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COVID-19: The Scientific Modality of Treatment Using High Energy Ionizing Radiation 10-15 MV X-Ray Photon

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Abstract

Introduction: The pandemic COVID-19 has emerged from Wuhan city of China in December 2019 and now spread all around the world till the end of March 2020. The World Health Organization (WHO) has named this corona virus disease as COVID-19 and defined it as the disease caused by severe acute respiratory syndrome corona virus -2 (SARS-CoV-2).

Aim: The aim of this study was to find out a possibility for the treatment of a patient infected with SARS-CoV-2 (COVID-19) using high energy ionizing radiation, 10-15 MV X-ray photon, based on biological facts and scientific evidences.

Materials and Methods: RNA is the integral part of SARS-CoV-2**.** And it is well-known fact that high energy ionizing radiation is able to break strand of both RNA and DNA causing cell death. SARS-CoV-2 enters into host cells using spike-glycoprotein consists of a large ectodomain. The ectodomain contains a receptor-binding unit S1 and a membrane-fusion unit S2.

Results: Several studies showed that there are basic similarities in chemical bonding of base of RNA and DNA. Adenine, Guanine, Cytocine and Uracil are common and identical components. These common components have weak hydrogen bonds. Single-stranded RNA (ss RNA) is the major structural component of SARS-CoV-2.

Discussion: The pandemic COVID-19 has panicked the world. There is no clinically approved medicine for this deadly disease up till now in the medical science. Only symptomatic treatment is given to the patients. On analyzing the several studies and literatures related to radio-biology, molecular biology, virology and radiation oncology, our medical physicist team found that DNA and RNA have many identical and common features. And high energy ionizing radiation (IR) is capable to break the strand of RNA, spike-protein, lipids and kill the viruses.

Conclusion: High energy ionizing radiation has a peculiar capability to damage the strand of RNA, proteins and lipids which are the integral parts of SARS-CoV-2. It is able to break the bond between ACE-2 of host cell and Spike- protein of SARS-CoV-2. Hence, it is concluded that 10-15 MV X-ray photon should be used for the treatment of patients infected with SARS-CoV-2 and it will surely give better result.

Keywords: SARS-CoV-2; Ionizing radiation; COVID-19; RNA; Receptor ACE-2; X-ray photon; Radio-biology

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Introduction

The pandemic COVID-19 has emerged from Wuhan city of China in December 2019 and now spread all around the world till the end of March 2020. The World Health Organization (WHO) has named this corona virus disease as COVID-19 and defined it as the disease caused by severe acute respiratory syndrome corona

virus -2 (SARS-CoV-2). The severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) belongs to the beta- corona virus family. Human corona viruses (HCoVs) spread in a similar fashion as Rhinoviruses, by direct contact with infected secretions or large aerosol droplets [1].

This virus belongs to a very important family of animal and human viruses that are in permanent circulation [2]. There are four common type human corona viruses identified which are NL63, OC43, E229 and HKU1. They are responsible for 10–20% of respiratory infections worldwide and are present in all continents [3-14]. In fact, mortality is poorly assessed, but it is clear that there are chronic carriers as well as asymptomatic carriers. Several studies have shown that there are as many asymptomatic carriers as symptomatic patients.

In 2003, a number of reports published with evidences of spreading the corona virus to many countries such as United States America, Hong Kong, Singapore, Thailand, Vietnam and in Taiwan. Several cases of SARS caused by corona and their deaths more than 1000 patient was reported in 2003. This was declared as the black year for microbiologist. This was the time when microbiologist started to understand the severity of these issues. After a deep study of the problem, they enabled to conclude and understand the pathogenesis of disease and discovered the cause as corona virus.

A report published on 24 Jan 2020 related to corona virus infected patient having many common symptoms such as fever, cough and fatigue; whereas diarrhea and dyspnoea were found to be as uncommon feature. A large number of patients infected with corona virus reported bilateral abnormalities. Corona virus was isolated from bronchoalveolar lavage fluid in china in 2020. It is also detected in blood samples. Corona virus is not firmly confirmed up till now in feces and urine sample of patient [15-17].

It was the Health Commission of Hubei province, China, first declared a cluster of peculiar cases of pneumonia in December, 2019. In beginning, total 27 patients were reported, which was further increased to 41 on Jan 11, 2020, with seven severe cases and one death [18,19]. Some of them were reported to have radiographic ground-glass lung changes; normal or lower than average white blood cell lymphocyte, and platelet counts; and deranged liver and renal function.

Most of them were found to be geo-graphically linked to the Huanan seafood wholesale market, which was further reported by journalists to be selling freshly slaughtered game animals [20]. Chinese health authority reported that the patients initially diagnosed negative for common respiratory viruses and bacteria, but few days later found positive for COVID-19. After that Chinese scientists studied about this virus at large scale and did sequencing its genome [21-23].

The aim of this study was to find out a possibility for the treatment of a patient infected with SARS-CoV-2 (COVID-19) using high energy ionizing radiation (10-15 MV X-ray photon) based on biological facts and scientific evidences.

Materials and Methods

The novel corona virus (COVID-19) is a virus enveloped with single-stranded RAN genome contains 29891 nucleotides, encoding for 9860 amino acids [24]. The structural details of novel corona virus (CoV) are shown in **Figure 1.** When virus enters the cell, the viral RNA genome is released into the cytoplasm and is transplanted into two poly-proteins and structural-proteins, after which the viral genome begins to replicate.

Similarities between DNA and RNA

RNA is the genetic material for SARS-CoV-2. The bases of DNA and RNA have similar chemical bonds like H-O, H-H, N-H and H-OH. The chemical bond of different components of RNA and DNA are identical, displayed in **Figure 2.**

Impact of radiation on RNA and DNA

This is the established fact that high energy ionizing radiation (IR)

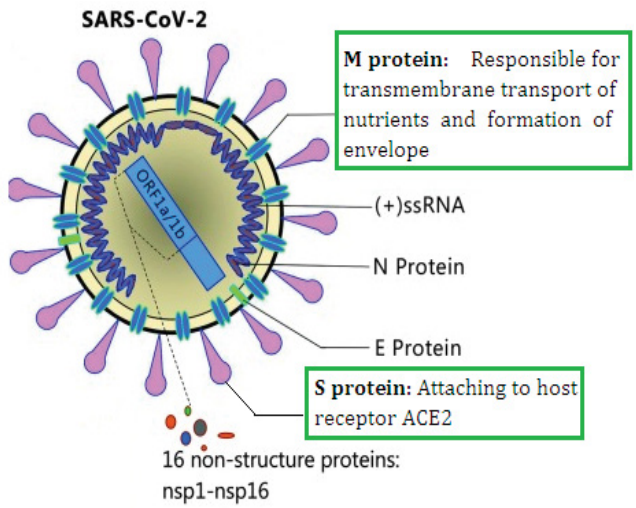

Figure 1 Structural details of SARS-CoV-2.

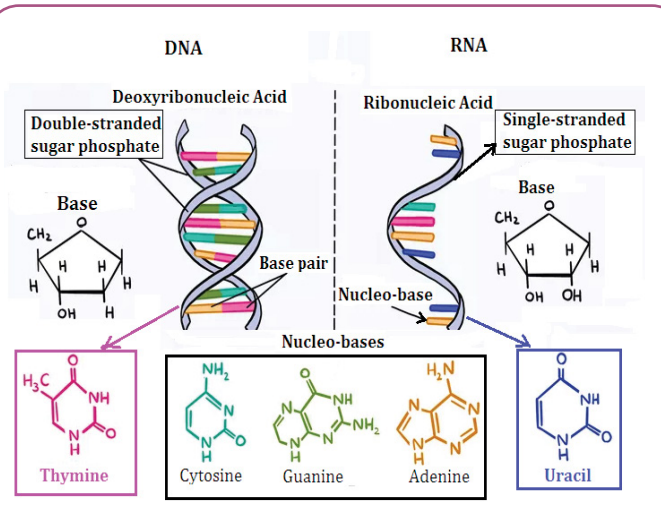

Figure 2 Basic similarities and differences between RNA and DNA.

is capable to break strands of DNA causing cell deaths. This is the primary biological basis of radiation therapy to treat cancer using high energy X-ray photons. Since the chemical structure of 'ss RNA' (major component of SARS-CoV-2) is very much similar to DNA. Scientifically, there is good chance that high energy ionizing radiation (IR) will certainly damage the RNA and Spike-protein of SARS-CoV-2 causing SARS-CoV-2 death, displayed in **Figure 3.**

The ionizing radiation may cause severe damage by breaking bonds or removing electrons in biological molecules, disrupting their physical structure and function. The damage can also be done indirectly on account of ionizing H_2O (the most abundant molecule in living organisms), which forms a H_2O^+ ion that reacts with water, forming a hydronium ion and a hydroxyl radical. The hydroxyl radicals further react with all kinds of biological molecules (RNA, proteins, and enzymes) and consequently bring physical damage to the molecules and disrupt the physiological processes of SARS-CoV-2.

Impact of radiation on receptor (ACE-2)

SARS-CoV-2 enters into host cells using spike-glycoprotein consists of a large ectodomain [25]. The ectodomain contains a receptor-binding unit S1 and a membrane-fusion unit S2. Angiotensin-converting enzymes-2(ACE-2) is the functional receptor of SARS-viruses. When a virus enters a host cell, S1 binds to cell surface receptor using its receptor-binding domain (RBD), and S2 fuses the host cell and viral membranes. Thus, the viral genomes enter into host cells. Spike- glycoprotein plays an important role in SARS-CoV-2 infection as attaching the corona virus to ACE-2 on the surface of host cell.

Hence there is need to block or damage the RBD and ACE-2 interaction to stop the corona-virus infection [26]. Several studies carried on Fukushima nuclear disaster survivors showed that ionizing radiation able to damage or break the physical structure of ACE-2 [27]. If small amount of radiation is given to the SARS-CoV-2 infected area, it will rupture the physical structure of ACE-2 and break the molecular bond between spike-glycoprotein and ACE-2 **(Figure 4).**

Selection of energy

We should be very specific in the selection of ionizing radiation (IR) in the treatment of a patient suffering with COVID-19. The major types of IR are alpha particles, beta particles, X-rays, and gamma rays. Since alpha- and beta- particles have very low penetrating power, while X- and y- rays have very high penetrating power and cause high degree of biological damage as compared to alpha- or beta-particles. However, all four types of radiation are successfully utilized for therapeutic purposes and are capable of causing significant cellular damage (RNA and DNA) [28,29].

The high energy X-ray photon beam (10 -15 MV) would be suitable for the treatment of COVID-19 patients as it is able to generate neutrons as well. And neutrons able to interact with hydrogenous materials found in the living organisms and damage them severely [30]. Hence, this is the basic reason and additional advantage of using 10-15 MV photons in the treatment of patients infected with SARS-CoV-2 the radiation weighting factors of suitable IR is tabulated in **Table 1** [31].

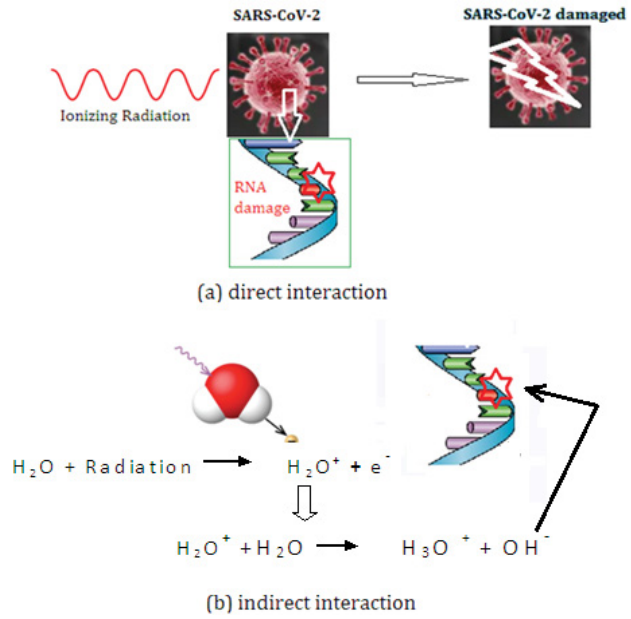

Figure 3 Pictorial representation of interaction of radiation with RNA and damage of SARS-CoV-2.

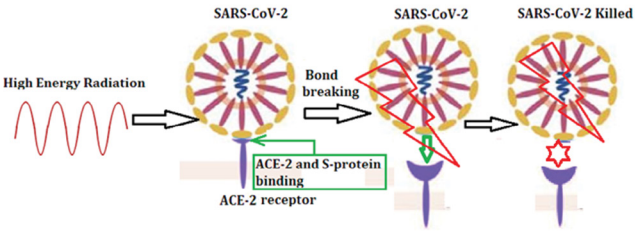

Figure 4 Displaying the breaking of bond between receptor ACE-2 and Spike-protein of SARS-CoV-2 due to high energy ionizing radiation.

Dose determination and treatment modality

After investigating a number of studies and literatures, our medical physicist team reached to a conclusion that 0.2-0.5Gy of IR dose is adequate dose to break the chemical bounding of base of RNA and double strands of DNA [32-34]. This amount of dose is also sufficient dose to break the lipids, spike- proteins and further lead to kill SARS-CoV-2.

As per clinical findings, SARS-CoV-2 holds in throat, nasal cavity and lungs of the patients having symptoms of cough, fever and dyspnoea. So, these areas would be treated as region of interest (ROI) for the treatment, and critical organs around ROI would be considered as organ at risk during the treatment. In general, radiation tolerance dose of organs at risk is very much higher than the dose recommended for the treatment of patients diagnosed COVID-19. The radiation tolerance dose of few important vital organs is tabulated in **Table 2** [35,36]. Hence, there is almost no chance of any side effect and damage of critical organs on account of irradiation.

The radiation dose can be delivered to the patients using linear accelerator (LINAC) easily available in radiation therapy department around the world. Source-to- Axis (SAD) technique using two beams at gantry angle 0° and 180° would be suitable for the treatment without using any immobilization device **(Figure 5).**

Results and Discussion

1. Several studies showed that there are basic similarities in chemical bonding of base of RNA and DNA. Adenine, Guanine, Cytosine and Uracil are common and identical component of RNA and DNA
2. Common components of RNA and DNA have weak hydrogen bonds.
3. Single-stranded RNA (ss RNA) is the major structural component of SARS-CoV-2
4. RNA and DNA strands get damage when exposed to 0.1-0.5Gy of ionizing radiation.
5. 0.2-0.5Gy radiation dose is able to damage 'ss RNA' of SARS-CoV-19 because its strand is similar to the strand of DNA.
6. Ionizing radiation 10-15MV X-ray photon is suitable energy for the treatment of patients diagnosed COVID-19.
7. Free neutrons emitted from LINAC due to use of 10-15 MV X-ray photons also interact with hydrogenous material abundant in living organism and damage its physical structure.
8. High energy ionizing radiation is capable to damage physical structure of receptor ACE-2, and can break the bond between ACE-2 and Spike- protein of SARS-CoV-2.
9. No immobilization device is needed as it is single fraction treatment with maximum opening field to cover both lungs and throat.
10. There is very less chance to occur any side effect due to irradiation of COVID-19 patients.

Table 1 Radiation weighting factor for different type of radiation.

Radiation Type and Energy Range	Radiation Weighting Factor (WR)
X-ray and γ-ray	1
Electrons	1
Neutrons :	
<10keV	5
10-100keV	10
>100keV- 2MeV	20
> 2MeV-20MeV	10
>20MeV	5

Table 2 Radiation tolerance dose for critical organs.

Organ	Maximum Dose(Gy)	Mean Dose(Gy)	Endpoint
Spinal cord	45	....	Myelopathy
Larynx	....	45	Edema
Oesophagus	....	34	Esophagitis
Heart	....	26	Pericarditis
Liver	....	≤30	Radiation-induced liver disease

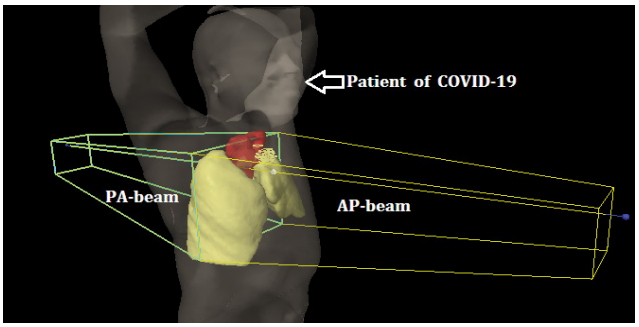

Figure 5 Treatment set up for the patient on LINAC.

The pandemic COVID-19 has panicked the world. There is no clinically approved medicine for this deadly disease up till now in the medical science. Only symptomatic treatment is being given to the patients infected with SARS-CoV-2. The countries affected with this disease are taking just pre-cautionary measures such as social distancing, lockdown across the nation, and advising their citizens to wash hands and mouth using soap and sanitizer.

The exact mode of transmission for SARS-CoV-2 has not yet been surely confirmed. However, many studies showed that the novel corona virus is transmitted by respiratory droplets formed when an infected person coughs or sneezes [37]. The respiratory droplets spread in air and get transmitted to other person through person-to-person contact or at a close distance. There is no drugs or biologics have been proven to be effective for the prevention or treatment of COVID-19. Various kind of antiviral agents, immune therapies, and vaccines are being under trials in different laboratories around the world as potential therapies, but no success has been reported up till now.

On analyzing the several studies and literatures related to radio-biology, molecular biology, virology and radiation oncology, our medical physicist team found that DNA and RNA have many identical and common features. And ionizing radiation (IR) is capable to breaks the strand of RNA, proteins, lipids and kills the living cells [38]. Moreover, IR is able to damage the receptor ACE-2 on the surface of host cell and breaks the bond between Spike –protein and the receptor. It badly damages the RBD, and binding units S1 and membrane fusion unit S2. This is the biological basis and scientific evidences to recommend the treatment of COVID-19 using high energy IR.

High energy electrons are already being used for virus irradiation. Ionizing radiation is capable to inactivate multiple biological parts of the viruses. This is also capable to break water molecules leads to the formation of H^+ and OH^- radicals together with more durable products, such as H_2O_2 and HO_2, in the presence of dissolved oxygen. These radicals severely damage the viruses and break the bond of various molecules.

Hence, these are sufficient scientific evidences which prove that patients infected with SARS-CoV-2 (COVID-19) should be treated by using high energy IR. And it will cause almost no side effect as the radiation dose recommended for the treatment is very less as compared to radiation tolerance dose of critical organs in the affected area like lungs and throat.

Conclusion

High energy IR has a peculiar capability to damage the strand of RNA, spike-proteins and lipids which are the integral parts of SARS-CoV-2. It is capable to break the bond between ACE-2 of host cell and Spike- protein of SARS-CoV-2. Hence, it is concluded that 10-15 MV X-ray photon should be used for the treatment of patients infected with SARS-CoV-2 and it will give definitely a better result as scientific facts indicated. The recommended dose for the treatment is 0.5 -1.0 Gy which is the sufficient radiation dose to kill the virus SARS-CoV-2. Patients diagnosed COVID-19 can be treated in two ways:

1. If the patient has diagnosed corona positive and has no symptoms of cough, fever, and respiratory distress; then deliver 0.5Gy dose using 15MV photon, AP-and PA- beam method (SAD-technique) in single fraction followed by multi-vitamin tablets or other medicines to boost the immune system as per clinical decisions.
2. If the patient has diagnosed corona positive and has severe symptoms of cough, fever and respiratory distress; then deliver 1.0Gy dose using 15MV photon AP-and PA- beam method (SAD-technique) in single fraction followed by medication of severe symptoms appeared in the patients just to recover them fast.

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Conflict of Interest

There is no conflict of interest.

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