Proton beam therapy for locally advanced pancreatic cancer

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Lecture : At diagnosis, approximately 30% of patients with pancreatic cancer present with locally advanced disease. Although chemotherapy and/or radiotherapy (RT) have usually been performed, the role of RT is controversial because of conflicting results from clinical trials over the past decades comparing concurrent chemoradiotherapy (CRT) with chemotherapy alone in these patients [1, 2]. In the LAP07 trial [2], although CRT after induction chemotherapy did not show a survival benefit compared with chemotherapy alone, CRT resulted in a significantly longer period without treatment (6.1 vs. 3.7 months) and reduction of the local tumour progression (32% vs. 46%) ($p<0.05$ for each). Additionally, several autopsy studies demonstrated that approximately 30% of patients with pancreatic cancer had no evidence of distant metastases at the time of death [3, 4]. One population-based study showed that 41% of patients with locally advanced cancer treated with chemotherapy died without evidence of distant metastases [5]. These findings suggested that RT could be a valuable treatment option for selected patients with locally advanced disease.
When administering RT for patients with locally advanced disease, conventional fractionated courses of RT with concurrent chemotherapy have been typically used which has been associated with a significant grade 3 or 4 toxicity rate and a median overall survival (OS) of 9–15 months [1, 2, 6, 7]. With recent advances in RT techniques, intensity-modulated RT (IMRT), stereotactic body RT (SBRT) and proton beam therapy (PBT) can deliver high doses to the tumour as well as minimising the radiation dose to surrounding normal tissues [8-17]. Because of the distinct physical characteristics of proton beams allowing deposition of high doses of radiation within the target and lacking an exit dose outside the target, PBT has been attracting attention. Conceptually, PBT can exploit the potential advantages of an accelerated form of RT in which different doses can be delivered to different targets at the same time. That is, a higher dose can be delivered to the tumour volume, while a lower dose is delivered simultaneously to nearby areas of surrounding normal tissue (ie, gastrointestinal structures). This accelerated hypofractionated RT can create a potential improvement in the therapeutic ratio compared with conventional fractionated RT due to the need for less repair of radiation damage of surrounding normal tissues and avoiding the need for prolonged chemotherapy breaks because there is shortened overall treatment time.

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