Engineered microparticles delivering oxygen to enhance radiotherapy efficacy

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In their recent paper (1), Seekell et al. describe the use of engineered microparticles to deliver oxygen to counter the high mortality rate of hypoxemia. We believe that these engineered microparticles could be extremely useful in radiation treatment, especially in anemic cancer patients.

One of the most well-recognized phenomena that counter the efficacy of radiotherapy is the lack of oxygen that is found in most solid tumors. Ionizing radiation induces DNA damage through the generation of oxygen radicals, thus explaining the fact that hypoxic tumors respond poorly to radiotherapy. Additionally, up to 40% of patients with solid tumors undergoing radiotherapy have anemia at presentation (2), and low pretreatment hemoglobin levels are a strong prognostic indicator of poor disease control and survival. Several different approaches have been used to resensitize hypoxic tumors, especially in anemic patients, such as hyperbaric oxygen treatment, erythropoietin, and red blood cell transfusions. These approaches have been largely unsuccessful or even counter-effective for a number of reasons (3, 4).

In our randomized phase III trial, using accelerated radiotherapy with carbogen and nicotinamide (ARCON) for laryngeal cancer ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00147732) number, NCT00147732) (5), we found that ARCON was extremely effective in

countering the poor prognosis of anemic patients (6). Five-year disease-free survival was 68% for patients treated with ARCON, versus 45% for controls. We explained this using the “reduced cord radius” model (7). This model assumes that the ability of cancer cells to survive at a distance from blood vessels is dependent upon the local supply and diffusion distance of oxygen and nutrients from each vessel. It has been proposed that anemia causes a reduced cord radius. Chronic restoration of oxygen levels by erythropoietin or blood transfusion will lead to an enhanced cord radius, as tumor cells will proliferate more actively until they once again outgrow their oxygen supply. Thus, similar hypoxic tumor regions will form, negating any radiosensitizing effect of these treatments. We hypothesized that in ARCON, the daily carbogen (98% O₂ + 2% CO₂) breathing immediately followed by radiotherapy will not cause this adaptive response because the oxygenation increase is too short and only for the duration of the radiation treatment (10–15 min).

Both the amount (12–18 mmHg) and time course (5 min) of increased oxygen tensions that are achieved using the engineered microparticles of Seekell et al. (1) would make this an exciting, new, clinically feasible approach to enhance the efficacy of radiotherapy.

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