



Revisiting radiotherapy for pancreatic cancer

Pancreatic cancer is the eighth most common cancer diagnosed in the United States (US) yet the third deadliest. This devastating disease is estimated to become the second leading cause of cancer deaths by 2030 largely due to the high rate of occult metastatic disease and significant tumor heterogeneity, rendering unselected therapies ineffective. Poor systemic control combined with high metastatic potential has likely contributed to the failure of multiple randomized controlled studies investigating the potential benefits of radiotherapy. As a result, the role of radiotherapy in the management of pancreatic cancer patients has been met with skepticism due to these conflicting clinical trial results from the US and Europe, leaving the scientific community at a crossroads.

During the past decade we have seen incremental but significant improvements in patient outcomes coincident with the widespread adoption of effective multi-agent chemotherapeutic regimens such as gemcitabine/Abiraterone and FOLFIRINOX in the metastatic, unresectable and most recently, resectable setting. It is likely that these regimens have in large part contributed to improving the 5-year survival rate to 9%. This recent progress in the control of known and occult micrometastatic disease has again highlighted the corresponding importance of local control. Indeed, in the recently reported ESPAC-4 trial comparing adjuvant standard of care gemcitabine to gemcitabine and capecitabine in patients with resected pancreatic cancer (Neoptolemos *et al.*, *Lancet* 2017), approximately 50% of patients had local recurrences, of which 28% were isolated. Simultaneous improvements in genomic assays, novel targeted small molecule and antibody-based therapies, as well as technologies used to deliver and assess response to radiotherapy have led to renewed investigation of radiotherapy for pancreatic cancer and are presented in this special issue of *Annals of Pancreatic Cancer (APC)*.

In this series, we will hear from gastrointestinal radiation oncology key thought leaders from distinguished academic centers across the US. Each field expert will provide a scientific review, a critical assessment and offer their opinion on chief topics within the pancreatic cancer and radiotherapy landscape.

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