Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 Rapid Letter

Low dose radiation therapy for COVID-19 pneumonia: A double-edged sword ☆

To the Editor

The COVID-19 pneumonia is a devastating disease without any approved treatment until now [1]. Kirkby and Mackenzie discussed the potential of lungs low dose radiation therapy (LDRT) for COVID-19 pneumonia treatment and suggested the re-examination of this forgotten therapeutic approach [2]. There are tempting reports from the early twentieth century which observed high efficacy of this method to treat pneumonia by X-ray [3,4]. This may open a new horizon in COVID-19 pneumonia treatment. However, some points should be taken into account to enhance the further clinical trials' outcome.

A comprehensive review of literature exhibited that all the publications about LDRT for pneumonia treatment are too old and haven't been established with satisfactory scientific reliability. Also, considerable limitations and defects in the animal experiments of these publications were observed. Besides, all the human studies were case reports, not reflecting modern randomization of subjects and blinded investigators [5].

The main recommended molecular mechanism by which LDRT treats pneumonia is the induction of anti-inflammatory effects [6]. Thus, the cost and benefit ratio for inhibition of inflammation at COVID-19 patients should be evaluated. Critically ill patients would be the first target for any possible clinical trials. Inflammatory cytokine storm affects a substantial number of these patients [7]. The LDRT is currently used for the decrease of limited inflammations in particular diseases like osteoarthritis and not a cytokine storm [8]. Thus, the anti-inflammatory effect of LDRT may not be very effective in controlling this storm in COVID-19. On the other hand, the most important concern about utilizing anti-inflammatory medications for controlling systemic inflammation is the suppression of immune response against infectious agents [9]. So, LDRT anti-inflammatory effects may disrupt immune system fighting against COVID-19 virus and delay virus elimination. Also, the window time of anti-inflammatory treatment is very important. According to reports, fatal COVID-19 cases are usually fast progressive and deteriorate under two weeks after onset. Therefore, prompt initiation of the anti-inflammatory therapy at this extremely short golden window time is determinative in the treatment outcome [10].

There is limited knowledge about the interaction of LDRT and viruses. Some studies have reported the significant increase of uptake, activation, transcription and spread of some viruses after radiation therapy [11–14]. Therefore, maybe it's better not to use the lungs as the target organ for radiation therapy due to high virus concentration. It should be mentioned that LDRT anti-inflammatory effects aren't limited to the irradiated site and LDRT exhibits systemic effects [5,6]. Therefore, maybe it's not necessary to just irradiate the lungs and total body LDRT may exhibit more efficacy.

Overall, it is necessary to completely investigate the LDRT effect on the COVID-19 virus and its cytokine storm in preclinical experiments to balance the risk and benefit ratio before designing further clinical trials. Also, inserting the LDRT anti-inflammatory effects at the right window time for each individual patient is determinative to reach the most favorable outcomes.

References

[1] Yang Y et al. The deadly coronaviruses: the 2003 SARS pandemic and the 2020 novel coronavirus epidemic in China. Journal of Autoimmunity 2020;109:102434. https://doi.org/10.1016/j.jaut.2020.102434.

[2] Kirkby C, Mackenzie MJR. Is low dose radiation therapy a potential treatment for COVID-19 pneumonia?. Radiotherapy & Oncology 2020. https://doi.org/10.1016/j.radonc.2020.04.004.

[3] McIntire F. Smith JHJTSJoM, X-ray therapy in the treatment of pneumonia. Radiology 1937;33:422–6. https://doi.org/10.1148/33.3.331.

[4] Scott WRJR, X-ray therapy in the treatment of acute pneumonia: report covering the use of X-ray therapy in the treatment of pneumonia at the Niagara Falls Memorial Hospital, from Oct. 1, 1937 to Sept. 30, 1938. Radiology 1939; 33: 331–349.

[5] Calabrese EJ. Dhawan GJTYjob, and medicine, How radiotherapy was historically used to treat pneumonia: could it be useful today?. Yale J Biol Med 2013;86(4):555–70.

[6] Arenas M et al. Anti-inflammatory effects of low-dose radiotherapy. Strahlentherapie und Onkologie 2012;188(11):975–81. https://doi.org/10.1007/s00066-012-0170-8.

[7] Mehta P et al. COVID-19: consider cytokine storm syndromes and immunosuppression. The Lancet 2020;395, 10229. https://doi.org/10.1016/S0140-6736(20)30628-0.

[8] Keller S et al. Efficacy of low-dose radiotherapy in painful gonarthritis: experiences from a retrospective East German bicenter study. Radiation Oncology 2013;8(1), 29. https://doi.org/10.1186/1748-717X-8-29.

[9] Schwartz DM et al. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nat Rev Drug Discov 2017;16(12):843–62.

[10] Zhang W et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): The experience of clinical immunologists from China. Clin Immunol 2020;214, 108393. https://doi.org/10.1016/j.clim.2020.108393.

[11] Iordanskiy S et al. Therapeutic doses of irradiation activate viral transcription and induce apoptosis in HIV-1 infected cells. Virology 2015;485:1–15. https://doi.org/10.1016/j.virol.2015.06.021.

[12] Mezhir JJ et al. Ionizing radiation activates late herpes simplex virus 1 promoters via the p38 pathway in tumors treated with oncolytic viruses. Cancer Res 2005;65(20):9479–84.

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https://doi.org/10.1016/j.radonc.2020.04.026

[13] Ramirez-Fort MK et al. Radiotherapy-induced reactivation of neurotrophic human herpes viruses: overview and management. J Clin Virol 2018;98:18–27. https://doi.org/10.1016/j.jcv.2017.11.004.
[14] Ceccaldi PJIjorb. Ionizing radiation modulates the spread of an apathogenic rabies virus in mouse brain. International Journal of Radiation Biology 1996;70:69–75.

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