CyberKnife Shows Promise in Delivering Painless, Non-Invasive Treatment for Pancreatic Cancer

Radical surgery, called the Whipple Procedure, has historically been the treatment of choice for localized pancreatic cancer. This procedure results in a median survival of about 11 months, with about 20 percent of patients surviving two years. Surgery carries about 5 percent mortality, and 80 percent morbidity risks. Local-regional recurrence, and distant metastates remain a major problem even when tumors are completely removed, as about half of patients develop local-regional recurrence.

Surgery (S) combined with post-operative external beam radiation therapy (XRT) and chemotherapy (CT) have been shown to reduce local-regional recurrence of pancreatic cancer and modestly improve survival (see results of studies below).

RESECTED PANCREATIC CANCER RESULTS
SURGERY ALONE VS. SURGERY + XRT + CT
RANDOMIZED TRIALS

STUDY		#PTS	TREATMENT	MEDIAN SURVIVAL (months)		2YRS
Kalser	(GITSG)	21	S	11		18%
		19	S + XRT + CT	21		46%
		30	S + XRT + CT	18		43%
Klinkenbijl		54	S	12.6		
		60	S + XRT + CT	17.1		
Demeure		31	S	16.9		
		30	S + XRT + CT	24.2		

Two large retrospective reviews, one from Johns Hopkins and the other from the Mayo Clinic, have demonstrated a statistically significant overall survival benefit with the addition of adjuvant XRT + CT (see chart below).

RESECTED PANCREATIC CANCER RESULTS
SURGERY ALONE VS. SURGERY + XRT + CT

STUDY		#PTS	TREATMENT	MEDIAN SURVIVAL (months)		5YRS
Johns Hopkins		908	S	14.4		14.40%
			S + XRT + CT	21.2		20.1%*
Mayo Clinic		472	S	19.2		17%
			S + XRT + CT	25.2		28%*

** $P < 0.001$*

Source: JCO, 2008 ; 26 [21] : 3503-3516

Results of the Johns Hopkins and Mayo Clinic studies are consistent with retrospective series, which also appear to show a benefit in median survival with S + XRT + CT vs. S-alone (see below).

RESECTED PANCREATIC RESULTS SURGERY ALONE VS. SURGERY + XRT + CT RETROSPECTIVE TRIALS			
STUDY	#PTS	TREATMENT	MEDIAN SURVIVAL (months)
Yeo	53	S	13.5
Yeo	120	S + XRT + CT	19.5
Whittington	28	S + XRT + CT	16
Foo	29	S + XRT + CT	23
Spitz	22	S + XRT + CT	22
Abrams	23	S + XRT + CT	15.9
Davis	34	S + XRT + CT	16

The mortality and morbidity of surgery denies or delays initiation of adjuvant XRT and chemotherapy in many patients. Therefore, there has been interest in recent years in evaluating pre-operative or neoadjuvant XRT + CT. This approach has not proven to improve survival compared to post-operative XRT + CT (see study results below).

RESULTS WITH NEOADJVUANT CT +/- XRT RETROSPECTIVE TRIALS			
STUDY	#PTS	TREATMENT	MEDIAN SURVIVAL (months)
Hoffman	11	XRT + CT + S	45
Hoffman	24	XRT + CT + S	16
Spitz	41	XRT + CT + S	19
Pisters	20	XRT + CT + S	16
Rajagopalan	12	XRT + CT + S	27
Allendorf	78	XRT + CT + S	24
Gillen*	4,394	XRT + CT + S	23
Rose	64	CT + S	24
Lee	43	CT + S	17

At best, only 25 percent of patients with pancreatic cancer have resectable disease at presentation. Factors such as the presence of distant metastases, or involvement of the superior mesenteric artery, make it almost impossible to cure patients of pancreatic cancer at diagnosis. XRT alone does not improve this figure. The GITSG conducted randomized trials in patients with unresectable disease at diagnosis. They compared XRT + CT, to XRT alone. The median survival was about 9 months in the combined treatment group, compared to about 4 months with XRT alone. The one-year survival was about 35 percent in the combined group, compared to 11 percent with XRT alone. Hall et al, reviewed the National Cancer Database for patients receiving XRT + chemotherapy for unresectable pancreatic cancer (J Gastroentest Oncol, 2014 ; 5[2] : 77-85). The median overall survival was 10 months.

Commented [GN1]: What does this stand for? Need to write out acronyms on first reference.

Intensity modulated radiation therapy (IMRT) permits variation of radiation energy, movement of radiation shielding, and rotation of the energy source, all at the same time during delivery of radiation treatment. With IMRT, dosimetry is tightly contoured, maximizing dose to the tumor and minimizing dose to normal tissues. While in this regard IMRT duplicates Gamma Knife, IMRT offers advantages: It can be given anywhere in the body and it can be delivered in fractions, which maximizes sparing of normal tissues. As a result, IMRT enables a higher radiation dose to be delivered to the tumor, and decreases exposure of normal tissue when compared with conventional XRT. These unique capabilities should result in higher tumor control, improved long-term survival and decreased complications.

Stereotactic body radiation therapy (SBRT) employs image-guided IMRT (IG-IMRT), only with more rapid fractionation. This results in a considerably higher radiobiologic dose, which could lead to improved tumor control, and in turn improved survival. Current medical literature has reported results of employing SBRT and chemotherapy (see chart below).

UNRESECTABLE PANCREATIC CANCER RESULTS
SBRT + CT
RETROSPECTIVE TRIALS

AUTHOR	#PTS	TREATMENT	MEDIAN SURVIVAL (months)	1-YEAR SURVIVAL	GRADE 3 COMPLICATIONS
Pollom	167	SBRT + CT	nr	33%	8%
Herman	49	SBRT + CT	14	78%	11%
Schellenberg	20	SBRT + CT	12	50%	5%
Chuong	77	SBRT + CT	15	72%	5%
Tozzi	30	SBRT + CT	11	47%	0%
Mahadevan	39	SBRT + CT	20	nr	9%
Goyal	20	SBRT + CT	nr	56%	5%
Moningi	88	SBRT + CT	18	nr	3%
Rombouts	1,164	SBRT	24	nr	0-25%
		RFA[1]	25.6	nr	4-22%
		IRE[2]	20.2	nr	9-15%
		HIFU[3]	12.6	nr	nr

1. Radio-Frequency Ablation
2. Irreversible Electoporation
3. High Intensity Focused Ultrasound

The CyberKnife System has been shown to be the SBRT delivery system providing the tightest radiation dose delivery. As a result, the CyberKnife System enables clinicians to give the maximum dose to the tumor target while minimizing dose to surrounding normal tissues.

The non-invasive, non-surgical nature of the CyberKnife System, treatments are often preferred for patients who have other health concerns and cannot undergo surgery. CyberKnife treatments are given daily for up to five days, on an outpatient basis. The treatments are painless and each session takes only about 45 minutes to deliver, resulting in fewer complications and minimal side effects when compared to other pancreatic cancer treatment options.