

# Is an R1 or R2 Resection of Pancreatic Adenocarcinoma of Any Benefit, or Does it Just Increase Morbidity?

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Diagnosis and Management of Pancreatic Cancer:  
Common Dilemmas

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# Agenda

- What is comparative survival in pancreatic cancer patients with R0, R1, and R2 resections?
- How accurate is the radiologic imaging for staging pancreatic cancer?
- Do R1 and R2 resections only occur in patients with borderline resectable tumors?
- Borderline resectable tumors
  - Definitions
  - Should they always receive preoperative therapy?
- Unresectable pancreatic tumors in younger individuals-Is aggressive therapy worth it for the patient?

# IN MY OPINION.....

The goal of surgery is to **CURE** the patient.

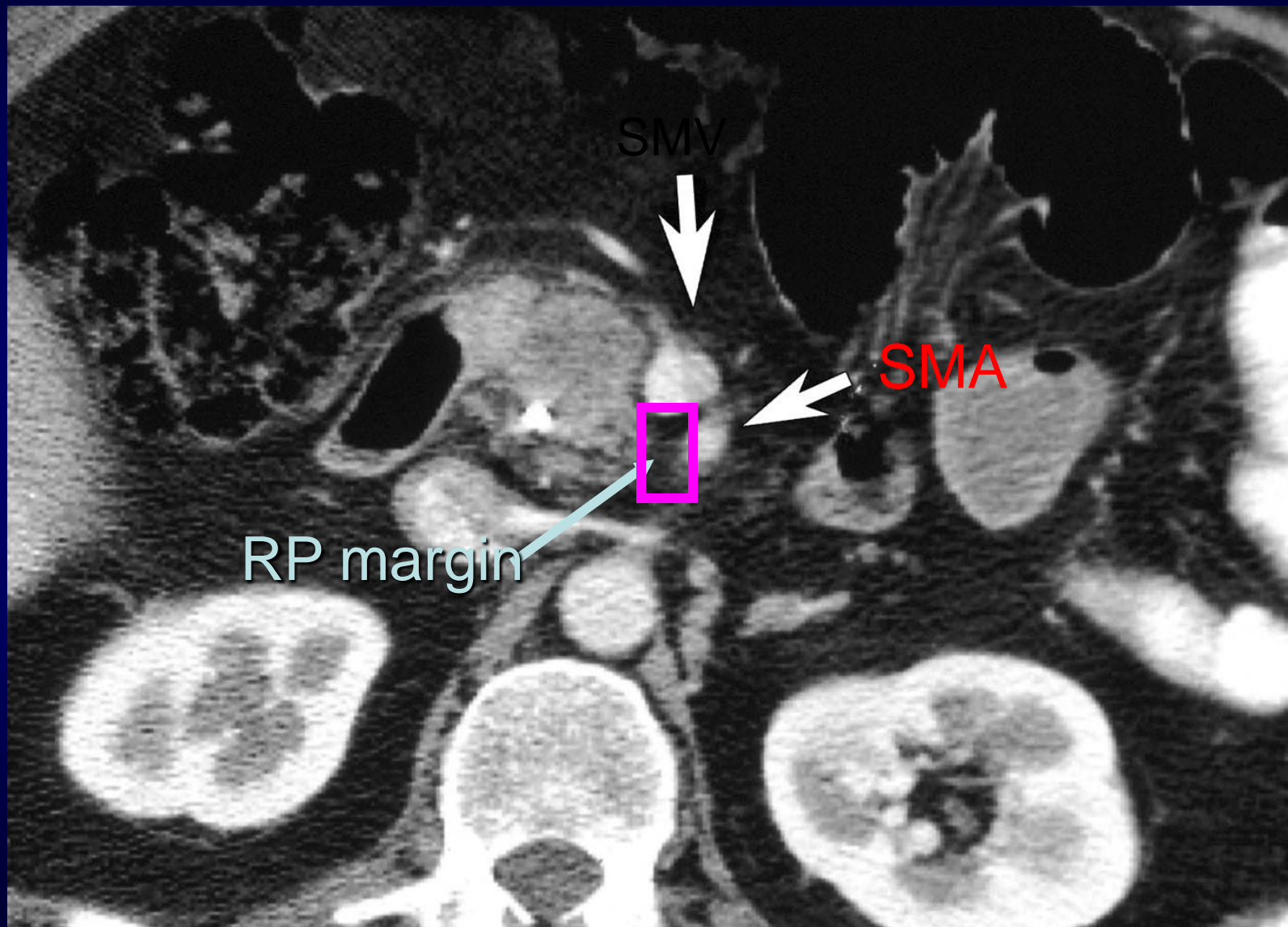
The goal of surgery is **NOT SIMPLY** to  
remove the tumor.

# Margin Status after pancreatic cancer resection

## R Status

R Designation	Gross Resection	Microscopic Margin
R0	complete	negative
R1	complete	positive
R2	incomplete	positive

# Retroperitoneal Margin



# Margin + Resections are Frequent and Associated with Poor Prognosis

<b>Author - Country</b>	<b>Number of Patients</b>	<b>Margin + Resection Rate</b>	<b>Median Survival</b>	<b>Independent Prognostic Factor</b>
Winter-U.S.	1175	42%	14 m	Yes
Richter-Germany	194	37%	12 m	Yes
Kuhlmann-Netherlands	160	50%	NS	Yes
Takai-Japan	89	47%	8 m	Yes

# R0 is better than R1 is better than R2

Institution	Margin + Rate	Median Survival R0	Median Survival R1	Median Survival “R2”
Mayo <sup>1</sup>	24%	18-19	15	10
Hopkins <sup>2</sup>	42%	20	14	
MGH <sup>3</sup>	30%	22	15	11

<sup>1</sup>Fatima J et al, Arch Surg, 2010

<sup>2</sup>Winter JM et al, J Gastrointest Surg, 2006

<sup>3</sup>Konstandinidis et al, GI ASCO 2010

# R0 is better than R1 is better than R2

Institution	Margin + Rate	Median Survival R0	Median Survival R1	Med. Survival "R2"
Mayo	24%	18-19	15	10
Hopkins	42%	20	14	
MGH	30%	22	15	11
<b>MDACC</b>	<b>17%</b>	<b>27.8</b>	<b>21.5</b>	

70% of MDACC patients received preoperative therapy!



Not all R1 resections are “true R1s” .....

Currently, R status is determined by surgeon and pathologist

# Lessons from Adjuvant Therapy Trials

## R1 resections are likely under-reported

<b>Study</b>	<b>N</b>	<b>%R</b>	<b>%T3</b>	<b>%N</b>	<b>%L</b>
		<b>1</b>		<b>1</b>	<b>F</b>
ESPAC-1 <sup>1</sup>	289	18	NS	54	63
CONKO-001 <sup>2</sup>	194	16	82	70	38

<sup>1</sup>Neoptolemos JP et al. NEJM, 2004

<sup>2</sup>Oettle H, et al. JAMA, 2007

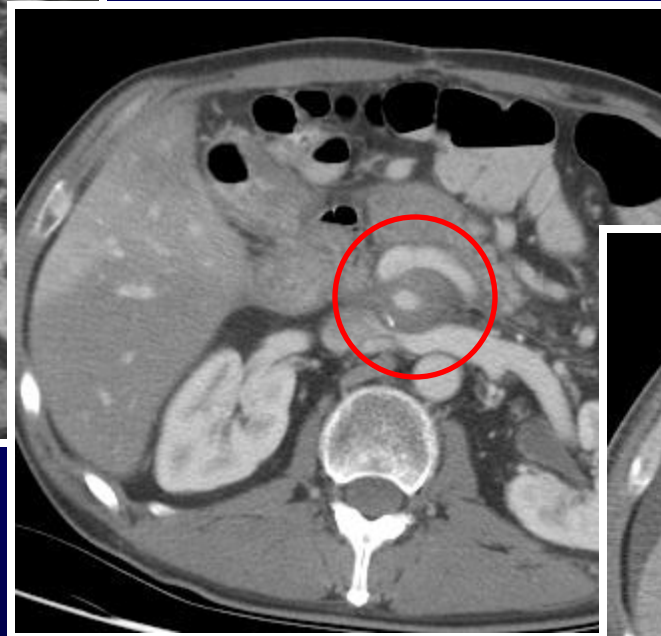
# Lessons from ACOSOG Z 5031 trial

- Only 68% described evaluation of the peritoneum
- SMA skeletonization was described in only 14%,
- Absence of residual macroscopic disease after resection was documented in 24%.
- Specimen inking was documented in 65% and histologic evaluation of the SMA margin reported in 47%.

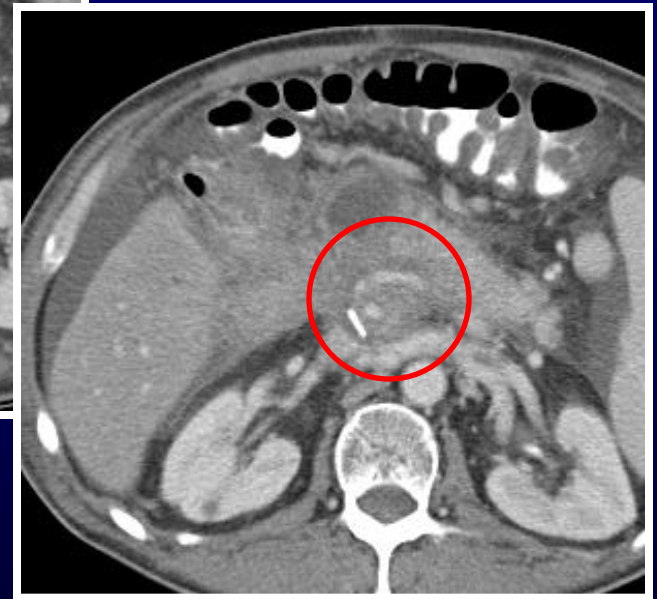
# Post-op CT images of a patient who reportedly underwent an R1 resection



6 weeks



6 Months



9 Months

# Pre-op CT images of a patient who reportedly underwent an R1 resection



Preoperative CT scans

Not all R1 resections are “true R1s”.....

In the future, R status should be determined by a RADIOLOGIST, a surgeon, and a pathologist.

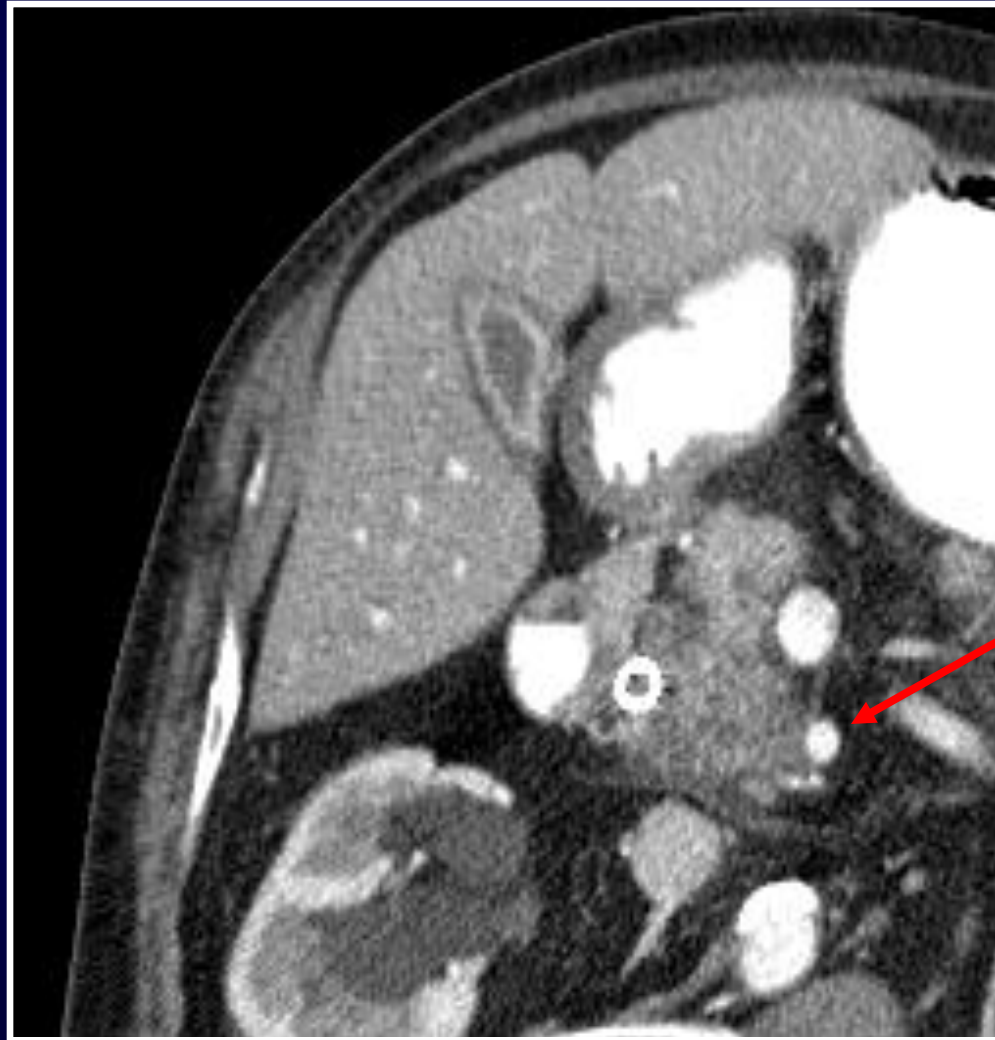
Strict radiographic criteria for resectability and standardization of surgery and specimen processing

# How accurate is high-quality preoperative Imaging?

- Predicts “resectability” about 90% of the time. Predicts unresectability close to 100% of the time.
- A CT scan is NOT a microscope.

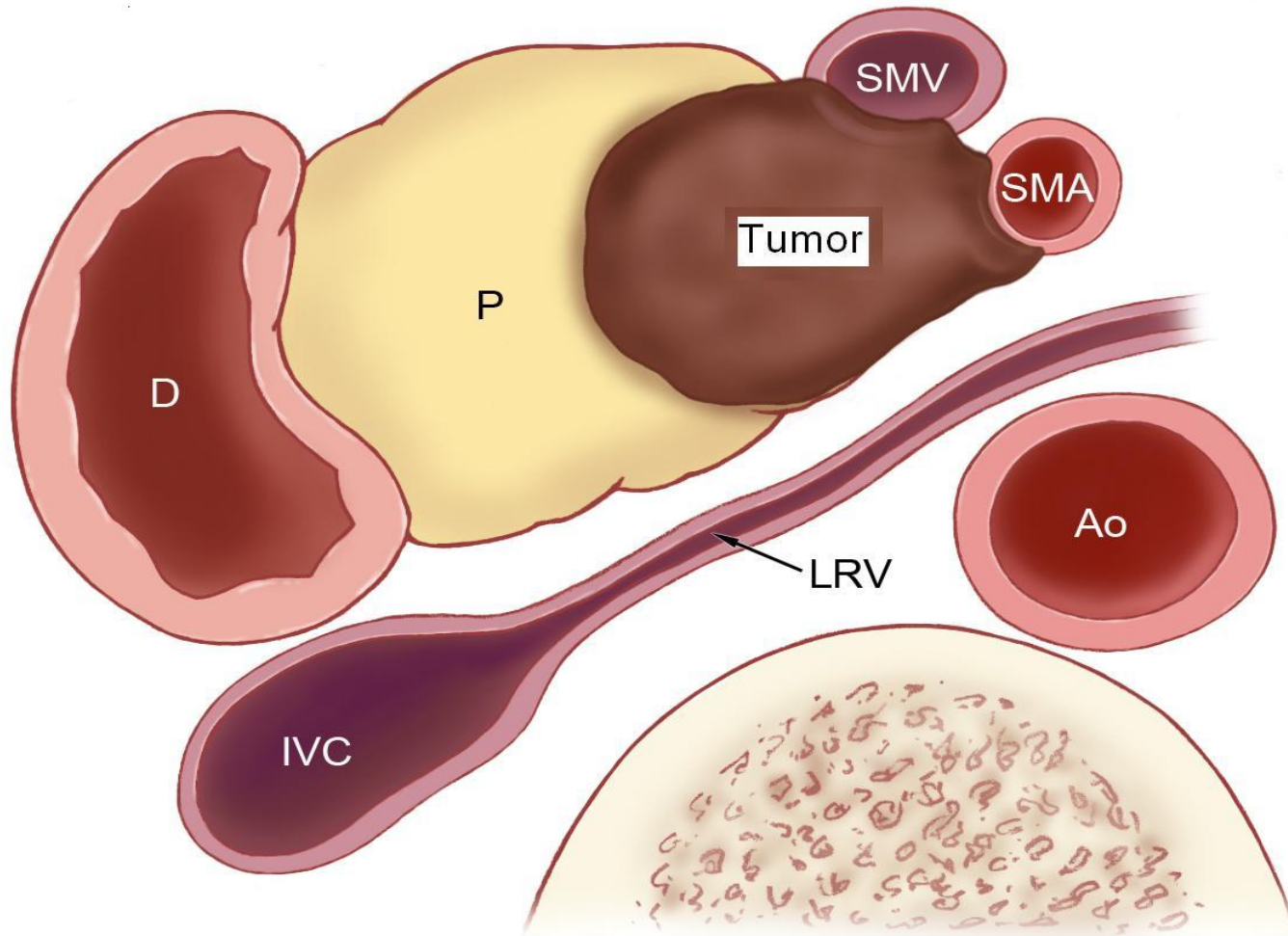
Institution	R1 Resection Rate with Upfront Surgery
MSKCC <sup>1</sup>	20%
MDACC	21%

Is this resectable at your hospital?

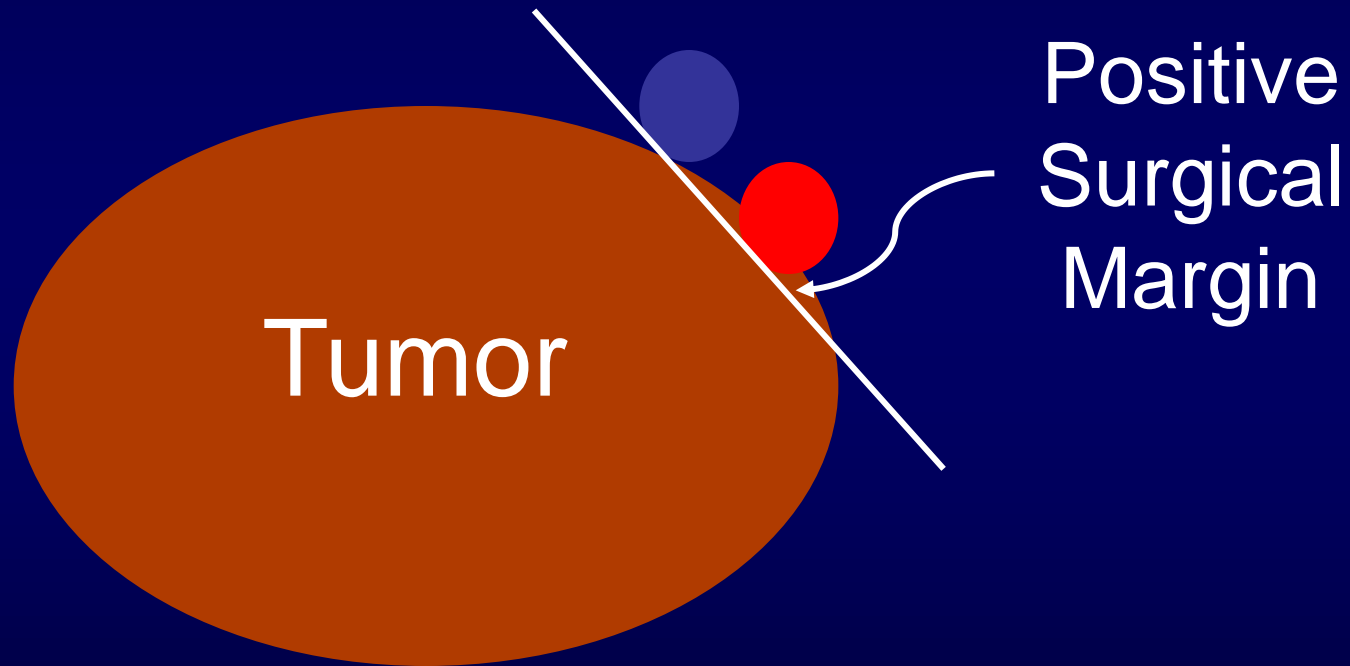


**SMA**





# Borderline Resectable Pancreatic Cancer



DOOM!!!!!!!!!!!!

## 2 Surgical Philosophies

“Tumor *wasn't clearly unresectable* so we attempted resection.”

**This may be unwise.**

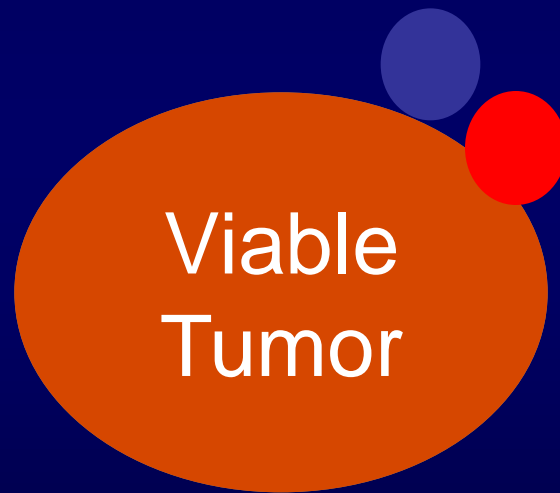
“Tumor *wasn't clearly resectable*, so we gave preoperative therapy.”

**Good move!!!!**

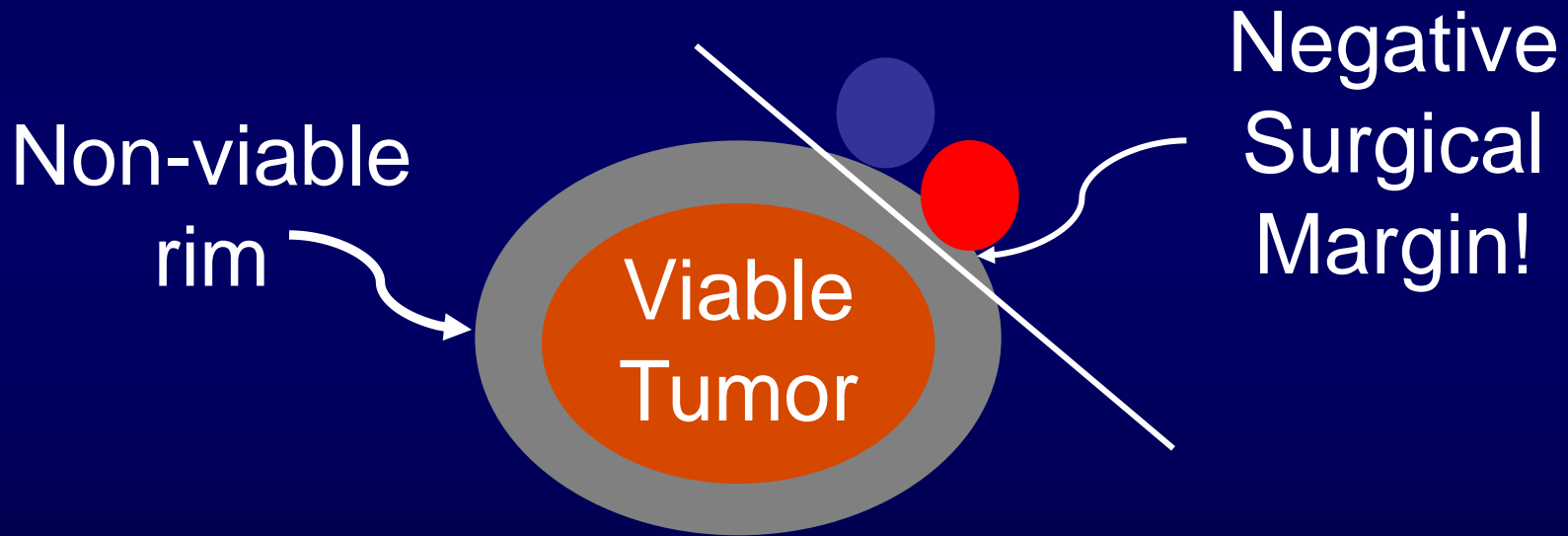
# Borderline Resectable Pancreatic Cancer

- Emerging entity due to the use of high quality CT imaging
  - Tumor abuts /involves the SMA for  $<180$  degrees
  - Short segment encasement of the common hepatic artery
  - Short segment venous occlusion with patent vein above and below
- Contaminate adjuvant and locally advanced PC trial results – needs to be studied separately
- Very high risk for margin positive resection – good candidates for preop therapy

# Borderline Resectable Pancreatic Cancer



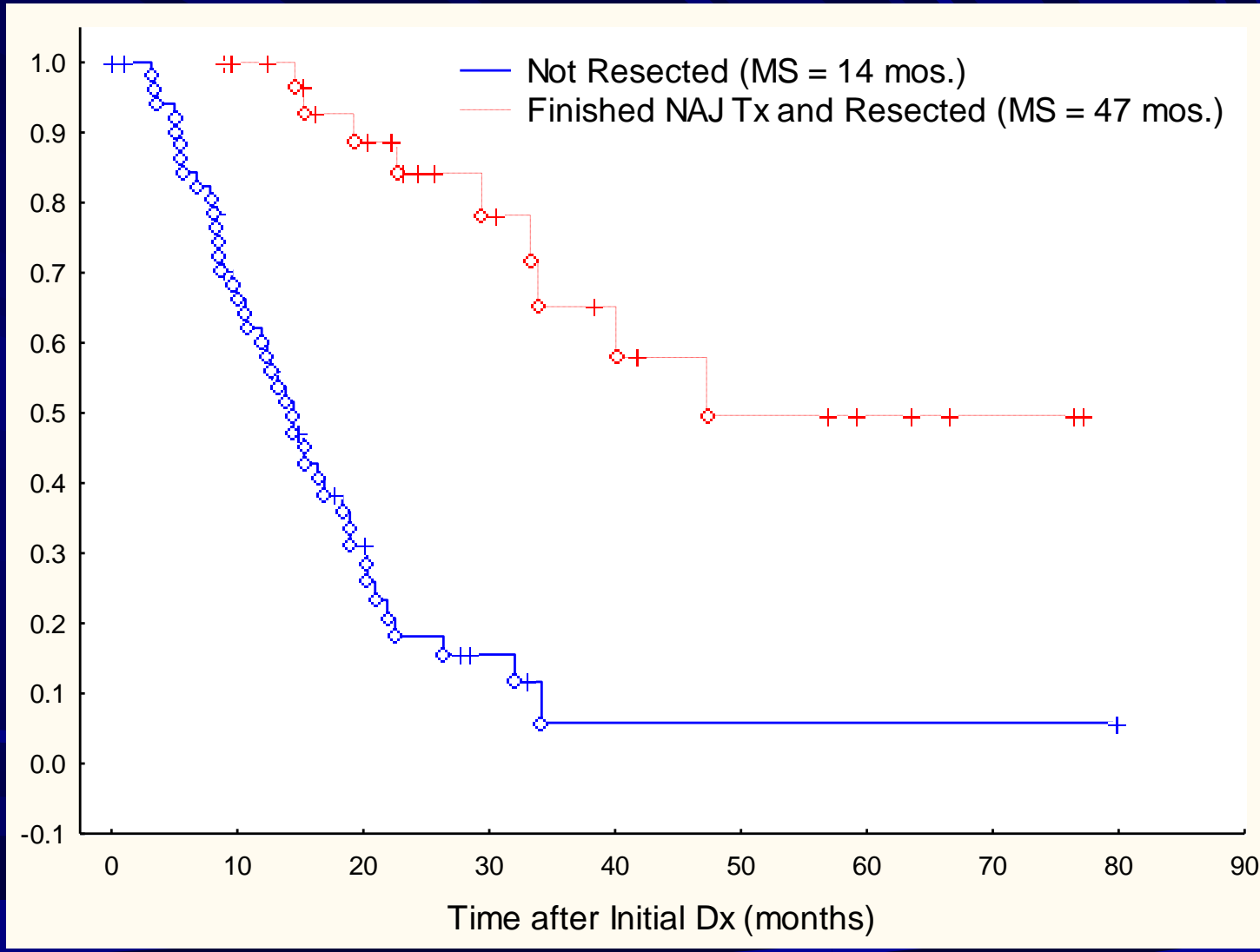
# After Preoperative Chemotherapy and ChemoXRT



**YIPPEE!!!!**

# Borderline Resectable Pancreatic Cancer

## MDACC Results for Type "A" Patients



Type A patients (95) operated v. not operated

# Making Progress with non-surgical rx?

UCSF<sup>1</sup>  
25 Pts

Induction Gem/Cis

Cape/XRT

17 mo

28% Progressed

10 mo

GERCOR<sup>2</sup>  
181 Pts

Induction ChemoRx

ChemoXRT

15 mo

29% Progressed

Continued Chemo

12 mo

MDACC<sup>3</sup>  
69 Pts

Gem/Ox/Cetuximab

ChemoXRT

19 mo

6% Progressed

<sup>1</sup>Ko A et al. *Int J Rad Oncol Biol Phys*, 2007

<sup>2</sup>Huguet F et al. *JCO*, 2007

<sup>3</sup>Crane CH et al. *GI ASCO 2010*



# To Summarize

- R0 resections do best.
- R1 resections are common (probably underreported).
- R1 resections do a little better than patients with locally advanced disease.
- R1 resection after preoperative radiation may have “attenuated” tumor biology.
- Patients with borderline resectable cancer are at high risk of a margin + resection with upfront surgery.
  - 40% can go onto have resection with >90% R0 after preop rx.
  - Excellent long term survival.
- Non-surgical treatment for locally advanced pancreatic cancer is slowly improving, using a chemo first approach.
- Performance status, not age is probably most important variable