While pancreatic cancer remains an almost uniformly fatal diagnosis, data suggest that advances in treatment have resulted in modest gains in overall survival for local (1,2) and metastatic (2,3) disease. Possible explanations for these observations include earlier detection (lead-time bias) through improved imaging techniques, more accurate staging, and an increase in the rate of curative resections. However, survival benefits have been most convincingly demonstrated in the realm of improved systemic therapies. That is, the increased survival seen is certainly due in part to the success of gemcitabine-based (4) and FOLFIRINOX (5) chemotherapy in slowing the systemic spread of disease.

This is not to say that local control is irrelevant to survival. Local control has been shown to significantly impact survival in other cancer types when systemic disease is effectively controlled (6). However, the typical method used to report local control can hide its importance in diseases that commonly metastasize systemically. Patients are generally censored from the analysis at the time of death. Thus, favorable-appearing rates of local control can be misleading, and as survival improves, local control can appear to worsen as there is more time for locally advancing disease to become clinically apparent. When systemic control improves, local control becomes a more important metric in disease and symptom control (7).

In pancreatic cancer, local progression is likely the direct cause of death in a large proportion of patients. It has been shown that around 30% of patients with pancreatic cancer die with local progression alone (8-10) and 10-25% more experience local progression along with distant spread before death (9-11). Furthermore, because of close proximity to vital organ systems, local progression from pancreatic cancer is extremely morbid, and current treatment options are limited. For these reasons it is imperative to investigate methods to improve local control in this disease.

In this issue of the Journal of Gastrointestinal Oncology, Wild and colleagues report their experience with re-irradiation using stereotactic body radiation therapy (SBRT). Eighteen patients treated at two institutions were identified. Patients received re-irradiation with SBRT for isolated local recurrence after surgery and multimodality therapy (15 patients), or isolated local progression after definitive chemotherapy and radiation (3 patients). All patients received gemcitabine maintenance therapy and had no evidence of distant metastasis prior to re-irradiation with SBRT. The median re-irradiation dose was 25 Gy in 5 fractions. The authors report a median survival from the time of SBRT of 8.8 months (95% CI of 1.2-16.4 months). Effective symptom palliation occurred in 4 of 7 patients who reported abdominal or back pain prior to SBRT. Rates of toxicity were acceptable with only 5 cases (28%) of grade ≥2 acute toxicity, no cases of grade ≥3 acute toxicity, and only 1 case (6%) of grade 3 late toxicity.

These results are encouraging, but proper patient selection is essential. The authors report that those patients who experienced local progression 9 months or more after definitive therapy survived significantly longer (11.3 vs. 3.4 months; P=0.019) than those who progressed earlier. For those patients who progress early, this finding is further disappointing evidence of our very limited ability to control aggressive pancreatic cancer. It also lends support to the principle that local therapy is most beneficial for those patients who betray less aggressive disease, as seen in the multimodality treatment of localized-unresectable pancreatic cancer (12-14). Differences in tumor markers such as Smad4 (Dpc4) are being investigated (8,15) to help select appropriate patients for more intense local therapy. Finally, the authors appropriately excluded patients with poor performance status.

SBRT has many advantages in the setting of locally recurrent pancreatic cancer. Compared to fractionated...
radiation therapy, SBRT shortens the treatment time, and may come with improved image guidance capabilities and dose conformality. Fears of high rates of late adverse effects from hypofractionation are not borne out in this study and seem to be less than 10–15% in other experiences of SBRT for pancreatic cancer in the recurrent (16), and definitive/adjuvant (17–19) settings. However, higher rates of toxicity have been seen with doses of 45 Gy in 3 fractions (20). Compared to surgery, SBRT offers the ability to resume chemotherapy faster, is less invasive, and avoids surgical morbidity. Finally, compared to chemotherapy alone or best supportive care, SBRT may theoretically improve freedom from further local progression and may even be cost effective if it can decrease the need for hospital admissions and interventional procedures to palliate pain and locally advancing disease.

In conclusion, local control is probably important for both symptom control and survival in pancreatic cancer but improving local control has been challenging. In the small retrospective series reported so far, re-irradiation with SBRT after local progression shows promise and adheres to the principle of “first, do no harm.” For now, appropriate patients include those with a moderate time from definitive treatment to local-only progression and good performance status. Certainly, further investigation of re-irradiation with SBRT is warranted and the work of Wild and colleagues should inform future trials. We should move away from the nihilistic attitude that attempting to gain local control is not worthwhile and move towards a personalized approach to the treatment of pancreatic cancer.

**Acknowledgements**

**Disclosure:** The authors declare no conflict of interest.

**References**

16. Lominska CE, Unger K, Nasr NM, et al. Stereotactic body radiation therapy for reirradiation of localized...