

# LOCALIZED INTRA-ARTERIAL GEMCITABINE: IMPACT ON SURVIVAL IN PATIENTS WITH LAPC—A NEW TREATMENT PARADIGM

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RenovoRx



# Local Control for Locally Advanced Pancreatic Cancer

- Local control appears to be important for symptoms and survival in LAPC
- Cure is unlikely
- Results for current treatment modalities are suboptimal
- As pancreatic cancer is generally considered to be a systemic disease, the current paradigm emphasizes chemotherapy
  - Combined regimens

# Many Forms of Local Control

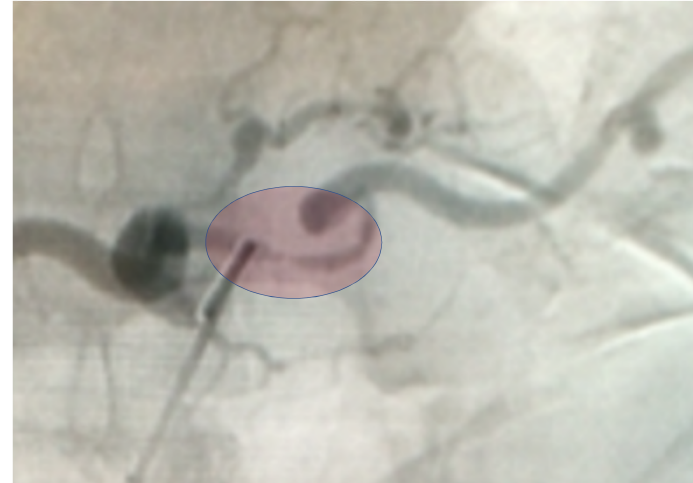
- IRE
- Radiation/SBRT
- Tumor Treating Electric Field
- Adenovirus/gene therapy
- High intensity focused ultrasound
- TACE

# Technical problem: liver vs. pancreas



## **Liver tumors highly vascularized:**

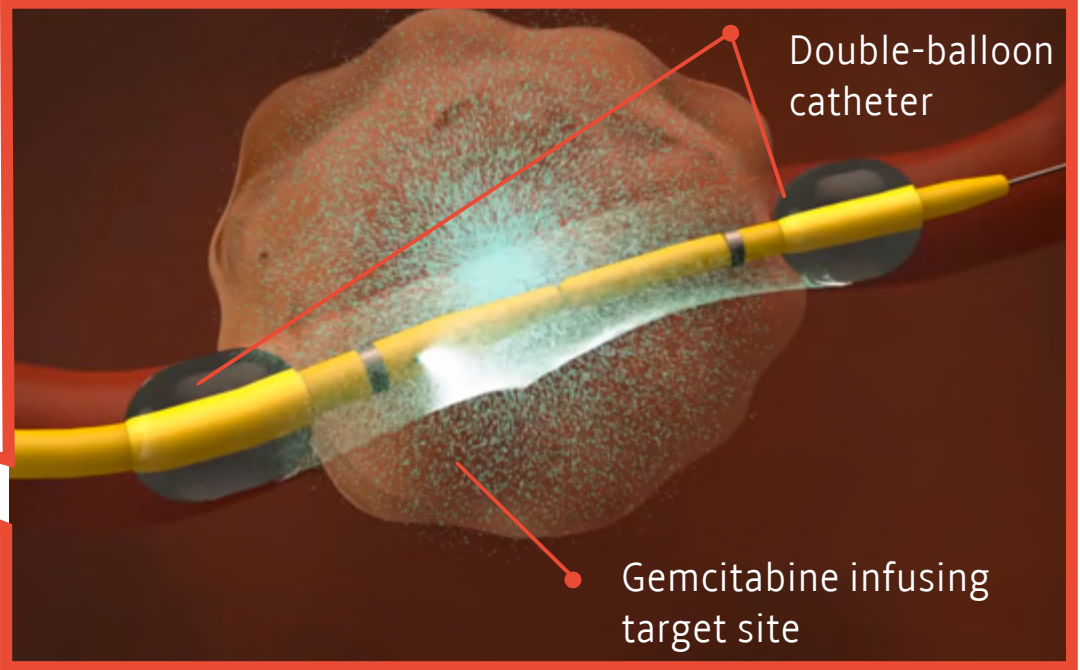
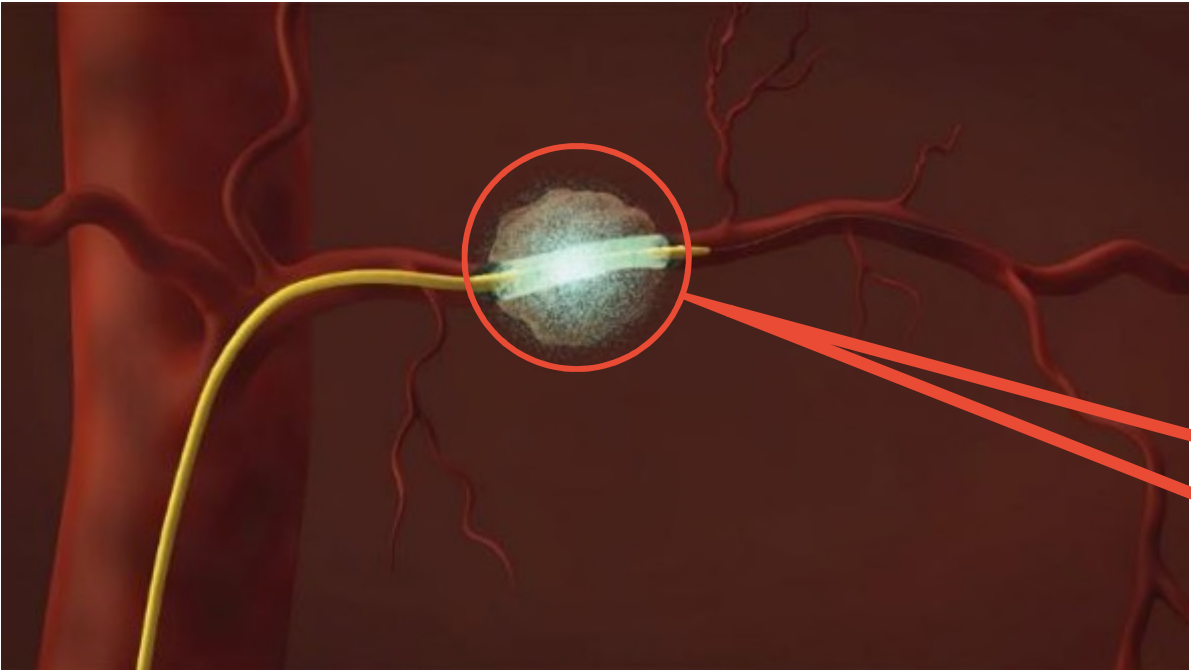
- Large tumor feeders – excellent targets for therapy
- Large branches within tumor - easily visualize tumor



## **Pancreas tumors: hypovascular**

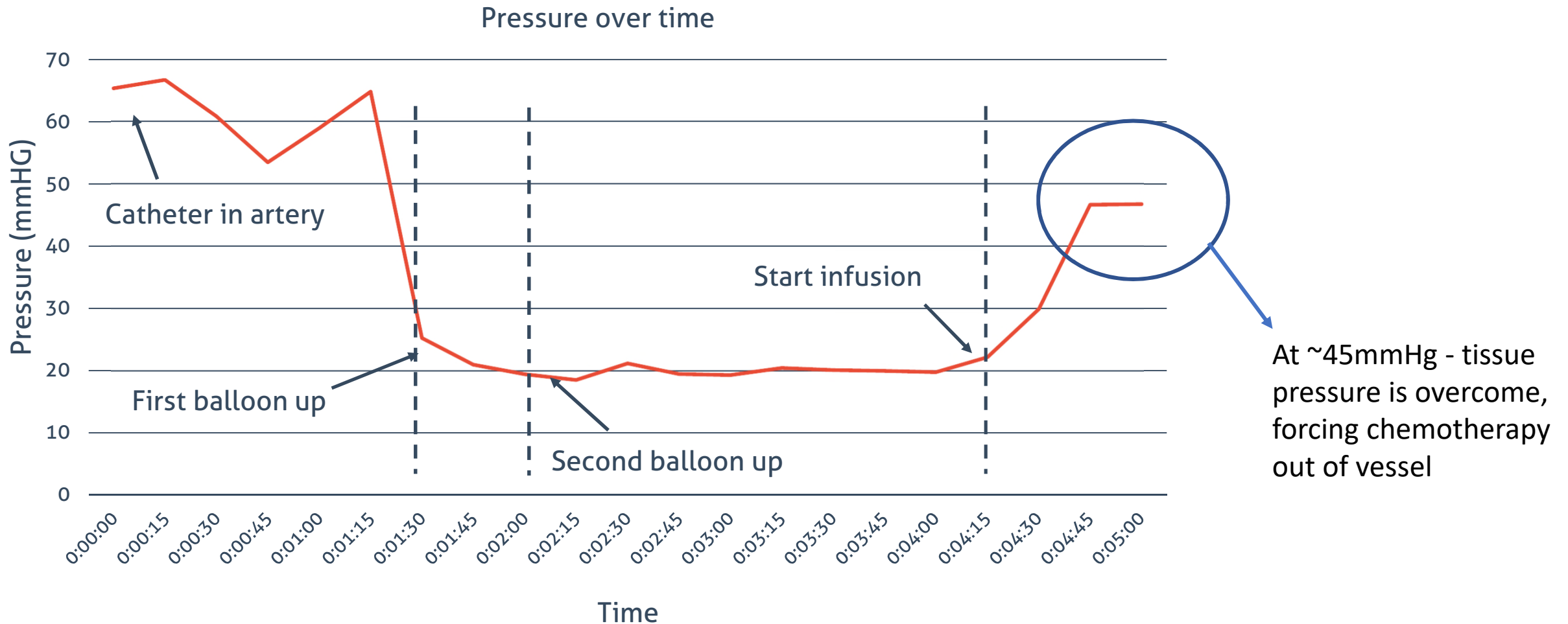
- Inability to identify or engage tumor feeder vessels

# RenovoRx found a way to make targeted therapy work

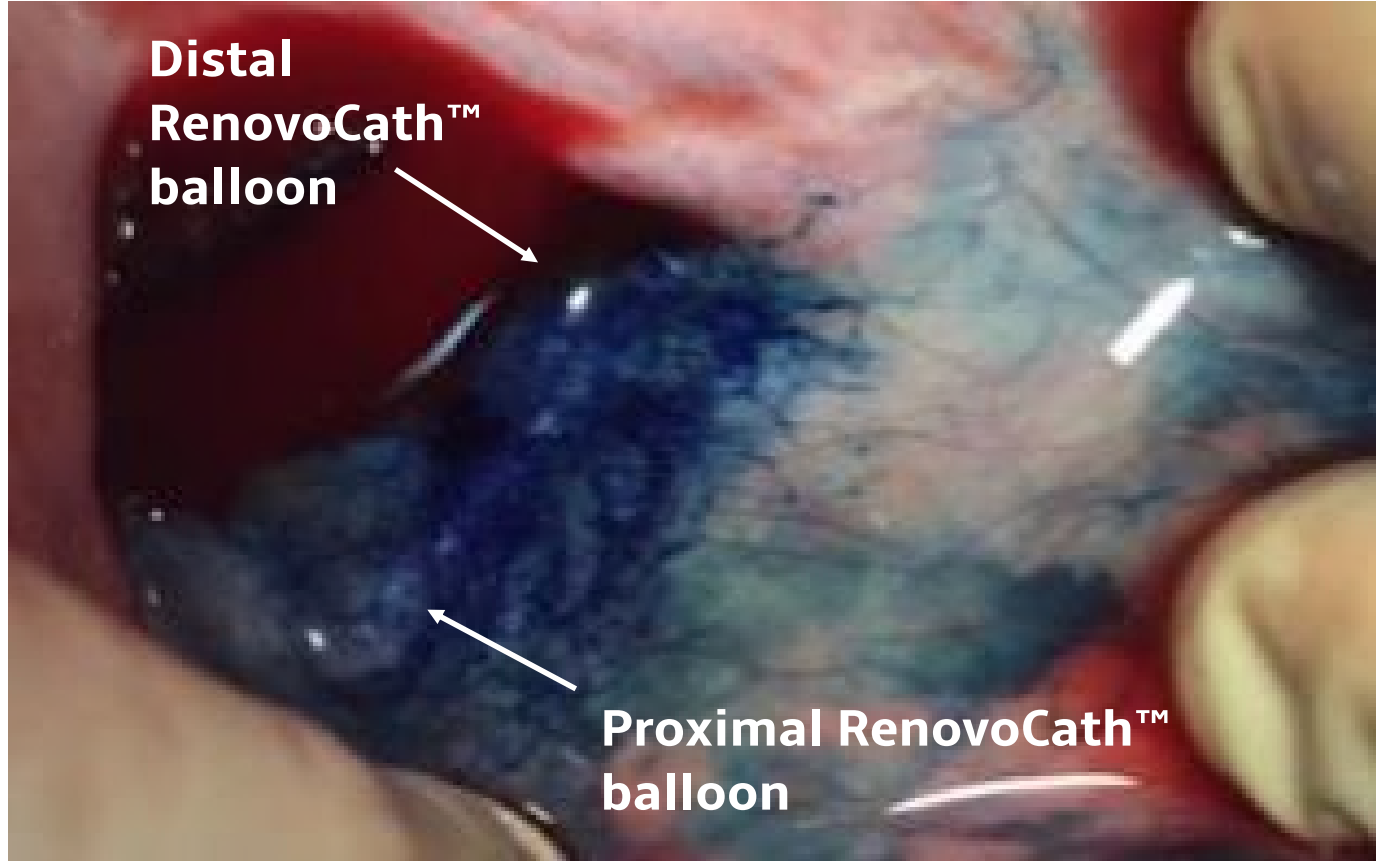


The **RenovoCath™ System** isolates the anatomy and micro-perfuses targeted tissue with gemcitabine

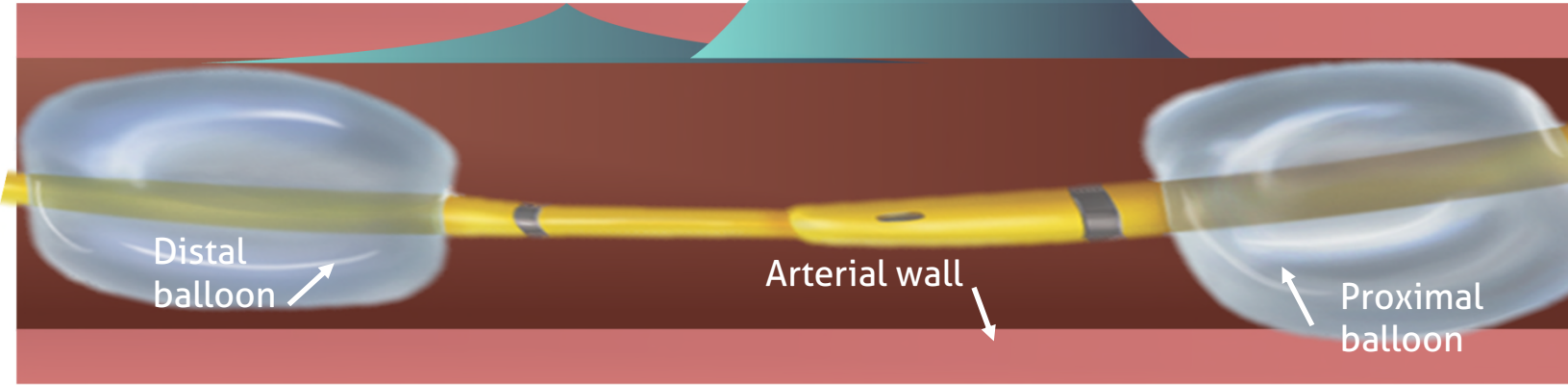
# Pressure mediated Trans-Arterial Micro-Perfusion (TAMP) Pressure over time



# Perfusion distribution



99.75% Permeating through arterial wall into tissue



# RenovoCath in pancreatic cancer: Phase I/II studies to explore clinical endpoints

## RR1- Dose Escalation Safety Study

- Primary Endpoint: Safety, MTD
- Secondary Endpoint: Survival
- Completed July 2016

**20 Patients**

• 101 Treatments



## RR2 – Post-Market Registry

- Primary endpoints: Survival, tumor response
- 6 centers Initiated Jan. 2016
- Limited to patient with Prior Radiation: March 2017
- Limited to one active site w/ Initiation of Phase 3 TIGeR-PaC: May 2018

**25 Patients**

• 96 Treatments



# Results

- To date, 43 pts. treated with IA Gemcitabine using RenovoCath between the 2 studies from May 2015 to Dec 2018 (*2 patients rolled over from safety to registry study*)
- Average age of patient enrolled was 73
- 24 of 43 patients had prior treatment before IA therapy :
  - chemotherapy (n=11 )
  - chemoradiation (n=12)
  - prior surgery (n=1).
- Median gemcitabine dose was 1000mg/m<sup>2</sup>
  - Full 1000mg/m<sup>2</sup> dose administered to 36 of the 43 patient cohort

## Results (Cont'd)

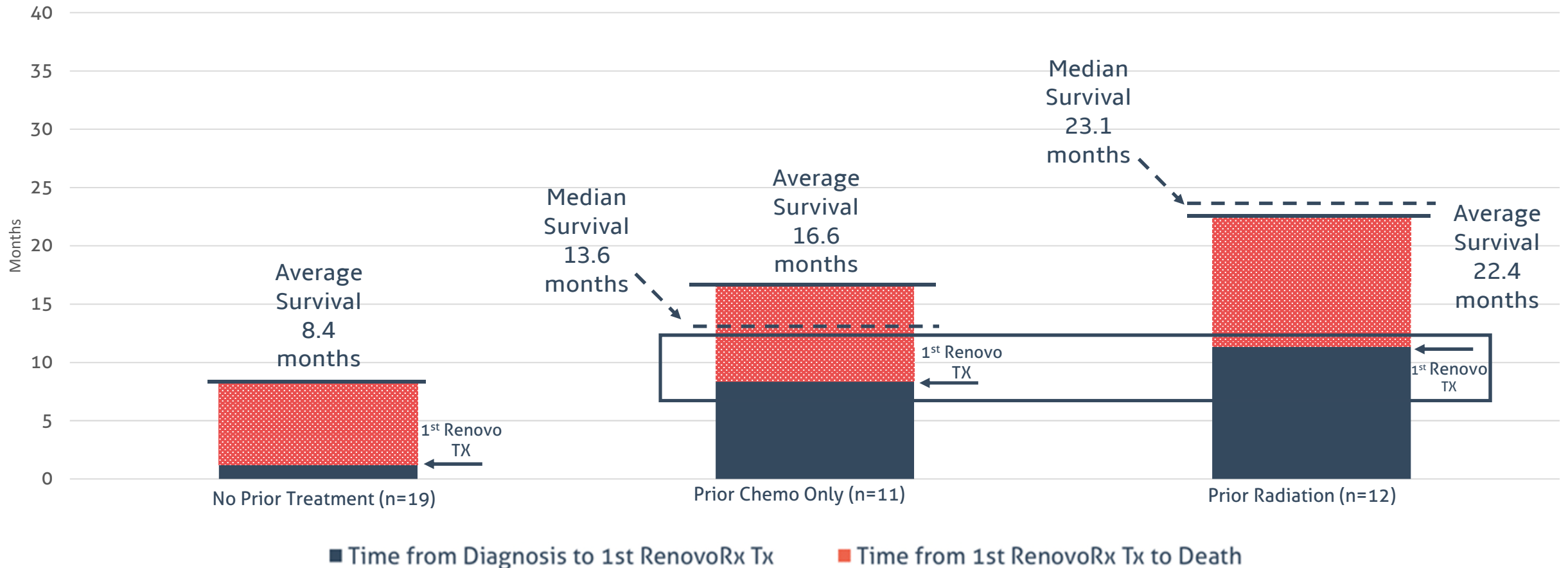
- On average each pt. received four IA treatments, ranging from 1-14 treatments
- 13 of 43 patients completed the planned 8 treatments of IA therapy
- Reasons for early discontinuation of IA therapy:
  - severe adverse events (n=12)
  - tumor progression (n=8)
  - patient/physician preference (n=6)
  - others (n=4)

## Results (Cont'd)

- In the overall cohort 6 of 43 patients are still alive, median overall survival 12.4 months
- Patients with prior chemoradiation showed the best clinical response in terms of tumor response (CT and tumor markers) and survival across both studies
  - Median survival of 27 months (5 of 12 patients still alive)

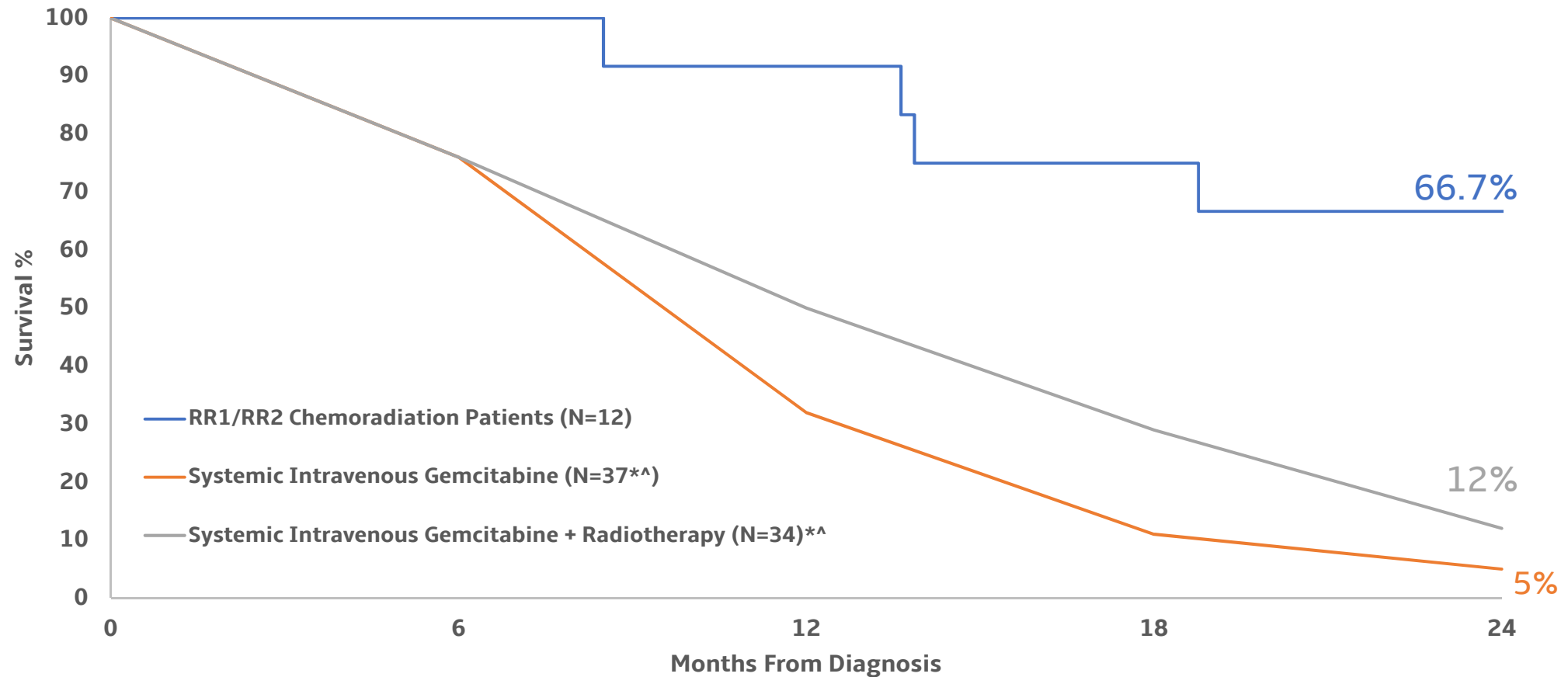
# Subset analysis lead to discovery of chemoradiation + Trans-Arterial Micro-Perfusion (TAMP)

The RR1 Safety Study and the RR2 Registry Study demonstrated survival benefit **after** RenovoCath™ treatments begin



Note: 1 patient with prior surgery not included in analysis above

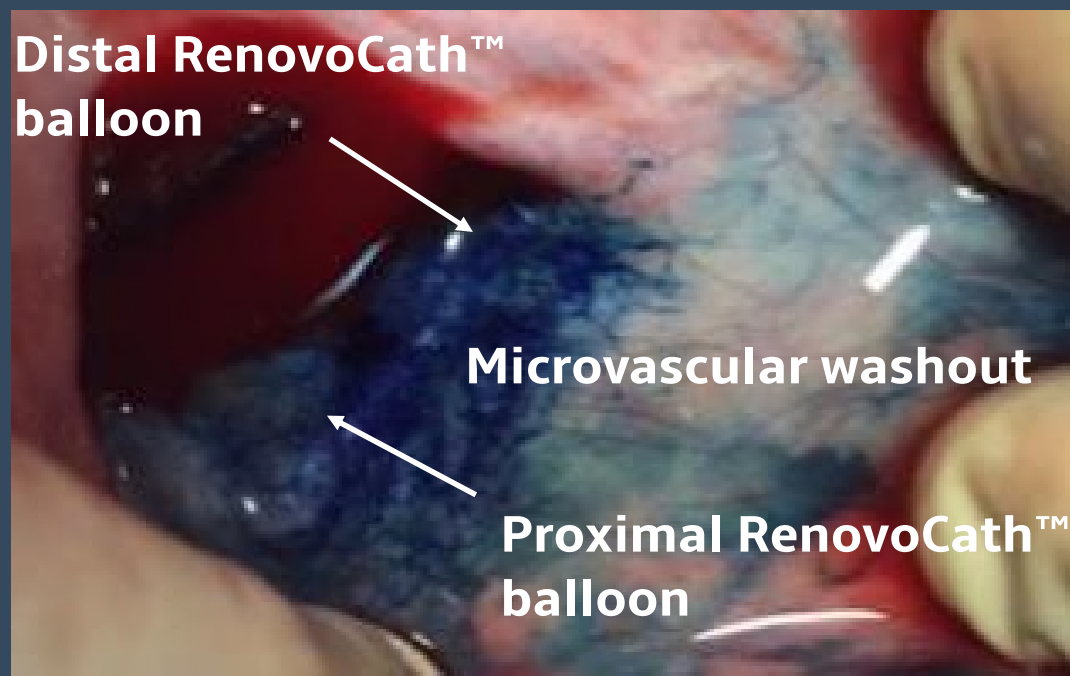
# Overall Survival of chemoradiation + RenovoCath (RR1 & RR2) vs. Historical Control (LAPC)



\*Chauffert, B. et al. Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000-01 FFCD/SFRO study. *Annals of Oncology* 19, 1592–1599 (2008).

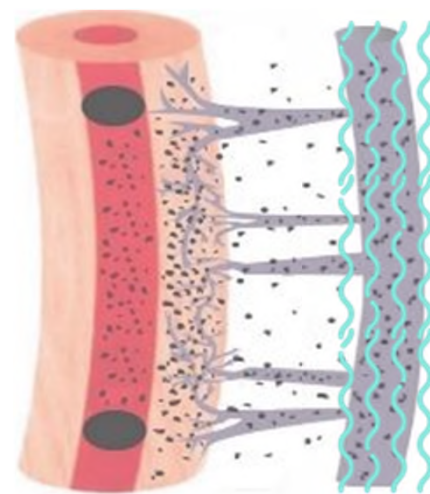
^ Loehrer, P. J. et al. Alone Versus Gemcitabine Plus Radiotherapy in Patients With Locally Advanced Pancreatic Cancer: An Eastern Cooperative Oncology Group Trial. *Journal of Clinical Oncology* 29, 4105–4112 (2011).

# Mechanism of action: Trans-Arterial Micro-Perfusion (TAMP) combined with radiation

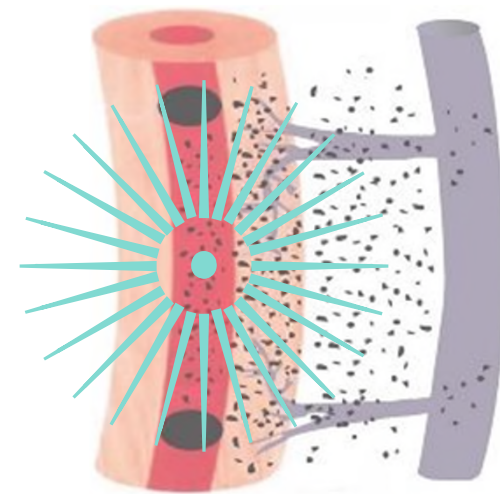


## Radiation reduces venous outflow by decreasing the microvasculature

Native vasculature and  
IA chemo lead to  
**Micro-vascular washout**



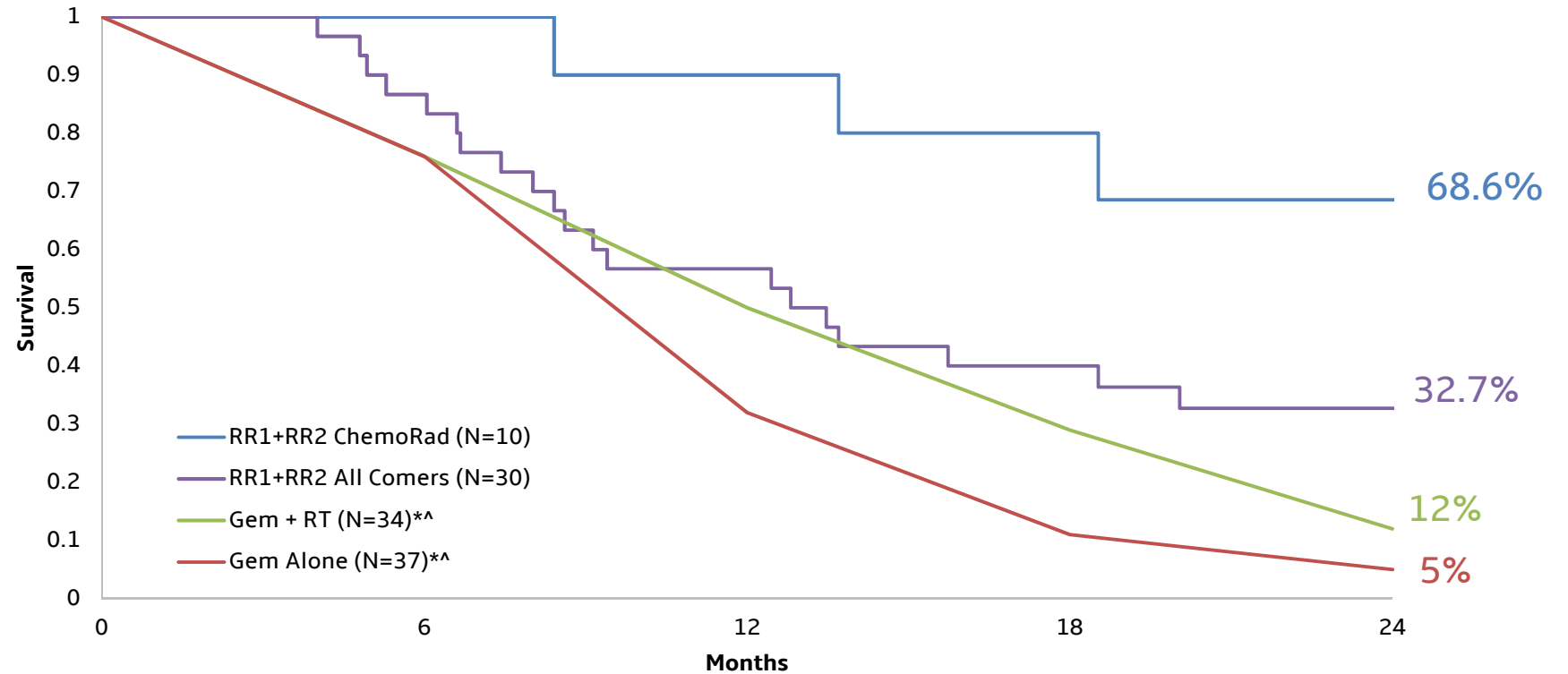
Irradiated vasculature  
and IA chemo lead to  
**Diffusion**



# K-M Plots of Overall Survival from Diagnosis Date by Different Sub-groups

RR1 and RR2 Subjects who Received  $\geq 3$  IA Treatments

Alive statuses of subjects are verified as of 01 JAN 2019



Number Alive (at Risk of Death)	RR1+RR2	RR1+RR2 ChemoRad	Gem + RT (N=34)*^	Gem Alone (N=37)*^
0	30	10	34	37
3	30	10	28	28
6	26	10	22	22
9	19	9	16	16
12	17	9	12	12
15	13	8	9	9
18	11	7	7	7
21	9	6	5	5
24	9	6	4	4

Group	Dead/N	Q1 (95% CI)	Median (95% CI)	Q3 (95% CI)
RR1+RR2	25/30	7.4 (5.3, 9.4)	13.1 (8.4, 20.0)	28.0 (15.7, NE)
RR1+RR2 ChemoRad	7/10	18.5 (8.4, 28.0)	27.8 (18.5, NE)	28.6 (27.8, NE)

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## Limitations

- Small numbers of patients
- Non-randomized
- Selection bias



# Conclusions

- Localized intra-arterial delivery of gemcitabine using RenovoCath demonstrates encouraging results in stabilizing local disease
- This benefit is especially pronounced in patients with prior induction therapy with radiation
- TIGeR-PaC (clinical trial.gov #NCT03257033)
  - Phase III multicenter randomized trial
  - 300 patients
  - IA gemcitabine versus gemcitabine +nab-paclitaxel (Abraxane) following 4 months chemo and chemoradiation for patients with LAPC
  - 12 of 30 planned centers have initiated enrollment into the study with expected completion of enrollment in 2021