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## **Letter to the Editor**

# **Low Dose Radiation to COVID-19 Patients to Ease the Disease Course and Reduce the Need of Intensive Care**

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Dear Sir,

Several recent relate to the use of PET/CT to assess pulmonary inflammation and precautions in general when COVID-19 patients are in need of nuclear medicine investigations. We would like to call attention to another, rather unnoticed, but potentially very promising, therapeutic application of what we have previously termed “the good rays” (1), i.e., the treatment of COVID-19 infected patients with low-dose radiation (LDR), which we believe will not only benefit these patients significantly, but also substantially improve the therapeutic capacity of the healthcare system.

An increasing body of evidence suggests that LDR has beneficial effects on the body’s DNA repair and immune systems (2). These properties may render LDR attractive for the treatment of COVID-19 patients. LDR has no short time side effects, is widely available, easy to administer, and cheap. This is in contrast to several of the currently discussed alternatives for treatment of COVID-19, many of which are under investigation in randomized controlled trials (RCTs), a circumstance that may be of particular interest in countries with limited resources and insufficient access to healthcare.

A hundred years of observations from studies of intended and unintended irradiation of animals and humans have consistently and almost unanimously demonstrated that effective doses to the body of up to 200 or 250 mSv are not only harmless, but beneficial in being associated with decreased rates of cancer and increased longevity (1). These many observations have not sufficed to make authorities slacken current rules of radiation protection that build on (unscientific) linear extrapolation from tissue damage observed with high radiation dose to the theoretical damage that the model claims is caused by LDR. This *linear no threshold (LNT)* model has never been validated in the LDR range. In contrast, it has consistently been contradicted by a multitude of observations (1).

Time has come to make up for this mistake and exploit LDR to fight COVID-19 – as a simple and stand-alone therapeutic procedure or as an adjunct to other forms of therapy being tested. Historically, X-rays have been used during the first half of the 20th century to successfully treat bacterial, sulfanilamide-resistant, interstitial, and atypical (including viral) pneumonia, a single treatment with low doses of X-ray quickly relieving respiratory distress and markedly reducing the risk of mortality, especially when given early in the disease course (3). With regard to the biological effects of ionizing radiation, multiple systems are involved, however, their net effect at doses of 100-300 mSv are anti-inflammatory actions minimizing toxicity, whereas increasing pro-inflammatory effects are observed at larger doses (4), i.e., a biphasic response consistent with Edward Calabrese's demonstration from thousands of biologic systems that this is nature's 'law' rather than a straight association as the one postulated by the LNT model (5).

We expect LDR irradiation to prevent or significantly relieve the severe pneumonia, which some COVID-19 patients develop and which may cause their death due to multi-organ failure because of insufficient oxygen supply. Quantifying the effect of LDR to be expected in COVID-19 patients is challenging due to lack of experience in comparable populations. However, the available evidence on the possible effect of LDR on short term and long term outcomes from clinical and animal studies suggests that substantial effects are not unlikely (3,6,7). A conservative guess would be that LDR will shorten the duration of the disease and reduce the number of patients in need of intensive care by one third and shorten the intensive care unit stay by at least 20%, i.e., something that will have a substantial benefit on health system capacity (8). Moreover, we can build on a long term experience with LDR as pre-treatment in patients with multiple myelomas and certain other cancer (9,10), which allows for monitoring and controlling the potential risk associated with the frequent exposure of the healthcare staff involved in administering LDR to COVID-19 patients.

It is probably rather safe to use LDR as an adjunct to other pharmacological interventions, because a direct interference with the pathways affected by pharmacological interventions is unlikely – in contrast to combining different pharmacological interventions. In this way, LDR also offers an opportunity to overcome the limitations implied by the limited effectiveness of any single intervention. For the same reasons, LDR can be tested in RCTs alongside a pharmacological intervention in a 2 x 2 factorial design, avoiding excluding participants from benefiting from other promising options and offering ¾ of all participants an active treatment. An RCT on effects of LDR in COVID-19 patients requires little preparation except for ethical approval and access to instruments able of providing LDR like planar X-ray or CT equipment and, hence, is fast to implement. The beneficial effect of LDR can be an advantage at all stages of disease, thus offering a wide spectrum for its application. It might be applied simultaneously to other interventions or may fill the time gap between them. To what extent FDG-PET/CT can come into use for examination of the lungs of these patients and in particular for monitoring effects of therapy is another, but also very interesting, question. We are very willing to collaborate with researchers who are interested in adding LDR as an adjunct to ongoing or coming RCTs on COVID-19 therapeutic options.

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