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Review Article

A Short Review of Benefits of Using Chest CT Characteristics for Early diagnoses to Corona Virus Disease 2019 (COVID-19)

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ABSTRACT

In 21st century, the year 2020 was expected with much development in India as well many other countries. But unfortunately, the world is facing many natural calamities. World is taking steps towards rescue mission of the disasters. Among of those calamities, deadly Corona Virus remains still all over the world as pandemic disease. Even the developed countries are struggling to come back to its normal routine. India is a country with developing technologies. Vaccines are yet to be developed for treatment of this Novel Corona Virus. As a diagnostic tool, Nasopharyngeal and Oropharyngeal swabs are taken from the person and tested using RT-PCR. This test is not 100 percent accurate. Confirmed COVID patients after few days are undergoing the medical imaging. This diagnostic imaging technique helps in showing the progression of this virus spread in Upper and Lower respiratory system. Chest Radiography is low cost modality but its sensitivity towards observation is 69%. Lung Ultrasound is used in Intensive Care patients and not used for routine diagnosing purpose. Computed Tomography plays a crucial role in three-dimensional chest imaging of COVID-19 patients. The sensitivity of CT is 98%. The aim of this paper is to consider CT as a tool for diagnosing COVID-19 patient than using the standard tool RT-PCR. A brief knowledge about imaging modality like X-ray, Ultrasound and Computed Tomography when used against COVID patient is explained. This paper gives reason for the ideal use of CT diagnosis for COVID 19.

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Introduction

The foundation of the year 2020 is with many global issues. The most important issue among those are Novel Corona Virus (COVID-19). It is a pandemic outbreak which initially began in December 2019. This virus is transmitting from human to human and is originated from sea market of Wuhan, China. The first country to report COVID-19 is United States in beginning of the year 2020. The name COVID-19 got its name from Corona Virus by International Committee of Taxonomy on Virus and World Health Organization. The number 19 represents the year of virus spread. Corona Virus is a communicable disease transmitting from animals to humans and humans to humans. It is a common cold which further leads to severe respiratory problems and it is officially named as SARS CoV-2 which causes COVID-19.

Fever, cough and shortness of breath are the symptoms of this infection. Day by day number of infected cases is increasing rapidly in all over the countries. This infection is leading to SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome). The Clinical physicians are doing their research in transmission of this infection. United States of America, Brazil, India, Russia, South Africa, Peru, Mexico, Chile, Spain, United Kingdom are the top ten countries which has high spread of this infectious virus in the world. As per information of World Health Organization Novel Corona virus by 2 August 2020, has infected 17,628,109 people all over the world. All over 216 countries are affected by this virus. The people who lost their life due to corona virus are 680,354. United States of America, Brazil, South Africa, Mexico, Peru, Chile, Iran, United Kingdom, Columbia and Bangladesh are the countries with social Corona virus spread. Corona virus is an infectious disease which spreads from human to human by

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saliva from the infected person. The transmission takes place by the droplets of COVID-19 to surrounding persons. Before the invention of medicine for its treatment, it is best to reduce the transmission and preventing it.

World Health Organization (WHO) is involving all the scientists and health professionals together to involve in research and development [1-3]. Every health professionals like virologist, epidemiologist are involved more in finding the cause of the infection as well as creating vaccine for eradicating the spread. The Research and Development blueprint has been activated to accelerate Vaccines, accelerate and therapeutics for this novel corona Virus. Food and Drug Administration (FDA) granted Emergency Use Authorization for the investigational antiviral drug "Remdesivir". FDA also approved Hydroxychloroquine and chloroquine (antimalaria drug) as EUA for the treatment of COVID-19 symptoms. Currently no approved medications or vaccines can cure SARS-CoV-2 infections. At present, Prevention is the better treatment.

People aged above 65 years and older, people with uncontrolled health conditions, weakened immune systems, people with severe obesity, people with renal and cardiac problems are at high risk of developing severe COVID-19. Patients with severe infection are taken into immediate medical treatments like mechanical ventilations, Intravenous treatment, sedative treatment. The ultimate things can be done now is to identify the infected person to be hospitalized soon as possible. In response of the spread of Corona virus, the laboratory for testing is very less. There occurs the development of multiple diagnostic tools which should be easy to use. WHO evaluated the immunodiagnostics test for COVID-19. Clinical diagnostics includes molecular and serology assays for further research development. The different types of COVID-19 tests are molecular test, antigen test and antibody test. The molecular test also known as RT-PCR (Reverse Transcription Polymerase Chain Reaction) includes Nasopharyngeal and Oropharyngeal swabs have been mostly preferred for the respiratory infection of COVID-19. These molecular based diagnostic tests can detect only the current and active infections of pathogens [4-11].

WHO advices to restrict the international travel. By restriction of travellers from one country helps in non-movement of people. This leads to reduce in transmission of infection. People are advised to wear masks and to maintain social distance. WHO is updating the daily reports of infected number of corona cases. Initially infected person and their contact was easily found out and sent to quarantine. Thermal scanner, thermometer acts as a primary screening method for suspecting the COVID-19. But temperature screening alone does not work out best for finding the COVID-19. By personal hygiene caring tends to keep oneself safe and secured. Soon there occurs the demand for hand sanitizer, gloves and masks. The PPE (Preventive Protective Emergency) Kit by doctors, nurses, radiologists and attendees are being used to protect themselves from COVID-19.

A report says that almost 50 million people of china tested for corona. Those people had symptoms of mild to severe. Chinese government implemented lockdown for the entire country. As there was an increase in number of infected cases, sooner they built temporary hospitals for treatment within a week. Sooner there was a drop in infected cases and made infected cases under control. That drop was possible because of their usage of diagnostic imaging technology. They used RT-PCR as a

primary kit for corona check. And later, as number of cases increased, they used Computed Radiography for finding the viral spread of patients. By June 8 2020, New Zealand was the first country to report no active cases in the world.

Novel Corona virus can exhibit in two forms. Many days it was believed that affected person will be having symptoms like fever, cough or any respiratory problems. Later it was revealed that persons without any symptoms also become victim of corona virus. For mild symptoms cases the recovery time is two weeks. For severe symptomatic patients the recovery time ranges from three weeks to six weeks. From the researchers' side, RT-PCR is considered as the golden standard of Novel COVID-19 diagnosis. Nucleic Amplification Acid Testing (NAAT) is a retrospective study for COVID-19. RT-PCR is one form of NAATs which is used as a primary diagnostic tool for preventing the spread of infection or to control the spread of infection.

Reverse Transcription- Polymerase Chain Reaction (RT PCR)

Reverse Transcription- Polymerase Chain Reaction is the measure of gene expression by amplifying cDNA reverse transcribed from RNA. Replication transcription and translation is mostly commonly known as "Central Dogma of Life" in molecular biology. There are two types of processes in qPCR: One step procedure and two step procedure. RT-PCR tests are very sensitive and reliable.

RT PCR is a test to detect the presence of viral RNA in sample collected. It is named as *in vivo* diagnostics (IVD) by FDA. For measuring the viral RNA, it has to be converted into DNA for multiple times. The sample has to withstand repeated temperature cycles in a PCR machine. Fluorescent markers will be used for identifying the virus. The presence of virus level is determined with respect to fluorescence. To reach the threshold value, the PCR machine undergoes many temperature cycles for evaluating the quantity of virus present in sample. The lesser number of cycles indicates presence of virus in more number. The test can be done quickly and results can be obtained within 3-4 hours. In real time, the results are delayed due to time taken for the samples to be tested in specialized laboratories. The results are produced after 6-8 hours from laboratories [12-15]. The practical way of eradicating the spread of SARS-CoV-2 is that millions of tests are required per week in a country says by epidemiologist. But it is not easy as words. The country should have standard laboratory, expertise personnel and expensive equipment for carrying out the test. This is the main cause of limited test in developing and under-developed countries. There is shortage of test kit available, materials like swabs, chemical agents. This leads to time delay on test results even in developed countries like USA.

The result is given as True positive and False negative. Positive test result shows that person has infected virus. Negative test results mean the absence of infected virus in person at that time. This leads to change in RT-PCR results which later increase the chance of incorrectly missing the infected person. RT-PCR test is a test to determine the presence of active virus. The test has sensitivity of 90 percent means; it can give 90 percent people with accurate results. Remaining 10 percent people will be shown as false negative even though with the presence of virus. This is one of the major drawbacks of diagnosing. It only tries to detect the presence of particular corona virus. No information will be provided for the symptoms felt by the patient who is with negative test results. The

evidence of many test results shows that sensitivity and specificity of RT-PCR gives false negative results. RT-PCR test is not 100 percent accurate. The sensitivity of RT-PCR is 65-95%. In current emerging situation, the low sensitivity of RT-PCR implicit a greater number of COVID-19 will be left free. These infected patients have to be isolated and should be monitored under medical expertise. RT-PCR test costs are expensive which is the major struggle diagnosing COVID-19.

According to WHO, it is possible that current antibody test may cross-react with other human corona viruses, resulting in false negative. Neither the RT-PCR test nor serological tests are perfect. But they are far better than nothing says the Medical expertise. So, Researchers

started moving to many other devising tests than RT-PCR. Infected patients are classified as symptomatic and asymptomatic. Asymptomatic patients do not have any symptoms, whereas symptomatic patients have mild, severe and critical symptoms. In mild illness, there will be little cough and fever. Involvement of lung damage for 50 percent, hypoxia and dyspnea are severe illness of COVID-19. Critical situation of COVID-19 patient includes respiratory problem and non-functioning of many organs and ultimately leading to death of patient. It is necessary to take utmost care on critical patients. Symptomatic patients can be found more or less with any diagnostic tests. But asymptomatic patients cannot be found that much easily which may result in severe situation for many.

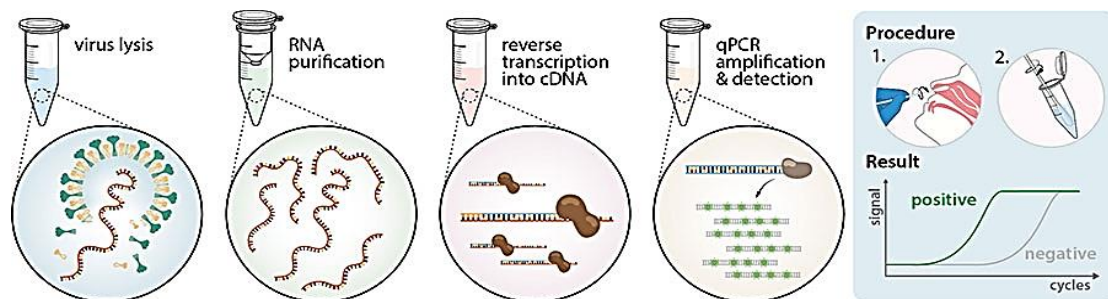


Figure 1: The procedure for RT PCR test to COVID-19 [23].

All symptoms of this virus are infecting throat, respiratory tract and lungs. Using the RT-PCR, identification of active corona virus is possible. But it does not give the information about the viral spread or aggregation of virus as shown in (Figure 1). The standard test and molecular test give delayed and false reports of Novel Corona-virus. The clinical presentation of COVID-19 coincides with much other respiratory illness. Early detection and isolation of patients is needed for controlling the spread of infection. Here comes the use of Medical imaging techniques for diagnostic purpose. SARS and MERS are infection occurring at Upper Respiratory System (URS) and Lower Respiratory System (LUS). Chest imaging is an early measure for caring the patients with suspected or confirmed COVID-19. Chest imaging plays major role in diagnosing the infected person with pneumonia or SARS CoV-2. Chest imaging can be done through modalities like radiography, Computed tomography and Ultrasound. Diagnosis of COVID-19 is a challenging method. In this Radiology plays a major role in investigating the infection.

Chest Radiography (CXR)

It is easily available in all hospitals. It is a low-cost modality for imaging investigations. A study says that "Patient in emergency situation with symptoms may have normal lungs in CXR but still with infected pneumonia". The doctors can further treat them with needed medication after knowing the internal anatomy of a patient. CXR is helpful in urgent diagnosis of patients widely. Chest radiograph can be considered for mild cases with required frequency of imaging before it develops to high risk of infection. CXR is taken as anterior-posterior for symptomatic patients. Unfortunately, many patients who found positive test results in RT-PCR were found as negative results in Chest radiograph. Using CXR, interpretation of X-ray films by radiologists goes wrong. A study says that initially radiologists were unable to confirm the symptomatic patients with proper findings. Many reports are re-read and resulted as abnormal which are previously said as normal. Even the experienced

radiologists who knew diagnostic well still re-read more than half percentage of X-ray films and reported back with abnormal or mild abnormality. The findings of CXR can be read for bacterial infection like bacterial pneumonia and pneumothorax. CXR cannot help up for COVID-19. CXRs rays are still useful for diagnosing with less sensitivity. Countries like China and Italy used CXR as primary screening method for COVID-19. The findings of abnormalities in CXR were delayed. From the onset of symptom to progression of diseases, CXR findings are delayed. This shows the low sensitivity of CXR. It has sensitivity of 69%.

Ultrasound

Ultrasound is an imaging modality which uses non-ionizing radiation. LUS is a lung ultrasound method for diagnosing lung. POCUS (Point of Care Ultrasound) is used for finding lung parenchyma. Ultrasound can be used in emergency personnel to triage and diagnose the suspected COVID patients. Lung Ultrasound is used for observing specific portion of lungs which can show only patchy bilateral spread of lesions. Lung Ultrasound can be used for only acute respiratory failure patients. End Stage Renal Disease patients are also at high risk. Ultrasound along with blood samples gives better results for SARS CoV-2. LUS can be done to patients who are tested with swabs. At early days of infected person, no pattern of LUS can be found. Evaluation of findings in LUS can be done only at later days of symptomatic patients. Ultrasound is helpful for COVID-19 patients at Intensive Care Unit (ICU). This modality test cannot be considered for early diagnosis of COVID-19 patients. One of the limitations is that it has low sensitivity and applicable only for symptomatic patients at high risk. LUS is used for patients with triaging symptoms in multiple setting such as symptomatic patients, emergency department and Intensive Care Unit. There will be risk of transmission of this disease since ultrasound makes closer contact of staff technologist and patient.

Computed Tomography (CT)

To get maximum sensitivity of diagnosis, there plays a role of Chest Computed Tomography. Computed Tomography uses X-ray machine which rotates in 360 degree to give cross section of body in images. CT uses ionizing radiation for obtaining the images. CT uses many detectors for detecting the images. Using CT, images of bones and internal organs can be viewed. CT gives detailed information about internal structure of the body than conventional X-ray. Conventional Radiography gives two-dimensional (2D) data whereas computed tomography gives three-dimensional (3D) data. Since Chest Computed Tomography for diagnosing pneumonia are routinely used. CT image may give better sensitivity than RT-PCR testing for novel corona virus. Patients with negative RT-PCR results show positive results in CT images. This makes the doctors to be confused. The main CT chest findings are Ground Glass Opacities and bilateral chest CT findings. CT can detect early diseases. Abnormalities are found in CT from the day of infection to progressive spread of infection. Morphology, distribution and severity are the specific features of CT scan. The sensitivity and specificity of CT scan varies over the time of infection. So, the rapid change in lung can be easily studied. The progression of CT lung scan shows the data from the onset of symptoms, i.e., from the day of suspect to the day of recovery. By the pattern of lung, it is easily found by the radiologists to report regarding the progression of Corona virus. In china, they were able to diagnose and report more number of infected cases with the help of imaging modality like Computed Tomography. CT can be taken to triage patients and for prediction of worsening condition. In severe illness of patient, CT scan show better sensitive image data. It is also used for improvement purpose. The frequency of CT imaging depends upon the clinical situation of patients. When the findings of CXR and CT are compared for lung, the abnormalities are found in later and early days respectively from the onset of symptoms. The sensitivity of CT is 98 percent and it is preferred as best diagnosis for novel corona virus.

Since Computed Tomography uses ionizing radiation, radiation delivered to patient has to be monitored carefully. Using ALARA principle, image acquisition can be done. Following all the radiation protection protocol, exposure should be reduced. Before letting the patient to leave, quality of image should be ensured. The report of the image should be sent to the physician immediately through PACs. After imaging of each suspected COVID-19 patients in CT couch, it has to be cleaned and disinfected.

The cure for this infection is not known still. Many new vaccines are being developed for welfare of humans. Early diagnosis and controlling the spread of infection is still possible. Early diagnosis like RT-PCR shows oscillating results. But chest Computed Tomography gives better results even for false negative RT-PCR test reports. Through diagnostic imaging, it is possible to know the severity of infection spread. The investigations involved in Computed tomography and radiography for finding the pathology of chest. Lung Ultrasound can also be used for only acute respiratory failure patients. Computed Tomography helps in monitoring and evaluating rigorously of the disease. Appearance of lung differs from the day of infection to recovery state. In recent studies, it is reported that sensitivity of CT is superior to RT-PCR. Lung Computed Tomography is considered a the better imaging modality for early diagnosis of pulmonary infection, which may easily cause SARS-

CoV-2. But the controversial argument is about CT is imaging modality which uses ionizing radiation may increase the patient dose.

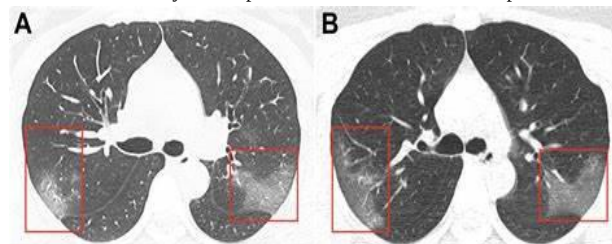
Radiation plays a major role in cancer treatment. Radiotherapy is the field where radiation is used as a beneficial way for controlling the spread of cancer cells. Radiation therapy uses high and low energy transfer radiation (gamma rays, protons) to kill the cancer cell. This works on the basis of radiobiology of cells. A better understanding of radiation and biological effects of cells when interacting with radiation has to be known. Radiation is useful when it is used with radiation protection protocols. Total dose, fractionation rate, Linear Energy Transfer (LET) and radiosensitivity of cells are the important factors of biological effects of radiation. Ionizing radiation has been used for cancer treatment from 19th century.

Ionizing radiation has more effects in proliferating cells than normal cells. CT can deliver maximum of 2mGy for COVID pneumonia patients. This low dose cannot lead to patient dose. The deposition of radiation has the potential to control the inflammatory response of the virus cell which is multiplying rapidly.

CT Scan and Imaging Analysis

Computed tomography is a non-invasive technique. It provides human anatomical data without superimposition of adjacent areas. Here in dealing with COVID-19 patients, CT plays a major role for diagnosing. The clinical characteristics of infected patients are well differentiated in chest CT image. In the early stage of pneumonia patient, there were SARS and later leads to ARDS (Acute Respiratory Distress Syndrome), MERS and other severe complications. Patients who underwent chest CT scan show bilateral pulmonary parenchymal ground-glass, pulmonary opacities. While reading the CT scan image, lung lesions can be observed. We know that there are persons infected with symptoms as well as without symptoms of corona virus infection.

Predominantly alveolar changes occur. Ground glass opacities, reverse halo sign, focal consolidations, peripheral distribution, septal thickening, pleural effusion are the signs of corona virus infection. CT scan helps in determining the early signs of virus infection to severity of spread. The early stage, progressive stage and peak stage of corona virus infection shows indications in chest CT of lung as shown in (Figure 2). Radiologists who are familiar with COVID-19 involvement spectrum as observant to identify and to provide treatment for infected persons.



Figures 2A & 2B: Unenhanced chest CT showed multiple peripheral ground-glass opacities in both lungs that did not spare the subpleural regions. On the basis of epidemiologic characteristics, clinical manifestations, chest images, and laboratory findings, the diagnosis of 2019-nCoV pneumonia was made. After receiving 3 days of treatment, combined with interferon inhalation, the patient was clinically worse with progressive pulmonary opacities found at repeat chest CT (B) [24].

Symptomatic COVID-19 Patients

Chest CT films are useful in the follow up of the disease. Symptomatic patients have 79% of characteristics of CT scan image. GGO (Ground Glass Opacities) are the predominant clinical representation of CT images from the symptom onset of infection. As infection increases by day, GGO reduces and consolidation becomes the most commonly occurring pattern. Along with consolidation, bronchiolectasis, irregular interlobular and septal thickening also occurs. As the disease progressed, pleural effusion adds on it. Continuous monitoring of CT scan images helps in change of disease in person [16-18].

Asymptomatic COVID-19 Patients

Chest CT in asymptomatic patient is a useful way of diagnosing. By using this imaging modality, asymptomatic patients can be isolated as soon as possible. Studies show that 50% of ground glass opacities and 20% of other abnormalities are the indications of Chest CT images. 54% of chest CT characteristics are observed for asymptomatic patients [19-22].

Duality of Radiation

Medical imaging is indispensable tool in medical field. Computed Tomography enables precise visualization of anatomical structures. Thus, Computed Tomography has its highest sensitivity of diagnosing the spread of infection in human. Since CT uses ionizing radiation for image acquisition. The use of radiation in diagnosis and treatment is increasing rapidly in recent years. Radiation therapy also uses ionizing radiation for curing cancer patients. Ionizing radiation plays dual role in medical field. We know Low dose ionizing radiation used for diagnostic imaging and high dose ionizing radiation used for therapeutic purpose. The amount of radiation received by tissue/organ is referred as absorbed dose usually measured in Gray (Gy). The effective dose refers to the measurement of ionizing radiation's biological response of causing harm. It is expressed in Sievert (Sv). High doses and high dose rate cause some side effects. When low dose is delivered for period of time (Low Dose Rate), the risk is low at the same time there is greater chance of repairing the specific damage. By using radiation protection rules, ionizing radiation can be used for diagnostic imaging and for reducing the spread the infection. The ALARA (As Low As Reasonably Achievable) principle is used for maintaining the exposure of radiation dose as low as possible and to ensure safety.

Conclusion

COVID-19 is an international health problem in recent times. Many researchers are involved in preparing vaccine for this deadly virus infection. At present, we are in need to save the lives of many people across the world. Focusing in diagnosing and isolating is preferred primarily in order to reduce the mortality rate. In mean time, person with symptom or asymptomatic are to be tested and quarantining them is important. RT-PCR is golden standard of testing the Novel Corona Virus. The result of RT-PCR is not same when the person is tested again. This shows less specificity of this diagnostic tool. In order to obtain the spread of virus infection, medical imaging techniques take part in this war. Sooner then, there arises many contradictions of using imaging modalities like X-rays, Ultrasound and Computed tomography for

COVID-19 patients. But in these pandemic times, we need to understand the situation and take necessary action for diagnosing and steps needed to recover from the Novel Corona Virus. Among all the imaging modalities, Computed Tomography shows the highest sensitivity of diagnosing corona virus. Every stages of infection can observe clearly and help in treatment to cure. Many conflicts occur in usage of Computed Tomography as a screening tool because of its ionizing radiation may increase in patient dose. But this modality which uses ionizing radiation does not give dose to patient; it acts as healing method by controlling the spread of corona virus. By understanding the impact of radiation in inflammatory response and immunity will help in recovering the rapid spread of corona virus in upper respiratory system. Everything is theoretically impossible until it is done.

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