Radiation treatment of localized tumors has evolved rapidly in recent decades, allowing radiation oncologists to deliver more focused treatments with significantly reduced side effects. One of the disruptive innovations led by physicists has been the development of intensity-modulated and image-guided radiation therapy (IMRT and IGRT), which has become the state of the art in radiation therapy with photons. At the next stage of the development, there is now growing interest in treating tumors with protons or heavier particles, which have the added physical benefit of the Bragg peak. However, proton and heavier particle therapy is available to fewer than 1% of the patients. The first reason for that is the higher cost and bigger size of particle therapy facilities. The second reason is uncertainty of the treatment delivery, which limits its accuracy and precision. To address the first point (higher cost), physicists are involved in developments to make the equipment much more compact and cheaper. Examples include superconducting accelerators, laser-accelerated accelerators, more compact “gantries” that rotate the beam around the patient, as well as other solutions to treat the patients form multiple directions of incidence. The uncertainties in positioning the Bragg peak in the patient are being addressed by in-vivo measurements of dose deposition, or surrogates thereof. Examples include the measurement of prompt gamma radiation produced by the proton beam as it traverses the patient. Positron-Emission-Tomography (PET) scans have also been used to measure the tissue activation by the proton beam. Finally, the measurement of sound waves produced by pulsed proton beams leading to rapid expansions of the irradiated tissue has recently been successfully pursued. After resolving the issue of aiming a treatment beam with high precision and low cost, such that the majority of the patients will benefit from it, one of the next challenges for physicists in medicine is to better identify the actual target of the treatment, and the dynamics of treating it optimally in a multi-modality approach.