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Ionizing Radiation as a Non-invasive Treatment for COVID-19 Patients-A Perspective Review

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Ionizing Radiation as a Non-invasive Treatment for COVID-19 Patients – A Perspective Review

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Abstract. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-stranded positive RNA virus surrounded by four structural proteins which are envelope, membrane, spike and nuclear capsid. This virus was identified at the end of 2019 and caused respiratory illness (i.e. coronavirus disease 2019: COVID-19). There is no specific vaccine or medication for the COVID-19 and current treatment relies on existing drugs including anti-viral and anti-inflammatory agents. Here, we describe the potential use electromagnetic radiation to treat COVID-19 infected individuals. The electromagnetic radiation, particularly UV-C has so far proved to be highly effective as coronavirus disinfectant method on medical instruments and material surfaces. Photochemical mechanisms of UV-C with human cell could alter the single strand RNA and effective to obtain photodimeric lesions in nucleic acid of the virus. Inactivation mechanisms by photodimers induced in genome commonly lead to mutagenesis, where base pairing during viral RNA replication will be interfere usually at pyrimidine dimers. Therefore, application of UV-C at moderate intensities within periodical irradiation on patient might be useful to inactivate RNA of SARS-CoV-2 and can be used as an alternative for non-invasive treatment of COVID-19 patients.

1. Introduction

There is no specific vaccine or medication for the coronavirus disease 2019 (COVID-19). Currently more than 100 clinical trials are under progress to treat COVID-19, including reassignment of existing drugs [1-8]. However, none of the repurposed drugs can conclusively be used to treat COVID-19 patients. Moreover, development of an effective and safe vaccine against COVID-19 that caused by SARS-CoV-2 coronavirus is also not yet promising [1]. Alternatively, the application of electromagnetic radiation in treating COVID-19 has been proposed and its clinical value will be further explored in this review [9].

Electromagnetic radiation can be classified into two main groups which are ionizing and non-ionizing radiation. The classification is based on its frequency and wavelength characteristics in generating energies as shown in Figure 1. Ionizing radiation can ionize or alter the structure of atoms but not for non-ionizing radiations. The ionizing radiation can further be categorized into two types which are ionizing particle (mass) and photons (massless). Theoretically, massive ionizing particle like α and β have a high possibility to interact with genetic materials as its energy is transferred linearly.

However, their penetration depth is much lower than photons and might not be suitable for internal tissues or cells. In contrast, ionizing photons including gamma ray, X-ray and ultraviolet type C (UV-C) have a higher penetration depth and thus ideal for targeting internal organ.

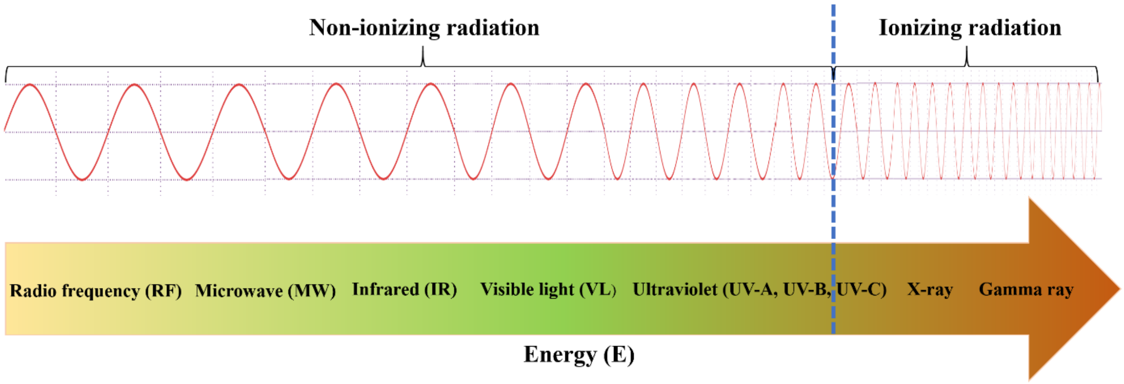

Figure 1. Electromagnetic radiation spectrum. Ionizing radiation started at UV-C, X-ray and gamma ray with short wavelength and high frequency propagation.

2. Material and methods

The methodology of this paper also includes literature search of related COVID-19 articles in Scopus, Pubmed, or Google Scholar. Specific keywords include but not limited to COVID-19, radiation, radiochemistry, RNA inhibition were used to discover the appropriate and significant information's related to this paper.

3. Results and discussion

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a single-stranded positive RNA virus surrounded by four structural proteins which are envelope, membrane, spike and nuclear capsid (Figure 2). The SARS-CoV-2 was first identified in December 2019. Human to human transmission of SAR-CoV-2 can be either via droplets or touching infected area.. The SAR-CoV-2 infect cells containing angiotensin-converting enzyme 2 (ACE2) such as lung epithelial cells and proliferate in the new host by copying its genetic (RNA) materials [10]. The SARS-CoV-2 replicate rapidly in a new host even before it can be properly recognised by our immune system. Thus, people with low immune system reactivity especially those who have chronic diseases such as heart disease, diabetic and hypertension may have high risk to get terrifying symptoms of chronic obstacle pulmonary disease (COPD) such as breathing problems and dry cough [11]. In this case, drug prescription either anti-viral, anti-bacteria or antibiotics can further weaken their immune system and cause further proliferation of SAR-CoV-2.

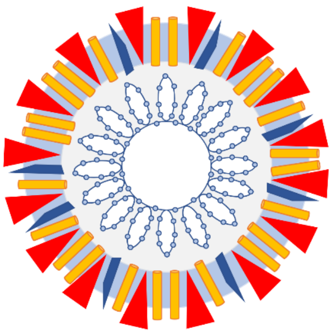

Figure 2. Schematic presentation of the COVID-19 structure. The figure was adopted from [12].

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Ionizing photons with high penetration power could be applied to inactivate the replication process of coronavirus RNA in an internal organ like lung. Energetic photons like gamma and X-rays as well as UV-C light enable to deposit their energies during interaction with coronavirus and break the RNA structure either directly by radiolytic cleavage of genetic material or indirectly by the action of radicals on the virus nucleic acids as shown in Figure 3 [13-14]. Therefore, virus replication and proliferation in COVID-19 patients can theoretically be abrupted by noninvasively irradiate the lung with certain intensities of gamma ray and UV-C light.

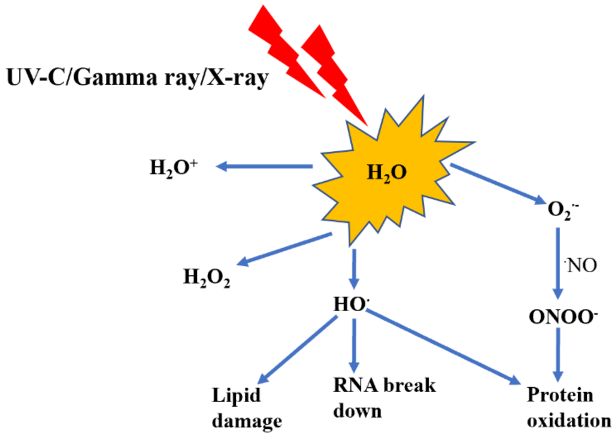

Figure 3. Ionizing radiation generates the potent intracellular free radical oxidants of H_2O_2, $O_2.^-$, and $OH.^-$. Oxidative stress lead to abruption the protein based formed RNA single strand [14].

Application of UV light with 240 nm and less can induces damage to a viral component other than nucleic acid and reduces viral infectivity [15]. In addition, Lytle and Sagripanti (2005) reported 254 nm UV with 3.1 J/m^2 capable to reduce viable Coronaviridae virus to 37% (D_{37}) [16]. Moreover, a few studies demonstrated that UV-C can inactivate coronaviruses including severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) within 5 minutes exposure time at 4 feet of source to target distance [17-18]. The UV-C was also beneficial to eliminate transfusion transmitted infectious agents (e.g. Nipah virus; NiV) and Crimean-Congo hemorrhagic fever virus; CCHFV) in blood and blood products [19-20]. The similar therapeutic effects were reported for gamma rays [13, 21]. However, UV-C seems more convenient and has low risk for clinical usage since no specific precaution or complex protection should be provided compare to energetic gamma and X-rays. Increasing the wavelength lead to reduce the single photons energy as stated in Equation 1, where E is the energy (J), h is Planck's constant ($h = 6.626 \times 10^{-34}$ Js), c is speed of light ($c = 2.998 \times 10^{8}$ m s^{-1}) and λ is the wavelength of the radiation (nm). Less energetic and far penetration characteristics of UV-C reduce adverse effects such as acute radiation syndrome.

$$E = hc/\lambda \qquad \text{Eq. 1}$$

UV-C light can be simply generated using UV light source power and can be regulated by adjusting specific frequency and wavelength for required energy ranges, making it economically practical for mass clinical applications. The focus beam can be manipulated to fit with the target area as well as its penetration and energy intensities in unit J/m^2. Photochemical mechanisms of UV-C with human cell could alter the single strand RNA and effective to obtain photodimeric lesions in nucleic acids [20, 22]. Inactivation mechanisms by photodimers induced in genome commonly lead to mutagenesis, where base pairing during RNA replication will be interfere usually at pyrimidine dimers [22]. Several earlier studies using UV for coronaviruses inactivation are listed in Table 1.

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Table 1. List of studies using UV light for for coronaviruses inactivation [23]

Virus	D_{90} J/m^2	UV k m^2/J	Source
Coronavirus	6.6	0.35120	Walker 2007 [24]
SARS-CoV-2 (Italy-INMI1)	12.3	0.18670	Bianco 2020 [25]
SARS Coronavirus (Frankfurt 1)	16.4	0.14040	Eickmann 2020 [20]
SARS Coronavirus (CoV-P9)	40.0	0.05750	Duan 2003 [26]
SARS-CoV-2 (SARS-CoV-2/Hu/DP/Kng/19-027)	41.7	0.05524	Inagaki 2020 [27]
Murine Coronavirus (MHV)	103.0	0.02240	Liu 2003 [28]
SARS Coronavirus (Hanoi)	133.9	0.01720	Kariwa 2004 [29]

Nonetheless, many are still skeptical on the medical potential of UV-C. They argued that the UV-C will generate extreme heat to the skin and induced inflammation as well as photokeratitis to the eye and skin cancer [30]. However, these adverse effects depending on the light intensities, wavelength, source to target distance, beam width etc. Theoretically, photokeratitis can be avoided by using UV protection glass which is available in the market. Skin cancer is stochastic effects and no threshold dose can be defined to determine the effects or symptoms. Commonly, long-term effects might be worst for continuous exposure and some precaution must be considered to minimize the risk.

4. Conclusion

Overall, UV-C has so far proved to be highly effective as coronavirus disinfectant method on medical instruments and material surfaces [31]. The irradiation dose for disinfections varies between minute to hours, depending on the intensities and surface area to be covered [32]. Therefore, application of UV-C with moderate intensities within periodical irradiation on patient might be useful to inactivate RNA of SARS-CoV-2 and can be used as an alternative for non-invasive treatment of COVID-19 patients.

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