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Radiobiological foundations of carbon ion radiotherapy: current perspectives and future challenges

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Cancer is the #2 killer in the US and is projected to overtake heart disease by 2030. More than 1.6 million new cancer cases and nearly 600,000 cancer deaths occur annually in the US. Radiotherapy is seeing increasing use in cancer treatment, largely because of improvements in dose distributions. The goal of radiotherapy is to deliver a lethal radiation dose to the tumor while sparing normal tissue. Most patients are treated with X-rays (photons) and in the US some receive proton (light ion) therapy. Following developmental work at Lawrence Berkeley National Laboratory, the Japan National Institute of Radiological Sciences brought carbon ion radiotherapy (CIRT; heavy charged particles) to clinical practice in 1994. Today there are 9 CIRT facilities in operation including five in Japan, three in Europe, and one in China. There are physical and radiobiological reasons why CIRT provides superior treatment outcomes for the most challenging tumors, such as those near sensitive structures (e.g., head and neck and near the spinal cord) and hypoxic tumors which are resistant to photons and protons. Carbon ions and protons are similar in providing superior dose distributions vs. photons, but the larger mass and charge of carbon ions offer several other benefits. These include more effective cell killing per unit dose reflecting more complex, clustered DNA damage that persists because it is difficult to repair. The superior local tumor control with CIRT translates to improved patient survival that is particularly evident in longer term studies. There are outstanding opportunities to build on these successes, including development of additional ion species such as helium, silicon and oxygen; and combination therapies with different ions, with radiosensitizing drugs that target specific DNA repair and/or DNA damage signaling pathways, and with the rapidly expanding arsenal of immunotherapies. This raises the question: how can scientists, clinicians, and society promote research and further development of these life-saving therapies?