



SPOTLIGHT ON Pancreatic Cancer

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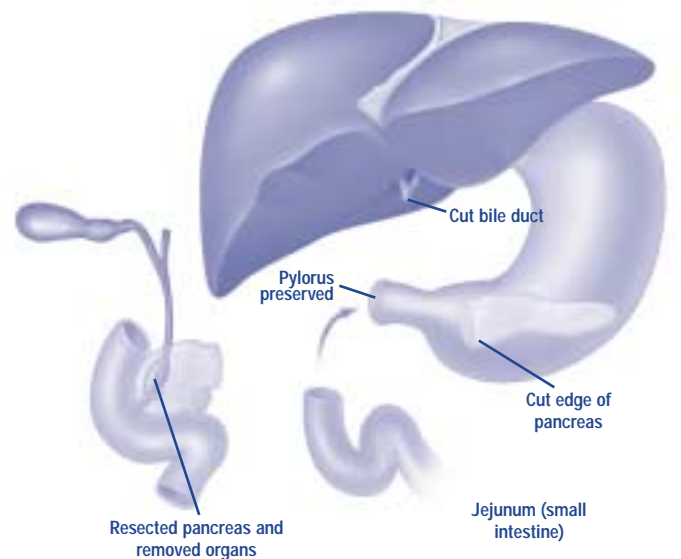
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Managing Chronic Viral
Hepatitis and Liver
Cancer on the Pacific
Rim Conference
July 19, 2003

New Technique for Whipple Procedure Improves Gastric Emptying

20% of Pancreatic Cancer Cases Eligible for Pancreaticoduodenectomy

by Assad Hassoun, M.D., Eric Becker and Laura Miyashita

More than 29,000 Americans are diagnosed with pancreatic cancer annually, the majority of whom are 65 or older. Smoking, diabetes, age, alcohol, chronic pancreatitis, familial pancreatitis and genetic factors, as well as dietary habits, are common risk factors associated with pancreatic cancer. Because of the location of the pancreas and treatment challenges, it represents the 4th leading cause of cancer death in men and women—a striking statistic given its low occurrence in comparison to other malignancies.



Incisions made for Whipple procedure

Cancers of the head of the pancreas typically originate in the pancreas tissue (63%), followed by the ampulla, distal bile duct and duodenum. About 20% of pancreatic cancer cases require a Whipple procedure, or resection of the pancreas head and neck, duodenum and distal bile duct with subsequent reconstruction.

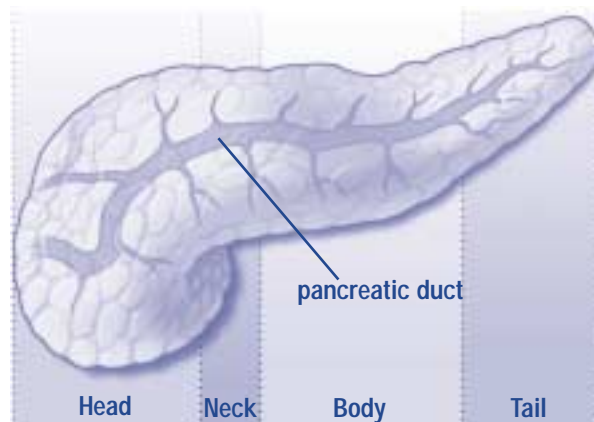


Fig. 1: Pancreas Segments

WHIPPLE PROCEDURE, continued on page 3

Endoscopic Ultrasound Superior for Pancreas Tumor Staging

Imaging Technique Helps Find, Stage and Sample Lesions

by Kenneth Binmoeller, M.D. and Robin O'Connor

Determining the extent of malignancy (staging) is essential to getting the best treatment for pancreatic cancer. An important tool in this staging, endoscopic ultrasound (EUS), offers excellent spatial resolution, thereby enabling physicians to detect the cancer's full extent.

Used for imaging the gastrointestinal tract and surrounding structures, EUS incorporates a tiny ultrasound transducer at the tip of the flexible endoscope. This transducer generates high-frequency sound waves that provide high spatial resolution. "By adjusting the position of the transducer within

the bowel lumen, we can scrutinize the entire pancreas from the uncinate process to the tail," explains Kenneth Binmoeller, M.D., director of California Pacific's Interventional Endoscopy Service.

The resolution of EUS far exceeds that of other imaging modalities such as CT and MRI. This enables not only the accurate staging of a known tumor, but also the detection of small tumors that other imaging studies may miss. Tumors less than 1 cm are readily visualized with EUS.

ENDOSCOPIC ULTRASOUND, continued on page 3

Team Approach Benefits Pancreatic Cancer Patients

New Research Protocols and Treatments Offer More Options

by Laura Miyashita

The development of innovative research protocols and treatment therapies provide new options for managing patients with pancreatic cancer. “Rather than compartmentalizing pancreatic cancer treatment to one specific specialist, California Pacific takes a more integrated approach to fully assess a patient’s needs, with many specialists working together to tailor an individualized program for each patient,” says Kathleen Grant, M.D., chief of California Pacific’s Division of Hematology and Medical Oncology.

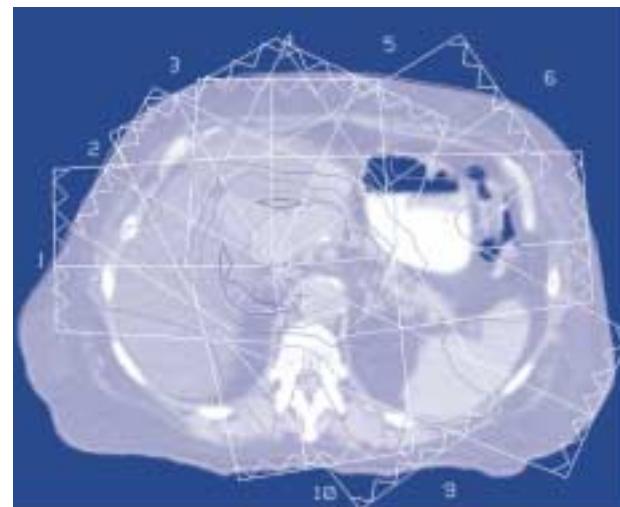
Among the specialists at California Pacific who work together in treating patients with pancreatic cancer include:

- Gastroenterologists (interventional endoscopists)
- Medical oncologists
- Radiation oncologists
- Radiologists (interventional and diagnostic)
- Pathologists
- Surgeons

intensity to accurately deliver higher doses of radiation to tumor tissues. “The benefit of IMRT is that it enables us to apply large doses of radiation while minimizing bowel toxicity and sparing tissue in surrounding organs such as the liver and kidney,” says Daniel Glaubiger, M.D., chair of California Pacific’s Department of Radiation Oncology. The Medical Center has two machines capable of delivering IMRT at present, with a third planned as well as a CT and MRI-based treatment planning system which employs a powerful, advanced computer system that evaluates many possible beam arrangements to create an optimized treatment plan for each patient’s anatomy.

Preliminary results of investigational trials using these advanced radiation techniques combined with chemotherapy appear to show some improvement in outcomes for pancreatic cancer patients when compared to previous experience. These combined treatments are intense and taxing for patients, and are best delivered at larger medical centers where all treatment modalities are available as well as the needed support services.

When given in coordination, chemotherapy enhances the impact of radiation. As Grant explains, “First, the IMRT delivers high doses of radiation to the pancreas tumor(s). Chemotherapy can complement radiation treatment by both sensitizing cancer cells to the effects



An example of beam arrangements for Intensity Modulated Radiation treatment of a pancreatic mass.

of radiation and by targeting cancer cells that can be outside of the radiation field.”

New Chemotherapeutic and Biologic Agents

Pancreatic cancer has historically had a poor prognosis because of both its ability to metastasize early and its relative resistance to many chemotherapy agents. Newer drugs such as gemcitabine and paclitaxel have been more effective. The addition of biologic therapies that target key intracellular pathways may also be an advance. On one research protocol, appropriate patients may receive the farnesyl transferase inhibitor R11577 to maintain remissions induced by radiation and chemotherapy.

To refer pancreatic cancer patients or for further details on treatment options, contact California Pacific’s Specialty Referral Program at 1-888-637-2762.



Intensity Modulated Radiation Therapy

This team approach offers patients the best treatment options for their situation. In addition, California Pacific’s expanding pancreatic cancer research program helps explore new therapies.

New research protocols for patients with pancreatic cancer include intensity modulated radiation therapy (IMRT) in conjunction with capecitabine, an oral chemotherapy drug. “This combination therapy may offer a better outcome than either radiation or chemotherapy independently,” explains Grant. (see accompanying box for other available research trials)

Intensity Modulated Radiation Therapy

Intensity Modulated Radiation Therapy (IMRT) is a newer radiation treatment technique using multiple x-ray beams that vary in

Pancreatic Cancer Clinical Trials for Patients at California Pacific Medical Center

A phase II trial of epothilone B analogue every 21 days in patients with advanced pancreas cancer

- Cytologically or pathologically confirmed adenocarcinoma of pancreas
- Locally advanced, distant metastatic or recurrent disease, not resectable, measurable or non-measurable
- No prior chemo, hormonal, immunotherapy, radiation or chemoradiotherapy as outside RT or at least 1 lesion has progressed since RT
- BMS-247550 50 mg/m² over 3hq21d with PK at baseline and cycle 1 hours 6 and either 24 or 36

A randomized phase II trial of weekly gemcitabine, paclitaxel and external irradiation followed by the farnesyl transferase inhibitor R115777 for local advanced pancreas cancer

- Pathologically confirmed adenocarcinoma of pancreas, unresectable
- No mets to major viscera, peritoneal seeding or ascites
- All malignant disease encompassable within single radiation field
- Radiographically assessable disease
- 50.4Gy/28 fractions + paclitaxel 40 mg/m²/wk x 6 + R115777 300 mg bid x 21dq28d starting 3-8 wk after RT complete

To refer possible patients in these trials, contact John Chard, R.N. at (415) 600-1475.

Whipple Procedure

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According to Surgeon Assad Hassoun, M.D., “With the use of advanced imaging techniques such as CT scan, ERCP and most importantly, endoscopic ultrasound (EUS), the outlook for pancreas cancer is more promising.” Hassoun relies on EUS (*see related article*) for evaluating the size, depth of invasion and proximity of cancer to mesenteric and portal vessels, as well as for sampling adjacent suspicious lymph nodes or liver lesions. “We can now eliminate the need for pre-operative diagnostic laparoscopy since EUS successfully delineates the plane between the tumor and the mesenteric vessels, and hence resectability,” explains Hassoun.

Whipple Procedure for Pancreatic Cancer

The Whipple procedure, first completed in 1935, is mainly performed for cancer in the pancreas head (*Figure 1*). Since then, surgeons have made further modifications to improve its outcome and diminish complications. Because of the procedure’s general success, it has been applied to premalignant conditions such as mucinous cyst of the pancreas and benign, yet very debilitating chronic pancreatitis and associated pancreatic head stricture.

At California Pacific Medical Center, surgeons have performed more than 50 Whipple procedures in the past year, with new modifications aimed at speedier recovery, decreased morbidity and complications.

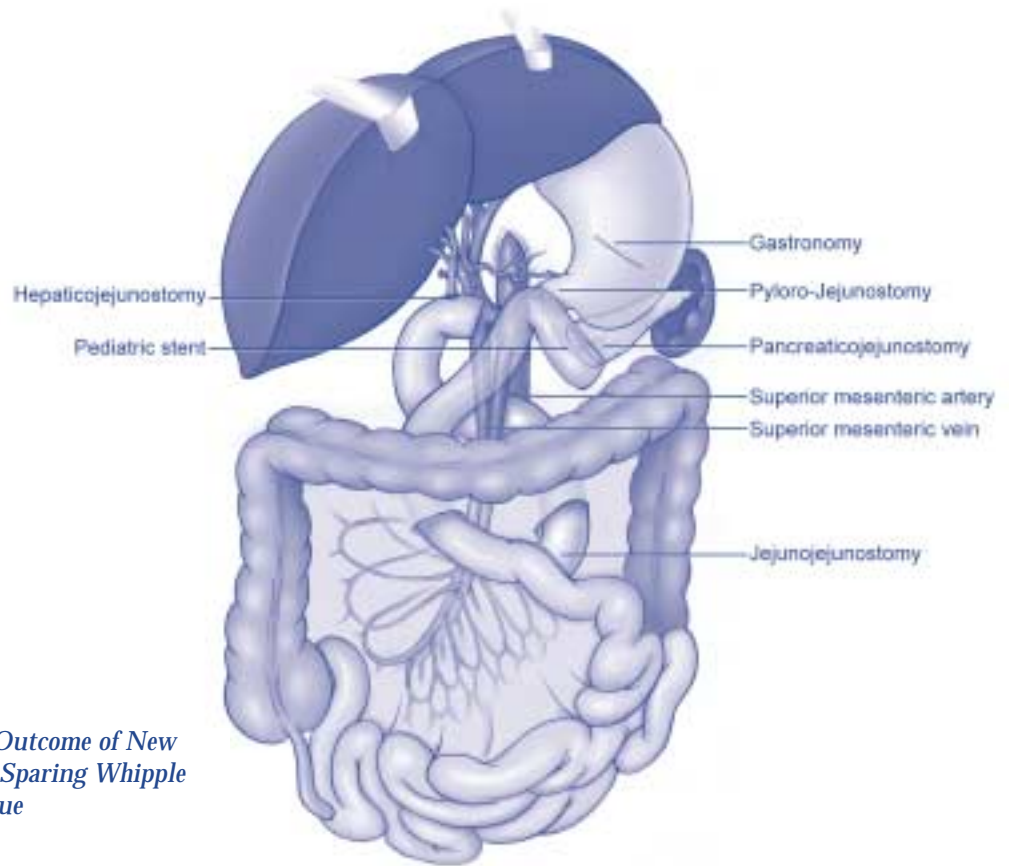


Fig. 2: Outcome of New Pyloric Sparing Whipple Technique

In most cases, California Pacific surgeons perform a “Pyloric Sparing Whipple.”

New Pyloric Sparing Whipple Technique

This new technique advances the first Limb of Jejunum (the Y Limb) toward the hepatic duct at the retro-mesenteric level and reconstructs a new Ligament of Trietz. Next, the second Limb of Jejunum (the Roux Limb) is divided and advanced in a retro-colic position toward the pancreas (pancreaticojejunostomy).

This same limb is then advanced toward the post-pyloric area of the stomach and a

pylorojejunostomy is performed. A partial inner pyloromyotomy is created during this anastomosis. The two limbs (both 40 cm in length) are then connected together, creating a jejunojejunostomy anastomosis. (*Figure 2*)

“We have found this modification very successful in achieving decreased bile gastritis, minimized reflux cholangitis and better gastric emptying,” explains Hassoun.

For further information on surgical treatments for pancreatic cancer, contact California Pacific’s Specialty Referral Program at 1-888-637-2762.

Endoscopic Ultrasound

continued from page 1

Recent adjustments to the staging classification by the American Joint Committee on Cancer (AJCC) classify the spread of pancreatic cancer as follows:

- T2: tumor invasion of the bile duct
- T3: tumor invasion of the portal vein, superior mesenteric vein and/or splenic vein
- T4: tumor invasion of the superior mesenteric artery and/or celiac axis

“In the past, surgical exploration was often necessary to identify the spread of cancer into adjacent structures,” explains Binmoeller.

“With EUS, however, we can avoid surgery and instead determine unresectable disease with a relatively painless imaging procedure.”

If, during EUS staging, the endoscopist determines one’s pancreatic cancer is unresectable, he will continue with EUS-guided fine needle aspiration (FNA). EUS again assists in attaining this biopsy specimen by enabling the endoscopist to precisely pinpoint needle placement. The FNA specimen obtained helps physicians determine adjuvant therapy and



Fig. 1: Echoendoscope with FNA needle projecting from the instrumentation channel.

can confirm metastatic spread to lymph nodes, liver, peritoneum, etc. Not only do patients benefit from this two-in-one procedure by avoiding unnecessary surgery and additional imaging, but it also results in additional cost savings to the payer.

For further information about endoscopic ultrasound or to refer patients for imaging, contact California Pacific’s Specialty Referral Program at 1-888-637-2762. You can also view our interventional endoscopy web site at www.cpmc.org/ies.



Fig. 2: Pancreatic head tumor invading and encasing the portal vein.



Fig. 3: FNA of a pancreatic tumor.

Save the Date: July 19, 2003

Managing Chronic Viral Hepatitis and
Liver Cancer on the Pacific Rim

Physicians and medical professionals are invited to an upcoming CME Conference at The Lodge at Sonoma focusing on liver cancer and new treatments for viral hepatitis. Among the topics presented include:

- State-of-the-art HCV Management: Is this Disease Curable?
- New HCC Options: Probes, Catheters and Transplant
- HBV: Why is This Virus So Hard to Treat and What Have We Learned?

For further details, contact Robert Gish, M.D. at (415) 600-1022.



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