in COVID-19 pandemic background[22]

System VR-based	Role
Management of pain	Assist COVID-19 patients with chronic pains to bring them relief.
VR based mobile application	Help in the treatment of COVID-19 infection diseases
VR based glasses	Help to get rid of any stress during long in-hospital treatment.
VR based recuperation therapies	Help for physical rehabilitation COVID-19 patients recoveries
VR based Healthcare Professional Training	Help training regarding COVID-19 virus

Our study's objective is to improve the diagnostic strategy of COVID-19 pandemic using VR for detection, segmentation, and quantification of the infected regions. We provide radiologists and doctors an interactive VR platform to visualize and interact with 3D infected COVID-19 lung from actual patients' CT-scan images. The paper's structure is given as follows. Section 1 briefly reviews the state-of-the-art segmentation and VR approaches for COVID-19. In Section 2, the proposed diagnostic method is discussed. Section 3 presents experimentations performed on COVID-19 infected patients, which discusses qualitative and quantitative measurements, respectively. Finally, Section 4 presents the conclusion by interpreting the obtained results.

2. PROPOSED FRAMEWORK

The proposed framework is composed of three modules: Segmentation Module (SM), 3D Reconstruction Module (3DRM), and Virtual Reality Rendering & Interaction Module (VR^2IM). The block diagram of the proposed method is illustrated in Figure 1.

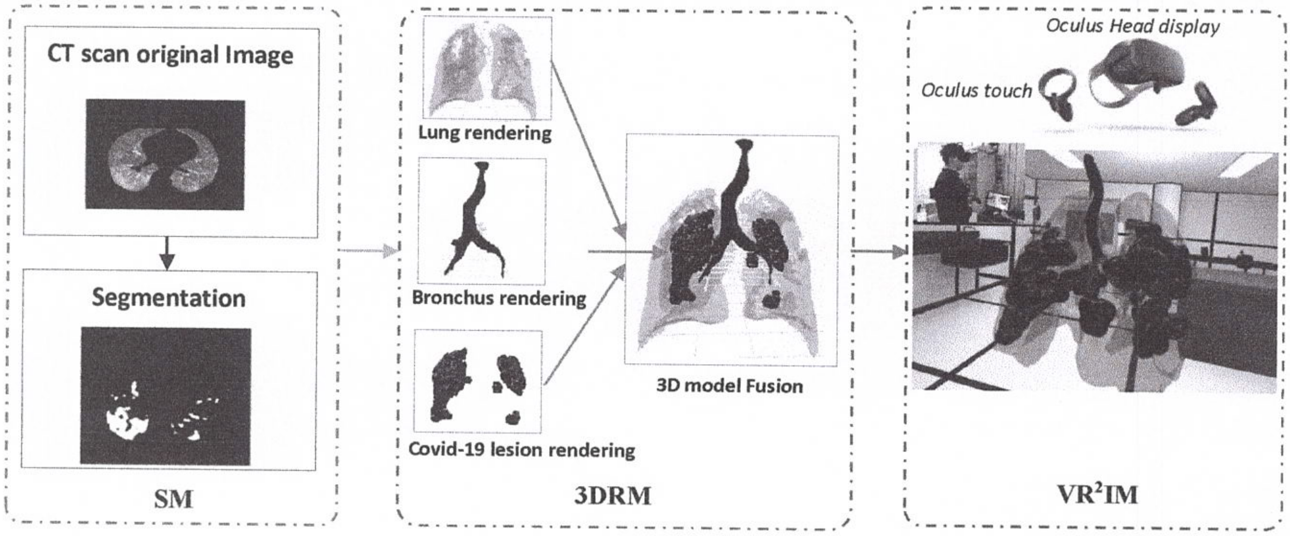

Figure 1. The proposed framework of Lung infection region quantification, recognition, and virtual reality rendering of CT scan of COVID-19.

In terms of SM, the first step was image contrast enhancement, followed by the segmentation step using the combination of Kapur's*[25] *and Tsallis' Entropy named KT-Entropy[26,27].

For contrast enhancement, The CT-scanned image enhancement technique for segmentation is proposed. Let $I_{i,j}$ denote a given CT scanned image, consisting of a grayscale level, $x = \{x_0, x_1, \dots, x_{L-1}\}$ and L represent the total number of intensity levels.

$$L_{i,j} = \left(\frac{E_{i,j} - x_{min}}{x_{max} - x_{min}}\right) \cdot x_{L-1} \tag{1}$$

$$E_{i,j} = \omega A_{i,j} + (1 - \omega) B_{i,j} \tag{2}$$

$$A_{i,j} = \left(\frac{a_{i,j}^2}{|C_{i,j}| + \phi}\right)^{\gamma_a} \quad ; \quad B_{i,j} = \log^{\gamma_b}\left(1 + \frac{a_{i,j}^2}{|C_{i,j}| + \phi}\right) \tag{3}$$

where x_{min} and x_{max} represent the minimum and the maximum intensity level of a fused image, $E_{i,j}$. ω denotes a fusion constant. $a_{i,j}$ is a denoised image. $C_{i,j}$ is directional contrast metric, $C_{i,j} = \max_k\left(I_{i,j} \otimes f_{m,n,k}\right)$. $f_{m,n,k}$ represents a directional filter. $I_{i,j}$ is a given image and $\otimes$ is a 2D convolution operator.

For segmentation, we used KT-Entropy-Based. The concept of entropy is linked (measure) with uncertainty, information, chaos, disorder, surprise, or complexity[25,26,27,28,29,30,31,32]. There are often different understandings of entropy in various fields. This section presents a new method that divides a CT image into lung infected and does not infect COVID regions using a combination of different entropies such as Kapur's Entropy[25] and Tsallis' Entropy[26,27].

Kapur's Entropy is an unsupervised thresholding technique that selects optimal thresholds based on segmented histograms' entropy [25]. The objective function of Kapur's Entropy is defined as:

$$T_K = \arg\max_t\left(K(t)\right) \quad ; \quad K(t) = H_0 + H_1 + \dots + H_n \tag{4}$$

where:

$$H_0 = -\sum_{t=0}^{t_1} \frac{p(t)}{c_0} \log\left(\frac{p(t)}{c_0}\right) \quad ; \quad c_0 = \sum_{t=0}^{t_1} p(t) \tag{5}$$

$$H_1 = -\sum_{t=t_1+1}^{t_2} \frac{p(t)}{c_1} \log\left(\frac{p(t)}{c_1}\right) \quad ; \quad c_1 = \sum_{t=t_1}^{t_2} p(t) \tag{6}$$

$$H_n = -\sum_{t=t_n}^{L-1} \frac{p(t)}{c_n} \log\left(\frac{p(t)}{c_n}\right) \quad ; \quad c_n = \sum_{t=t_n}^{L-1} p(t) \tag{7}$$

$H_0, H_1, \ldots, H_n$ represent the entropy value with $\{t_1, t_2, \ldots, t_n\}$ some thresholds. $p(t)$ denotes a probability density function of an image, c_n is a cumulative density function.

Tsallis' Entropy is the extension of Boltzmann/Gibbs Entropy[26]. Costanito Tsallis applied it as a support for generalizing the standard statistical mechanics[27], which could be utilized in a non-extensive system as:

$$T_T = \arg\max_t (s_1(t) + s_2(t) + (1-q)s_1(t)s_2(t)) \tag{5}$$

$$s_1(t) = \frac{1}{q-1}(1 - \sum_{l=1}^{t} h(l)) \quad ; \quad s_2(t) = \frac{1}{q-1}(1 - \sum_{l=t+1}^{L-1} h(l)) \tag{7}$$

$$h(l) = \sum_s (H(s,t)) \quad ; \quad H(s,t) = card(P_{i,j}) \tag{8}$$

where $P_{i,j}$ represents a paired image between a given image, $I_{i,j}$, and a denoised image, $a_{i,j}$. $card(\cdot)$ is a cardinality operator. $H(s,t)$ denotes a matched histogram on a 2D luminance plain, $x_0 \leq s, t \leq x_{L-1}$.

KT-Entropy is a combination of Kapur's Entropy and Tsallis' Entropy:

$$T = \alpha \cdot T_K + (1-\alpha) \cdot T_T \quad ; \quad 0 \leq \alpha \leq 1 \tag{9}$$

where

$$T_K(x) = \arg\max_{t,x}(K(t)) \quad ; \quad K(t) = Lmax\left(\sum_{n=0}^{n} H_n\right)$$

$Lmax(\cdot)$ denotes the local maximum operator, which is applied for searching the total number of local maximum positions, x. and α is a thresholding weight.

Figure 2 Illustrative example of lung tissue regions; a) original lung tissue; b) lung tissue segmented using Kapur's Entropy; c) lung tissue segmented using Tsallis' Entropy; d) lung tissue segmented using Non-Parametric KT-Entropy

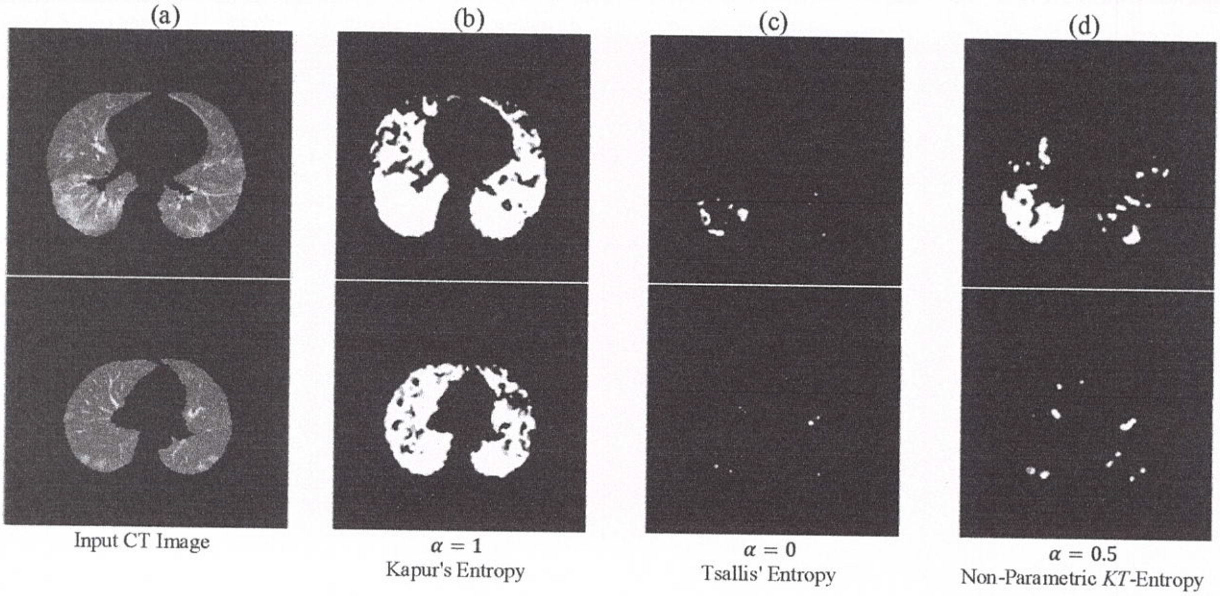

Figure 2. lung tissue regions with three segmentation methods

Following by defining a region threshold, T. Finally, we generate the local mask of sub-regions as presented in the equation below.

$$m_{i,j,k} = \begin{cases} x_{L-1}, & card(R_{i,j,k}) \leq T \\ x_0, & card(R_{i,j,k}) > T \end{cases} \tag{10}$$

where $R_{i,j,k}$ denotes the number of pixels in sub-region k. T is a threshold. x_0 and x_{L-1} represent the initial and the last grayscale levels of an image.

To generate the global mask of sub-regions, we rely on

$$M_{i,j} = \max_k (m_{i,j,k}) \tag{11}$$

where $m_{i,j,k}$ represents the local mask of the sub-region. i, j denotes the size of a given image. k is the index of $m_{i,j,k}$.

In terms of 3DRM, a 3D mesh using a 3D slicer based on the original CT scans was generated. 3D Slicer is a free, open-source platform specialized in medical image versatile visualization, computation, and research in image-guided therapy[33, 34]. After that, COVID-19 segmented lesions from row DICOM images were contoured in a slice-by-slice fashion in the transverse plane. Reconstruction of segmentation images of COVID-19 lesions was generated through 3D-Slicer, and we obtain a 3D mesh model. The user can then save the results in [.STL] or [OBJ] formats are sent to a 3D printer for printing or used as the input for VR^{2}IM. Finely, the digital 3D reconstructed model generated from 3D Slicer can be imported into various digital modeling software that allows further manipulation of the digital infected lung model.

In terms of VR2IM, we integrated Virtual Reality with CT-scan imaging to provide a three-dimensional, realistic and comprehensive display of infected lung, including COVID-19 lesions. We developed an interactive & immersive VR viewer software application using a multiplatform Unity3D graphical engine, supported by several Operating Systems, SDKs (Software Development Kits), and programming languages. This module transformed OBJ and STL format and generated FBX format directly usable to provide 3D infected lung visualization and interaction.

Through Unity 3D, we imported FBX formats and designed VR infected lungs where COVID-19 lesions were3D segmented and delineated. We used *Oculus Rift S* Head Mounted Display (HMD) (an updated version of *Oculus Rift*[35]), including sensors to recognize user movement when rotating his head in the three axes. We also use two Oculus Rift S touches devices to manipulate 3D lesions. Oculus SDK managed 3D visualization and hand interaction (translation and translation). A medical staff composed of doctors and radiologists could be provided a complete immersion in the virtual environment allowing even diving into the 3D infected lung and visualizing the 3D Covid-19 lesions, with hand manipulation of the structure (translation and rotation). They could visualize and manipulate 3D lungs on an accurate scale as if printed in 3D.

3. RESULTS AND DISCUSSIONS

The objective of our work is to provide COVID-19 lesions view in three dimensions. We focused on infected lung segmentation algorithms. We use the medical images from El-BAYANE center for radiology and medical imaging. Figure 3 shows 3D Slicer reconstructed lung images using the proposed segmentation method, with the segmented regions of the covid-19 lesions, bronchi, veins, and arteries. The images correspond to *OBJ* files. The color map that transforms the Hounsfield scale's intensities into color was manually adjusted so that the lung, covid-19 lesions, bronchi, and veins can be observed from a different scale.

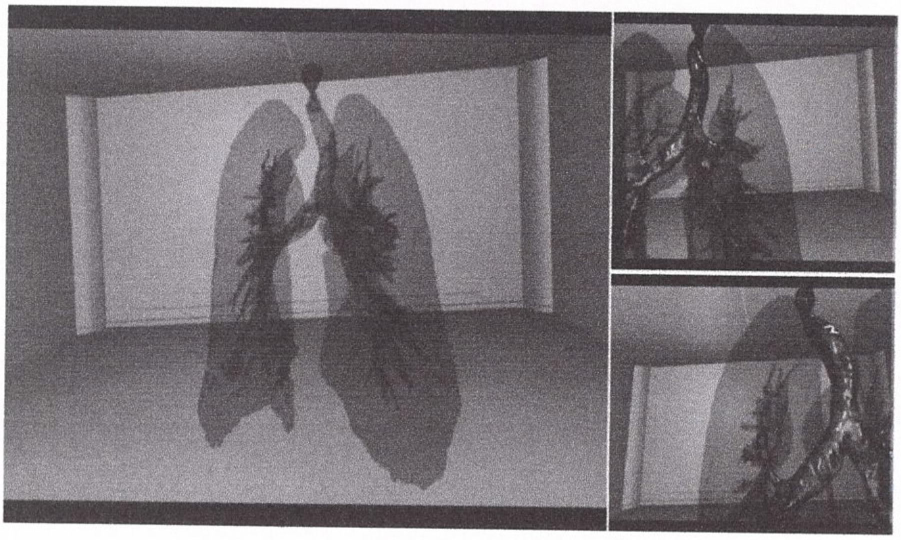

Figure 3. Volume representation of the lung segmentation with blood vessels and COVID lesion left: entire lung with veins and arteries. Upper right: an enlargement of an area with a detected Covid-19 lesion (in red color). Lower right: enlarged view of a non-infected region.

The hardware platform necessary to develop this platform should support VR rendering capacity for tablet, smartphone, and the workstation connected to the Oculus display.

The processor used was an Intel i7 at a maximum frequency of 3.60 GHz, working with a RAM memory of 08 GB with 08 GB graphical card's memory.

Once the segmentation region of Covid-19 lesions was done, we generate DICOM images converted into a smooth 3D mesh to offer doctors the most appropriate tools for visualizing the 3D model of infected lungs. Then, we transform the 3D mesh models into OBJ and STL formats which are lighter and easier to render in the 3D environment. Blender software framework imports OBJ and STL format and generates FBX format directly usable to provide 3D lung visualization. We use the Unity 3D game engine to import FBX formats and design interactive VR applications of infected lungs where COVID-19 lesions are well-segmented, and 3D described. The users could use Oculus touch to manipulate (translation, rotation, and zoom) and access the 3D lung's internal structure. Figure 4 shows the 3D visualization of COVID-19 disease of four patients' lungs using the VR platform.

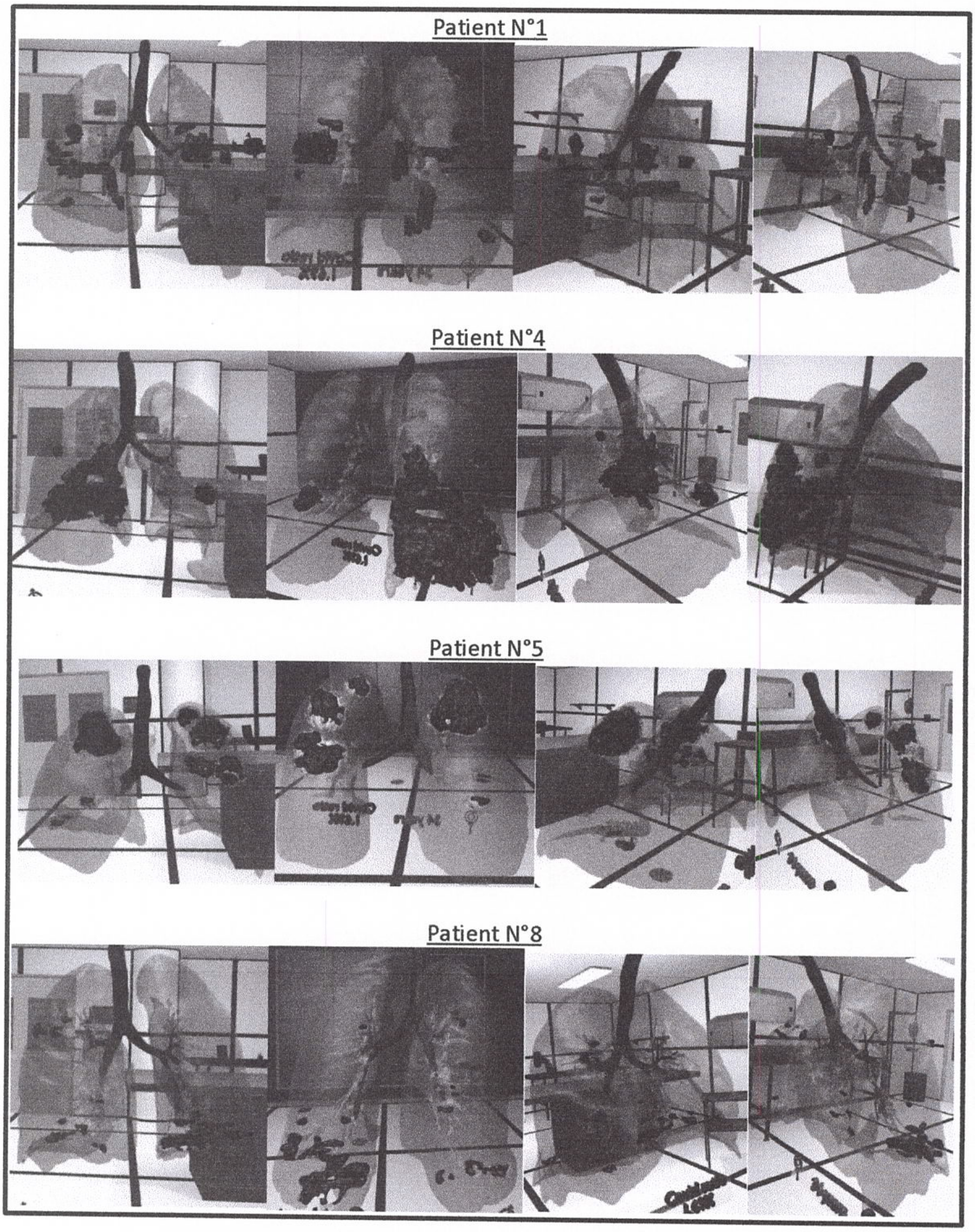

Figure 4. Virtual Reality Rendering of segmented lung with Covid-19 lesion of four patients.

To explore our proposed VR advanced CT scan diagnostic system's efficiency, we made a subjective evaluation based on the experimentations of nine COVID-19 infected patients. A set of six (06) subjects composed of doctors and researchers tested VR experiences and provided their opinions. All subjects were asked to diagnostic the nine infected patients using the VR prototype. At the beginning of the experiments, the subjects were instructed to correctly use the Oculus Rifts S HMD and the two Oculus touches. Then, they were immersed in the VR environment for two times five minutes to be familiar with the VR prototype. The experimenters were also asked to use a smartphone and an interactive Tablet to compare with HMD in terms of COVID-19 diagnosis.

Once the experimenters completed their trials, we asked them to fill a questionnaire individually. They responded using a 7-point Likert scale: 1. Strongly Disagree, 2. Disagree, 3. Somewhat Disagree, 4. Fair, 5. Somewhat Agree, 6. Agree, 7. Strongly Agree. Five parameters were evaluated through the VR experience (Table 2 shows the results of the subjective questionnaire):

Q1: Immersion sensation,

Q2: Realistic view of the lung and the infected regions,

Q3: Localization of lesions,

Q4: Enhance diagnostic and provide appropriate medical treatments to patients,

Q5: Ease to use.

Table 2: Representation of the agreement levels in response to 5 parameters for the assessment of our VR application

Question	**Subject N°1**			**Subject N°2**			**Subject N°3**			**Subject N°4**			**Subject N°5**			**Subject N°6**			**Average**		
	*H**	*S**	*T**	*H*	*S*	*T*	*H*	*S*	*T*	*H*	*S*	*T*	*H*	*S*	*T*	*H*	*S*	*T*	*H*	*S*	*T*
Q1	6	2	2	6	1	2	6	2	2	7	1	1	6	1	2	7	1	2	6.33	1.33	1.83
Q2	6	3	4	6	4	4	7	3	4	6	3	3	6	2	2	6	3	3	6.16	3.00	3.33
Q3	7	5	5	7	5	5	6	4	4	6	4	5	7	4	5	7	4	4	6.66	4.33	4.66
Q4	6	4	4	7	4	4	6	4	5	7	4	4	6	5	5	6	4	4	6.33	4.16	4.33
Q5	7	6	6	7	5	6	6	4	5	6	5	5	7	4	5	6	5	5	6.50	4.83	5.33

**H: Oculus Rift S HMD, S: Smartphone, T: Tablet*

According to question 1 (Q1), all participants feel immersed in the VR environment, and they view the 3D lung of nine patients with the infected regions when they use Oculus Rift S display. They estimated that the 3D view provided, let's imagine, as if we are in front of actual lungs. These participants noticed that, even if it was possible to see a 3D lung with infection, there no immersion through smartphones and tablets. Most of the experimenters found the 3D covid-19 lesion clear, visible, and realistic (Q2). They perceive a realistic 3D view of the COVID-19 lesion and its volume and distribution within the lung (Q2). They, however, preferred using the Oculus display since it provides a more realistic and clear view than Smartphone and Tablet. With oculus touch, they have a free hand to access inside the 3D lungs and manipulate them. With the two handheld displays, their navigation space and interaction possibilities are significantly reduced. VR viewer is a relevant tool to locate (Q3) the lesions compared to 2D view CT scan. With Oculus, the experimenters believed that it was possible to view and find the COVID-19 lesions in more detail and the tiny lesions that could hardly be viewed with CT scan. The precise location of these lesions could be well perceived with Oculus more than Smartphone and Tablet. The participants believed that 3D technology improves disease knowledge and provides appropriate medical treatment for patients (Q4). They also found the VR system easy to use (Q5). Finally, most participants found these experiences agreeable and improve their understanding of the disease. They express their ability to conduct the same experience if necessary and advise this application to medical staff.

4. CONCLUSION

Over the last decade, the VR technology emergence allowed us to work with 3D models to describe a patient's disease realistically. We can visualize and interact with 3D models entirely from the classic existing technologies and methods with these technologies. The ongoing Covid-19 pandemic made the use of these technologies highly recommended. This paper has developed an innovative system with which 3D visualization and interaction with three-dimensional infected lungs will be offered as a more accessible diagnostic tool for radiologists and doctors instead of using 2D CT scan images. The proposed system provides an alternative to complete segmentation and visualize the results with a realistic three-dimensional view. Our proposal could be considered one of the first tools that integrate virtual reality technology for COVID-19 disease diagnosis from CT-scan imaging to plan appropriate medical treatments. With the developed VR application, radiologists can analyze COVID-19' 3D models and provide a more appropriate diagnosis than 2D images. As different experimenters conclude that 3D visualization of CT-scan images using virtual reality offers a better interpretation of the radiological results and can be a breakthrough for medical treatment planning. Finally, we believe that professionals in medical fields could widely use VR in the following years to analyze radiological results since VR tends to become the general public.

REFERENCES

[1] Voronin, V. , Marchuk, V., Semenishchev, E., Cen Yigang. and Agaian, S., "Medical image segmentation using 3D MRI data," Proc. SPIE 10221, Mobile Multimedia/Image Processing, Security, and Applications 2017, 102210A (2017).

[2] Tahamtan, A. and Ardebili, A., "Real-time RT-PCR in COVID-19 detection: issues affecting the results," Expert review of molecular diagnostics, vol. 20, no 5, p. 453-454 (2020).

[3] Bollineni, V., Nieboer, K. H., Döring, S., Buls, N., & De Mey, J., "The role of CT imaging for management of COVID-19 in epidemic area: early experience from a University Hospital," Insights into Imaging, vol. 12, no 1, p. 1-5 (2021).

[4] Ozsahin, I., Sekeroglu, B., Musa, M. S., et al., "Review on diagnosis of COVID-19 from chest CT images using artificial intelligence, " Computational and Mathematical Methods in Medicine (2020).

[5] Shi, F., Wang, J., Shi, J., et al., "Review of artificial intelligence techniques in imaging data acquisition, segmentation and diagnosis for covid-19," IEEE reviews in biomedical engineering (2020).

[6] Oulefki, A., Agaian, S., Trongtirakul, T., et al., "Automatic COVID-19 lung infected region segmentation and measurement using CT-scans images, " Pattern recognition, p. 107747 (2020).

[7] Akbari, Y., Hassen, H., Al-Maadeed, S., et al., "COVID-19 Lesion Segmentation using Lung CT Scan Images: Comparative Study based on Active Contour Models," (2020).

[8] Alom, M. Z., Rahman, M. M. S., Nasrin, M. S., Taha, T. M., and Asari, V. K. "COVID MTNet: COVID-19 detection with multi-task deep learning approaches, " arXiv preprint arXiv, https://arxiv.org/abs/2004.03747 (2004).

[9] Hu, R., Ruan, G., Xiang, S., Huang, M., Liang, Q. and Li, J.., "Automated Diagnosis of COVID-19 Using Deep Learning and Data Augmentation on Chest CT, " medRxiv (2020).

[10] Ma, N., Zhang, X., Zheng, H., and Sun, J., "ShuffleNet V2: practical guidelines for efficient CNN architecture design, " in Springer International Publishing, vol. 11218, pp. 122–138 (2018).

[11] Gozes, O., Frid-Adar, M., Greenspan H., et al., "Rapid AI development cycle for the coronavirus (COVID-19) pandemic: initial results for automated detection & patient monitoring using deep learning CT image analysis, " arXiv (2020).

[12] Jaiswal, A., Gianchandani, N., Singh, D., Kumar, V., and Kaur, M., "Classification of the COVID-19 infected patients using DenseNet201 based deep transfer learning, " Journal of Biomolecular Structure & Dynamics, pp. 1–8 (2020).

[13] Singh, D., Kumar, V., Vaishali, M. K., and Kaur, M., "Classification of COVID-19 patients from chest CT images using multi-objective differential evolution–based convolutional neural networks," European Journal of Clinical Microbiology & Infectious Diseases, vol. 39, no. 7, pp. 1379–1389 (2020).

[14] Amyar, A., Modzelewski, R., and Ruan, S., "Multi-task deep learning based ct imaging analysis for covid-19: classification and segmentation," medRxiv (2020).

[15] McCann, RA., Armstrong, CM., Skopp, NA., Edwards-Stewart, A., Smolenski, DJ., June, JD., et al., "Virtual reality exposure therapy for the treatment of anxiety disorders: an evaluation of research quality, " J Anxiety Disord, 28:625–31. doi: 10.1016/j.janxdis.2014.05.010 (2014).
[16] Moreno, A., Wall, KJ., Thangaveluf, K., Craveng, L., Ward, E., Dissanayakaf, NN., "A systematic review of the use of virtual reality and its effects on cognition in individuals with neurocognitive disorders," Alzheimers Dement (N Y), 5:834–50. doi: 10.1016/j.trci.2019.09.016 (2019).
[17] Aouam, D., Zenati-Henda, N., Benbelkacem, S., Hamitouche, C., "An Interactive VR System for Anatomy Training, " In : Mixed Reality. IntechOpen (2020).
[18] Touel, S., Mekkadem, M., Kenoui, M., Benbelkacem S., "Collocated learning experience within collaborative augmented environment (anatomy course), " In: 2017 5th International Conference on Electrical Engineering-Boumerdes (ICEE-B). IEEE, p. 1-5 (2017).
[19] Yeung, A. W. K., Tosevska, A., Klager, E., et al., "Virtual and Augmented Reality Applications in Medicine: Analysis of the Scientific Literature," Journal of medical internet research, vol. 23, no 2, p. e25499 (2021).
[20] Pareek, T. G., Mehta, U., Gupta, A., et al., "A survey: Virtual reality model for medical diagnosis," Biomedical and Pharmacology Journal, vol. 11, no 4, p. 2091-2100 (2018).
[21] Ueda, M., Martins, R., Hendrie, PC., McDonnell, T., Crews, JR., Wong, TL., McCreery, B., Jagels, B., Crane, A., Byrd, DR., Pergam, SA., "Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal," J Natl Compr Canc Netw (2020).
[22] Haleem, A., Javaid, M., Vaishya, R., Deshmukh, SG., "Areas of academic research with the impact of COVID-19, " AJEM (Am J Emerg Med), https://doi.org/ 10.1016/j.ajem.2020.04.022 (2020).
[23] Singh, R. P., Javaid, M., Kataria, R., et al., "Significant applications of virtual reality for COVID-19 pandemic," Diabetes & Metabolic Syndrome: Clinical Research & Reviews, vol. 14, no 4, p. 661-664 (2020).
[24] Mantovani, E., Zucchella, C., Bottiroli, S., et al., "Telemedicine and virtual reality for cognitive rehabilitation: a roadmap for the COVID-19 pandemic, " Frontiers in neurology, vol. 11 (2020).
[25] Kapura, J.N.; Sahoob, P.K.; Wongc, A.K.C. A new method for gray-level picture thresholding using the entropy of the histogram. Comput. Vis. Graph. Image Proc. 1985, 29, 273–285.
[26] L. A. Passos et al., "κ-Entropy Based Restricted Boltzmann Machines," 2019 International Joint Conference on Neural Networks (IJCNN), Budapest, Hungary, 2019, pp. 1-8.
[27] S. Sharma and I. Bassi, "Efficacy of Tsallis Entropy in Clustering Categorical Data," 2019 IEEE Bombay Section Signature Conference (IBSSC), Mumbai, India, 2019, pp. 1-5.
[28] Shannon, C.E. The mathematical theory of communications, I and II. Bell Syst. Tech. J. 1948, 27, 379–423.
[29] Singh, V.P.; Oh, J. A Tsallis entropy-based redundancy measure for water distribution network. Physica A 2014, 421, 360–376.
[30] Singh, V.P. Entropy Theory in Hydrologic Science and Engineering; McGraw-Hill Education: New York, NY, USA, 2015.
[31] Papalexiou, S.M.; Koutsoyiannis, D. Entropy based derivation of probability distributions: A case study to daily rainfall. Adv. Water Resour. 2012, 45, 51–57.
[32] Tsallis, C. Possible generalization of Boltzmann-Gibbs statistics. J. Stat. Phys. 1988, 52, 479–487.
[33] Hata, N., Piper, S., Jolesz, F. A., et al., Application of open source image guided therapy software in MR-guided therapies," In: International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Berlin, Heidelberg, p. 491-498 (2007).
[34] Fedorov, A., Beichel, R., Kalpathy-Cramer, J., et al., "3D Slicer as an image computing platform for the Quantitative Imaging Network. Magnetic resonance imaging, " vol. 30, no 9, p. 1323-1341 (2012).
[35] Chessa, M., Maiello, G., Borsari, A., et al., "The perceptual quality of the oculus rift for immersive virtual reality," Human–computer interaction, vol. 34, no 1, p. 51-82 (2019).