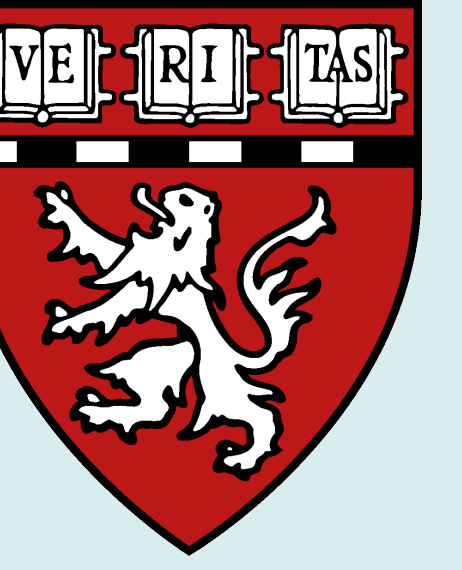


# Retrospective analysis of patients treated with adjuvant chemoradiotherapy for resected pancreatic cancer



Jona Hattangadi, Beow Yeap, Harvey J. Mamon

Department of Radiation Oncology, Brigham and Women's Hospital, Dana Farber Cancer Institute, Boston, Massachusetts

## BACKGROUND

- The rationale for adjuvant chemotherapy and radiation following resection of pancreatic adenocarcinoma is to treat residual microscopic disease.
- Consensus on the benefit of such therapy remains elusive, as results from randomized trials are conflicting.
- While the GITSG trial showed improved survival with adjuvant chemoradiation, the EORTC failed to show a statistically significant survival benefit, and ESPAC-1 suggested a deleterious effect of radiation.
- Nonetheless, adjuvant chemoradiation with 5-fluorouracil (5-FU) continues to be commonly used in the United States, and remains the standard treatment at our institution.

## STUDY OBJECTIVE

- To assess overall survival (OS), progression-free survival (PFS), and patterns of failure in a consecutive, unselected series of patients treated with adjuvant 5-FU and radiation therapy for resected pancreatic cancer.

## MATERIALS and METHODS

- 44 consecutively treated patients with resected pancreatic adenocarcinoma (n=42) or acinar cell carcinoma (n=2) who underwent adjuvant therapy between 1998 and 2004 at the Brigham & Women's Hospital were identified.
- Demographic data, tumor characteristics, treatment information, and sites of disease progression were obtained by review of medical records.
- All patients were followed after adjuvant therapy with interval bloodwork and imaging every three to four months to look for disease progression and metastases.
- Survival probabilities were estimated with the Kaplan-Meier method and patterns of failure were analyzed.

Table 1: Patient demographics and surgery

Characteristic	# patients
Age (yr)	Median: 63 Range: 34-79
Gender	M 18 (41%) F 26 (59%)
Surgery	Pancreaticoduodenectomy (Whipple) 27 (61%) Pylorus-preserving 6 (14%) Distal pancreatectomy 9 (20%) Total pancreatectomy 2 (5%)

## RESULTS

- Patient characteristics are shown in Table 1 and Table 2.
- Treatment characteristics are shown in Table 2. 84% of patients were treated with external beam RT to 5040 cGy.
- Table 3 shows overall and progression-free survival.
- Disease recurrence was documented in 35 patients.
- Patterns of failure are displayed graphically in Figure 1. Considering both initial and subsequent sites of failure, the majority of patients recurred with peritoneal carcinomatosis (60%) and/or liver metastases (54%). Local failures in the pancreatic bed (34%) or regional lymph nodes (23%) were also common.

Table 2: Tumor characteristics and treatment

Characteristic	# patients
Histology type	Ductal adenocarcinoma 41 (93%) Mucinous adenocarcinoma 1 (2%) Acinar cell carcinoma 2 (5%)
Tumor size (longest diameter, cm)	Median: 2.6 Range: 1.2-7.0
Site of tumor	Head 33 (75%) Body 5 (11%) Tail 6 (14%)
Resection margins	Positive (including <1mm) 16 (36%) Negative 28 (64%)
Postoperative tumor stage	T2 8 (18%) T3 33 (75%) T4 3 (7%)
Postoperative nodal status	N0 15 (34%) N1 28 (64%) N2 1 (2%)
Grade/degree of differentiation	Poor 6 (14%) NX 6 (14%) Moderate to poor 26 (59%) Moderate 5 (11%) Moderate 1 (2%)
Lymphovascular involvement	Yes 19 (43%) Well 14 (32%) No 11 (25%)
Days between resection and adjuvant therapy	Unknown 62 Median: 63 Range: 33-118
ECOG Performance Status at initiation of therapy	0 27 (61%) 1 15 (34%) 2 2 (5%)
Follow-up from resection (months)	Median: 12.2 Range: 4.4-39.1
Concurrent 5-FU with XRT	Continuous infusion 37 (84%) Bolus infusion 7 (16%)
Other Adjuvant Chemotherapy	Capecitabine 16 (36%) Leucovorin 2 (5%) Continuous 5-FU post-XRT 1 (2%)

Table 3: Overall Survival (OS) and Progression-free Survival (PFS)

Factor	Median (months)	95% CI	1-yr	2-yr
OS (n=44)	16.9	12.7 - 23.2	67%	25%
PFS (n=44)	9.1	6.8 - 11.0	35%	13%

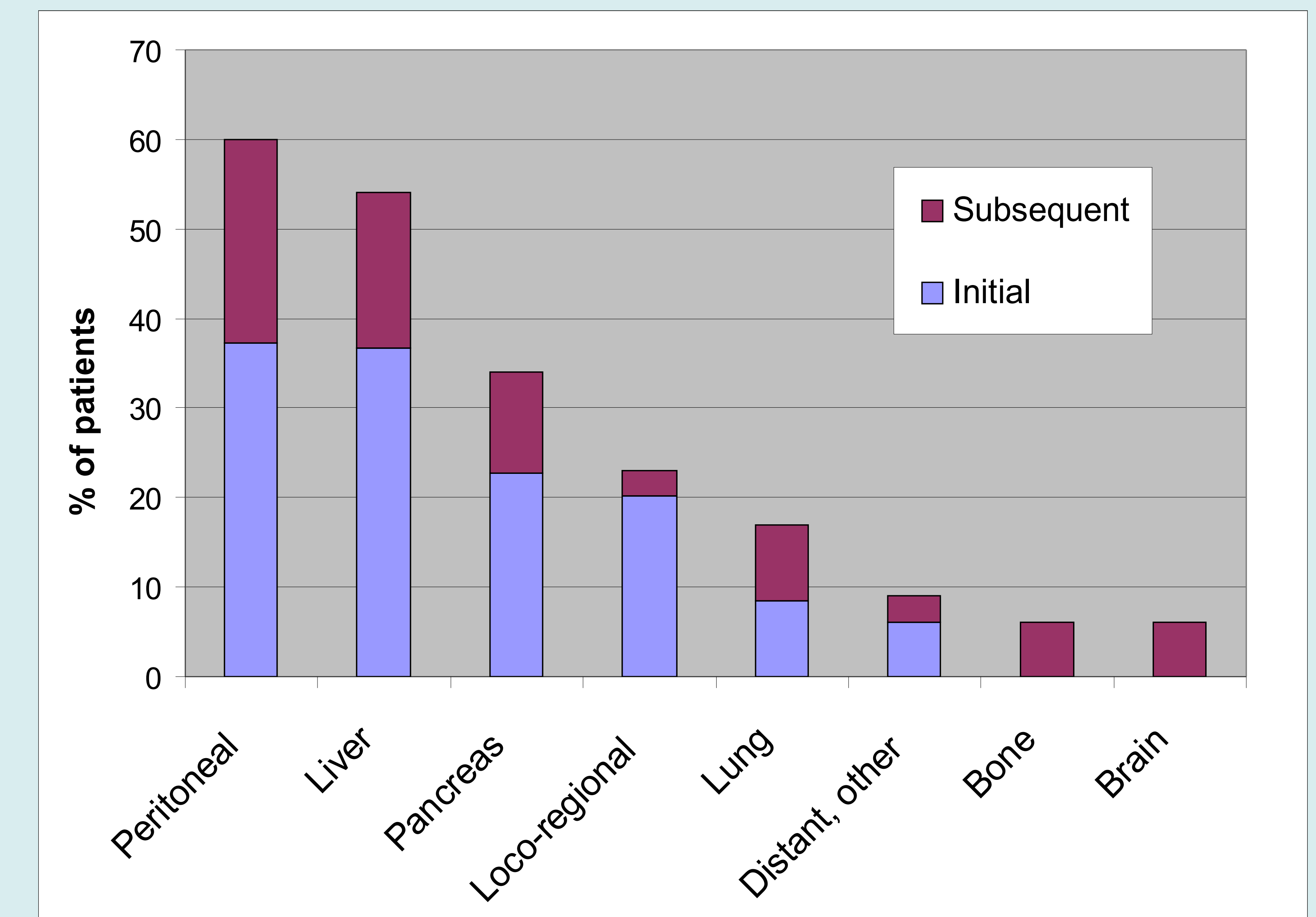


Figure 1: Patterns of Failure. The lower portion of each bar indicates the percentage of patients who experienced their initial site of recurrence at that site; the upper portion indicates the percentage of patients who subsequently recurred in that site after an initial recurrence elsewhere.

## CONCLUSIONS

- Median survival of this cohort is less than that of the chemoradiation arm in the GITSG trial (20 months)<sup>1</sup>, which required negative margins and similar to the EORTC study (17.1 months)<sup>2</sup> which allowed positive margins.
- Our results do not support the hypothesis that properly delivered radiation has a negative effect on survival in the adjuvant therapy of pancreatic cancer.
- However, the wide confidence interval of our cohort overlaps the range of median survivals seen in the adjuvant arms of all of these studies.
- We plan to analyze a larger number of patients to further refine this analysis.

## REFERENCES

- Kaiser MH, Ellenberg SS. Pancreatic cancer. Adjuvant combined radiation and chemotherapy following curative resection [Published Erratum Appears in Arch Surg 1986 Sep;121(9):1045]. Arch Surg 1985; 120:899.
- Klinkenbil JH, Jeekel J, Sahnoud T, et al. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and periampullary region: phase III trial of the EORTC gastrointestinal tract cancer cooperative group. Ann Surg 1999; 230:776.
- Neoptolemos JP, Dunn JA, Stocken DD, et al. Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: a randomised controlled trial. Lancet 2001; 358:1576.