Clinical and Immunologic effect of IORT in Pancreatic Cancer Surgery

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Disclosure Statement of Financial Interest

“No COI”

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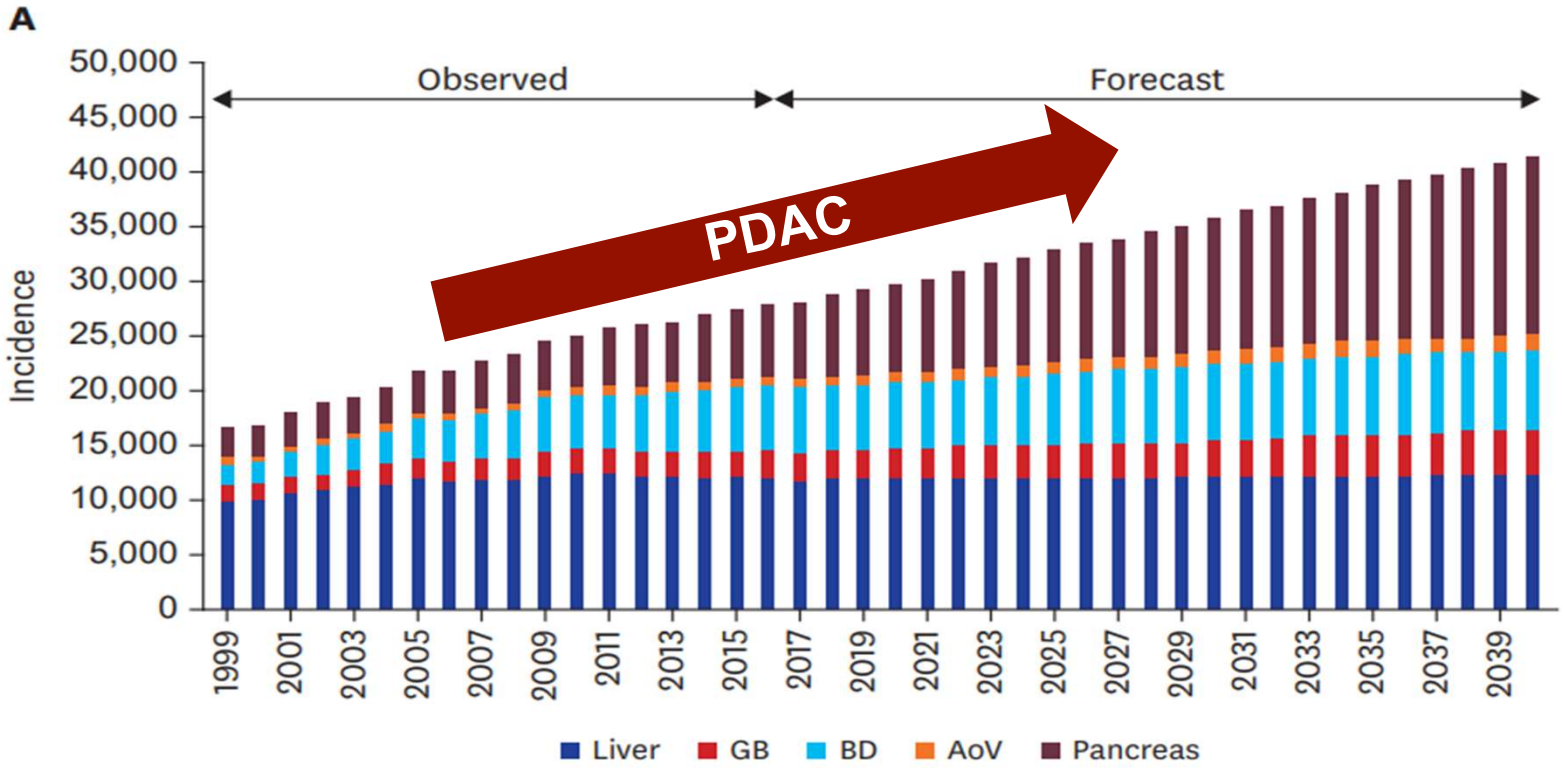
Expected Incidence of PDAC in Korea



Annual number of incidence of PDAC is rapidly increasing

Park HM et al. J Korean Med Sci, 2022

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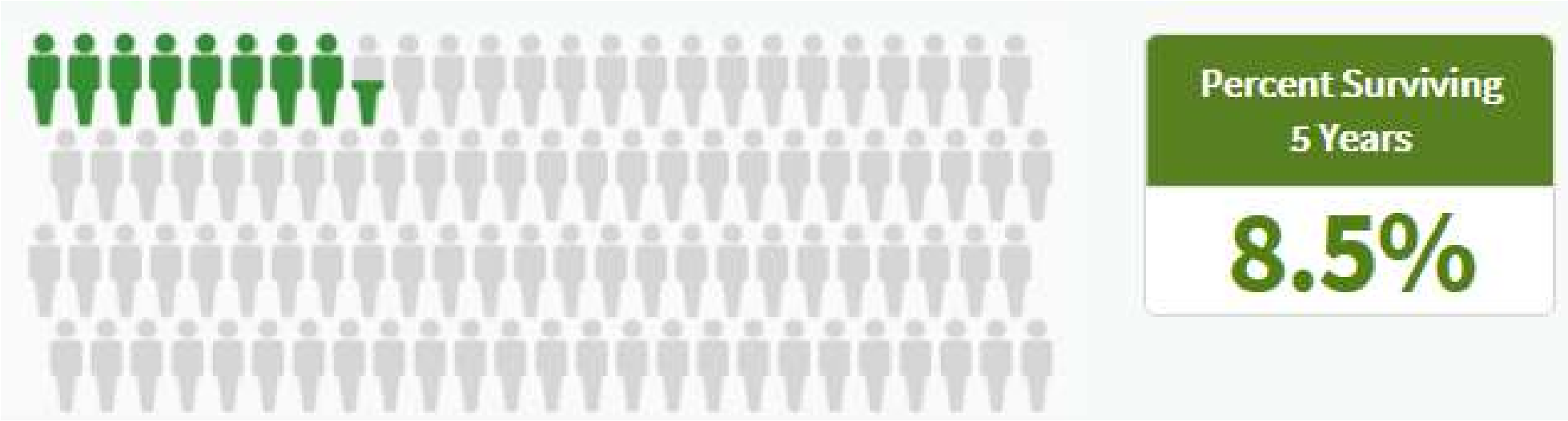
Pancreatic cancer is still poor prognosis



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Negative margins are the goal

with Radical Resection for PDAC

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Definition of resection margin

- **Tumor free margin > 1mm**
- Ink marking of the different Resection margin
- Axial dissection technique
- Remaining difficulty in differentiation of pancreatic, ampullar and distal bile duct cancers

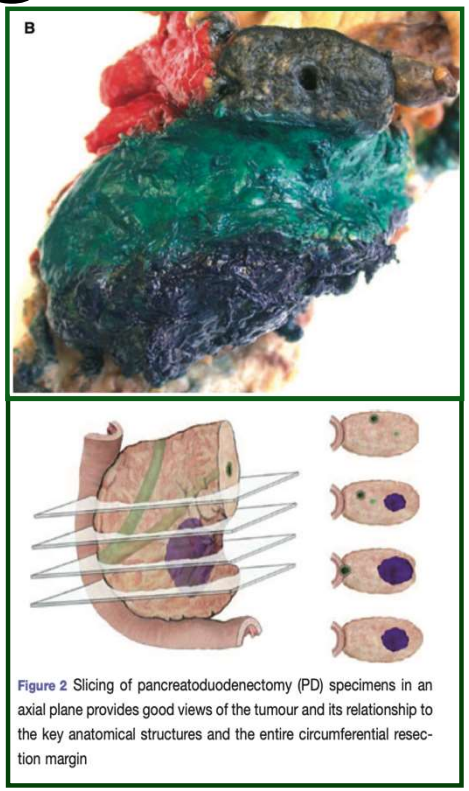

Figure 2 Slicing of pancreatoduodenectomy (PD) specimens in an axial plane provides good views of the tumour and its relationship to the key anatomical structures and the entire circumferential resection margin

Verbeke CS. Histopatholgoy 2008:52;787-796

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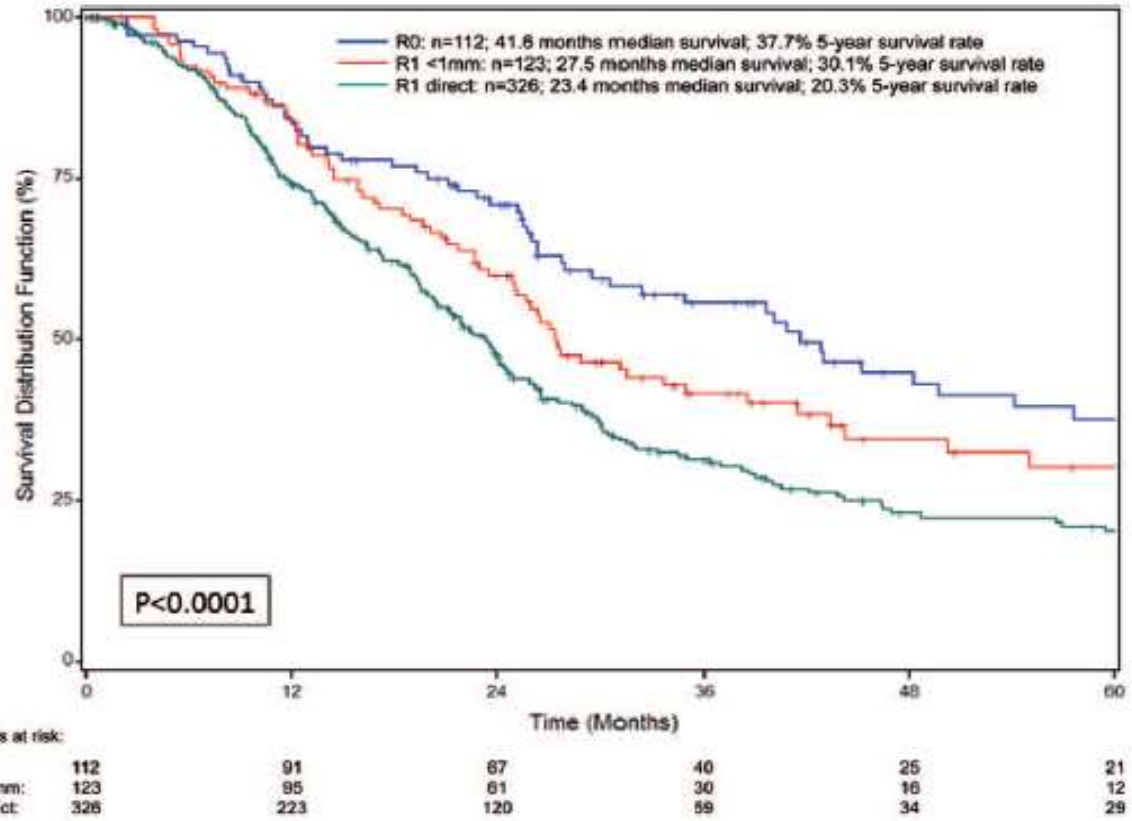
Pancreatic Cancer Surgery

The New R-status Counts

Oliver Strobel, MD, Thomas Hank, MD,* Ulf Hinz, MSc,* Frank Bergmann, MD,† Lutz Schneider, MD,* Christoph Springfeld, MD, PhD,‡ Dirk Jäger, MD,‡ Peter Schirmacher, MD,† Thilo Hackert, MD,* and Markus W. Büchler, MD**



Patients at risk:

R0:	112	91	67	40	25	21
R1 <1mm:	123	95	61	30	16	12
R1 direct:	326	223	120	59	34	29

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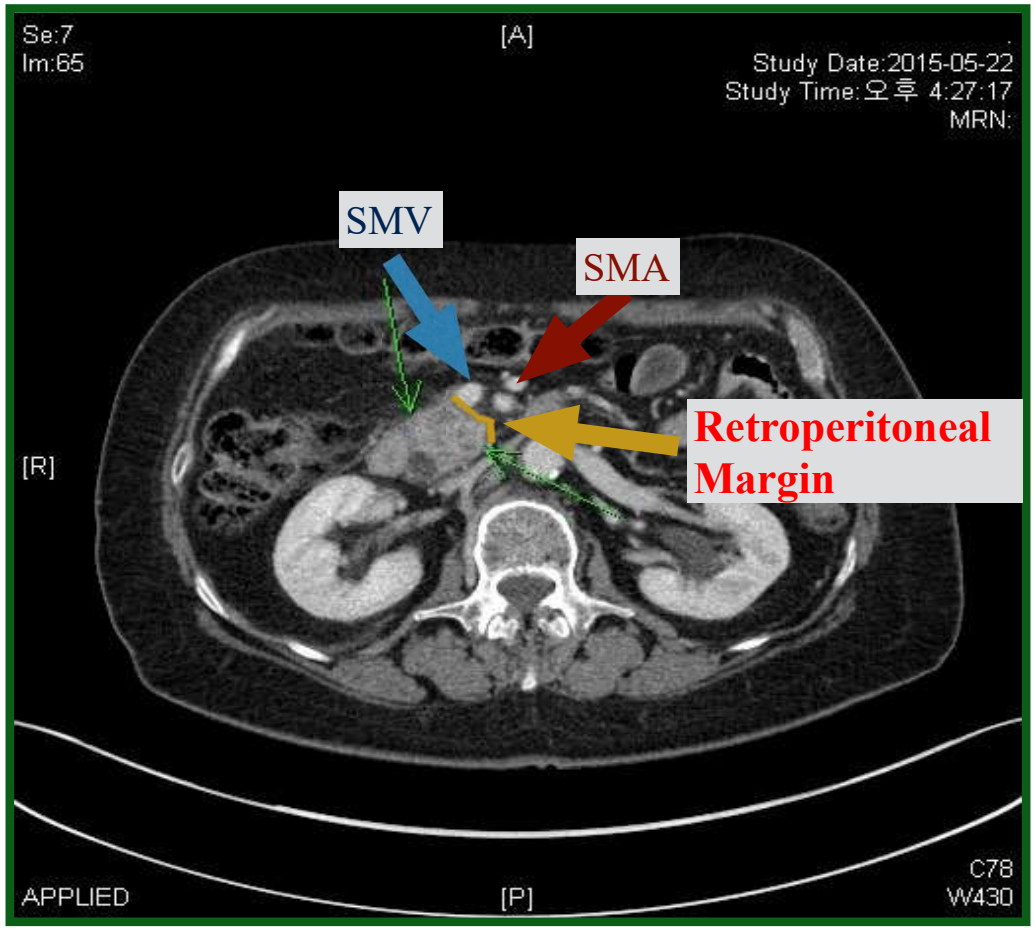
Retroperitoneal Resection Margin ?



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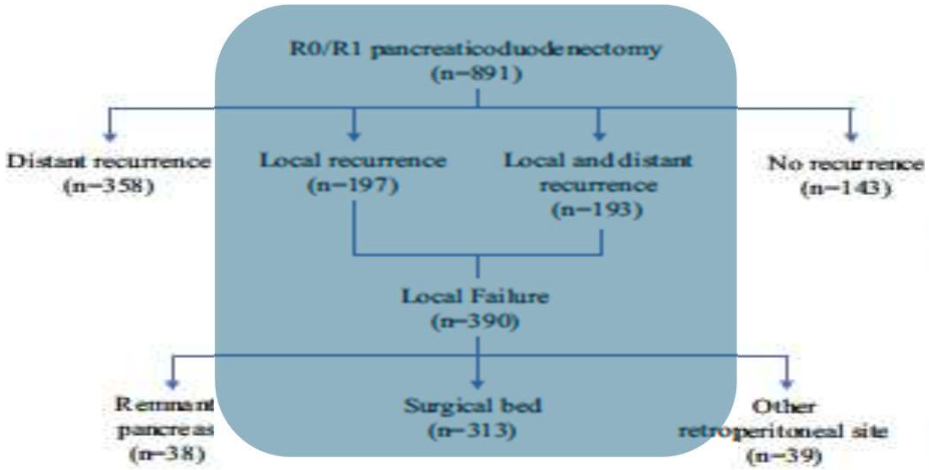
Detailed Analysis of Margin Positivity and the Site of Local Recurrence After Pancreaticoduodenectomy

Caitlin A. McIntyre, MD[1], Constantinos P. Zambirinis, MD, MRes[1], Alessandra Pulvirenti, MD[1], Joanne F. Chou, MPH[2], Mithat Gonen, PhD[2], Vinod P. Balachandran, MD[1], T. Peter Kingham, MD[1], Michael I. D'Angelica, MD[1], Murray F. Brennan, MD[1], Jeffrey A. Drebin, MD, PhD[1], William R. Jarnagin, MD[1], and Peter J. Allen, MD[1,3]

- **Local failure rate : 44.8%**
- **Retroperitoneal margin positive**



	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Positive posterior margin	1.50 (1.17–1.91)	*0.001*	1.41 (1.09–1.81)	*0.009*
Positive pancreatic margin	1.06 (0.78–1.43)	0.707		
Positive bile duct margin	0.85 (0.42–1.72)	0.654		
Positive anterior peritoneal margin	1.02 (0.65–1.59)	0.913		
Positive lymph nodes	1.36 (1.06–1.75)	*0.017*	1.13 (0.85–1.49)	0.400
Tumor size	1.09 (0.99–1.19)	0.068	1.06 (0.97–1.17)	0.210
Poor tumor differentiation	0.96 (0.75–1.24)	0.766		
Lymphovascular invasion	1.26 (1.00–1.60)	0.054	1.08 (0.84–1.39)	0.550
Perineural invasion	1.61 (0.97–2.65)	0.063	1.35 (0.81–2.24)	0.250

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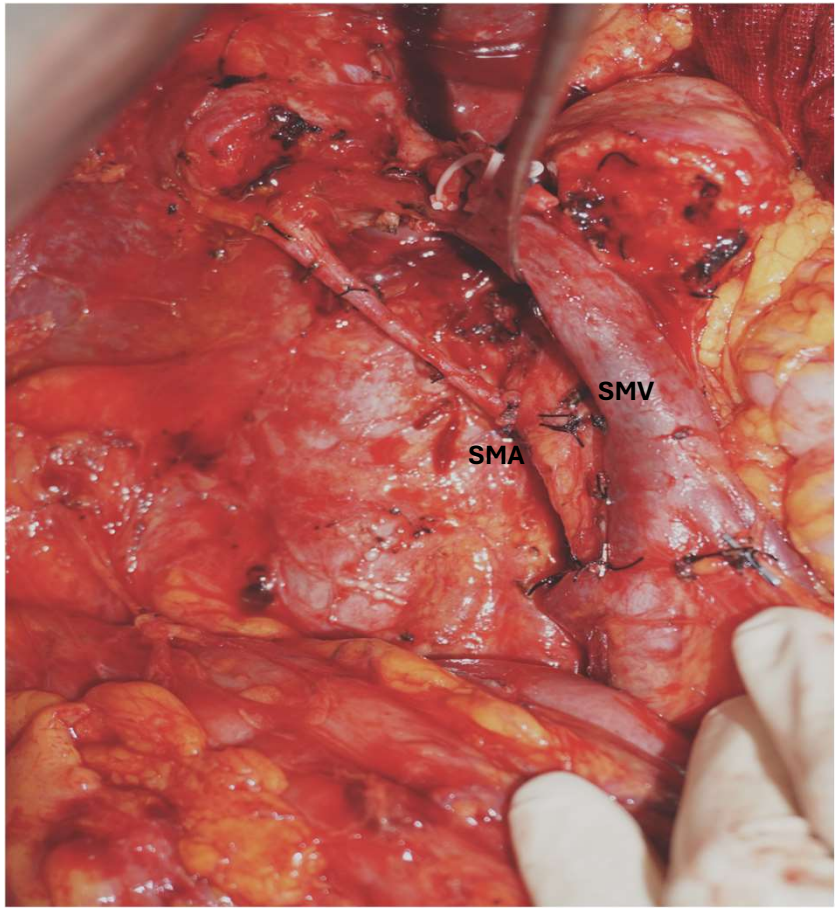
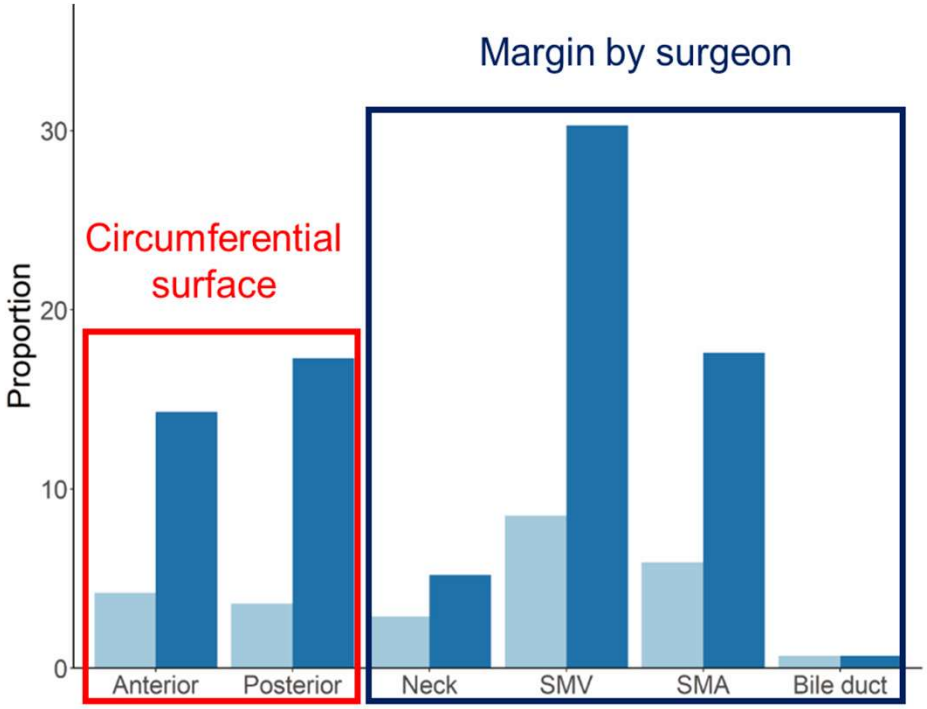
Margin status & Prognosis after pancreatectomy(SNUH)





1 mm margin (+) 43%

0 mm margin (+) 17%

Unpublished

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IORT [Intraoperative radiation therapy]

- **High doses of radiation therapy while excluding part or all of the nearby dose-limiting sensitive structures**

- **The effective radiation dose is increased and local tumor control potentially improved**

- **In pancreatic cancer, IORT has been offered for unresectable tumors to provide local tumor control and palliation of pain, and for resectable tumors in an effort to improve local control and survival after PD**

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Advantages of IORT

1. **Reduce the chance of residual tumor** at the site of surgery, thus maximizing local control and reducing of local recurrence

2. **Maximizes the radiobiological effect** of a single high dose

3. **Faster treatment time**

4. **Minimal exposure of surrounding tissues** to radiation, thus reducing normal tissue toxicity

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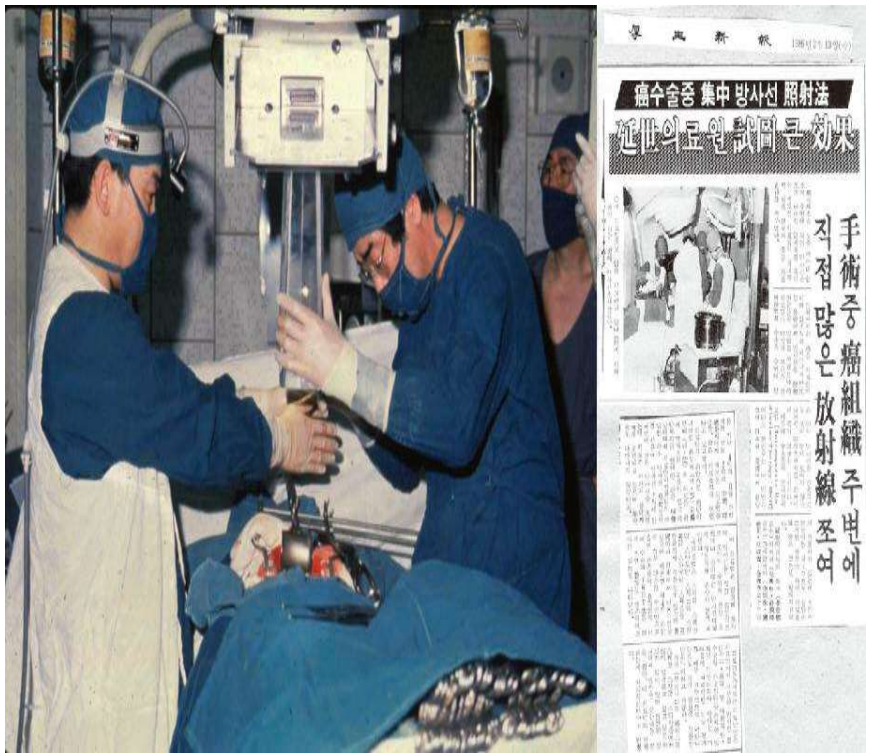
First IORT in Korea (1986)
Electron IORT for Gastric cancer

- 20-Gy single fraction equivalent to 40-60 Gy at 2 Gy/fx
- **Advantage**
  - ✓ Normal tissue sparing, early application of RT, visual target, increased effective dose to tumor bed
- **Disadvantage**
  - ✓ No pre-treatment planning, uncertainty in dose distribution, **patient transport**, development of IMRT



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NIH U.S. National Library of Medicine

ClinicalTrials.gov

First case of IORT : Sep-26-2017

Intraoperative Radiation Therapy for Resectable Pancreatic Cancer

- Resectable Pancreatic Adenocarcinoma
- Radiation: Intraoperative radiation therapy (IORT)
- Gangnam Severance Hospital Seoul, Korea, Republic of

Arm
Experimental: IORT group Intraoperative radiation therapy of 10 Gy delivered during surgery followed by adjuvant gemcitabine chemotherapy

ClinicalTrials.gov Identifier: NCT03273374

Recruitment Status : Recruiting
First Posted : September 6, 2017
Last Update Posted : September 11, 2017

See Contacts and Locations

STUDY PROTOCOL Open Access

A phase II study of intraoperative radiotherapy using a low-energy x-ray source for resectable pancreatic cancer: a study protocol

Jun Won Kim[1], Yeona Cho[1], Hyung Sun Kim[2], Won Hoon Choi[1], Joon Seong Park[2*] and Ik Jae Lee[1*]

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Curative resection

Determination of IORT Target volume

Selection of applicator
(3.0, 3.5, or 4.0 cm)

Placement of applicator

Irradiation with a single dose of
10 Gy into the tumor bed

Removal of applicator

30-40mins

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Intraoperative Radiotherapy for Resectable Pancreatic Cancer Using a Low-Energy X-Ray Source: Postoperative Complications and Early Outcomes

Yeona Cho[1], Jun Won Kim[1], Hyung Sun Kim[2], Jbon Seong Park[2], and Ik Jae Lee[1]

Departments of [1]Radiation Oncology and [2]Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea.

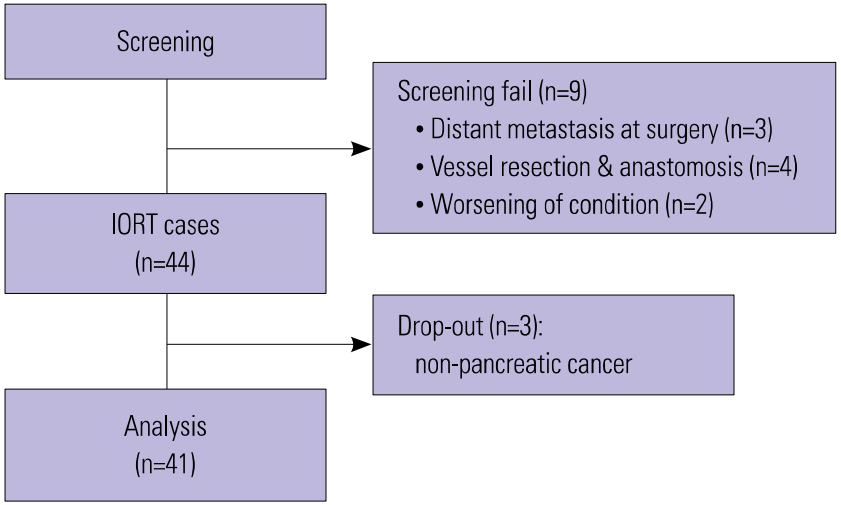

Fig. 2. Patients selection for this analysis. IORT, intraoperative radiotherapy.

Table 3. Postoperative Complications (n=41)

Checklist	Grade	n (%)
Delayed Gastric emptying*	A	1 (2.4)
	B	4 (9.8)
Postoperative pancreatic fistula†	A	1 (2.4)
	B	1 (2.4)
Chyle leakage	2	2 (4.9)
Duodenal ulcer perforation	3b	1 (2.4)

Other acute postoperative complications were evaluated using Clavien-Dindo classification.

*Delayed gastric emptying was graded according to the International Study Group of Pancreatic Surgery consensus definition; †We use the consensus of International Study Group on Pancreatic Fistula (ISGPF) for the definition and grading of postoperative pancreatic fistula.

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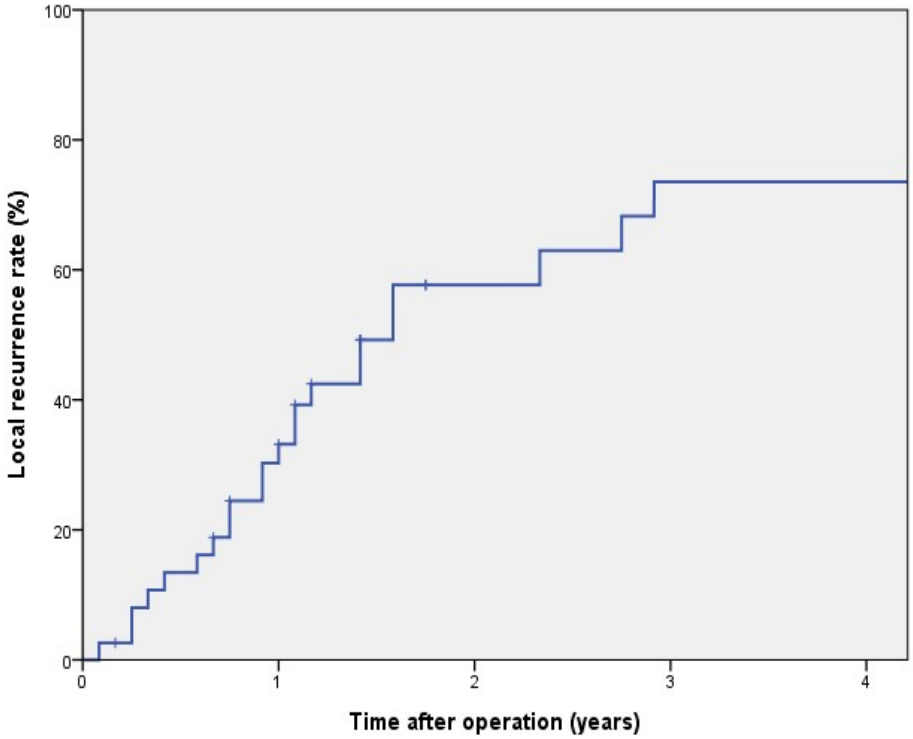
IORT for Resectable PDAC : Final Results

Table 2 Local recurrence rate and survival rates

	1 year	2 years	3 years
Local recurrence rate (%)	28.2	54.9	70.8
Disease-free survival (%)	48.1	19.5	13.5
Overall survival (%)	92.2	63.6	53.4



Average Local Recurrence Rate ≈ 40% at 1yr

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The Physiological Effects of IORT

- **Abscopal effect :**

  Effects of ionizing radiation at a distance from the irradiated volume but within the same organism

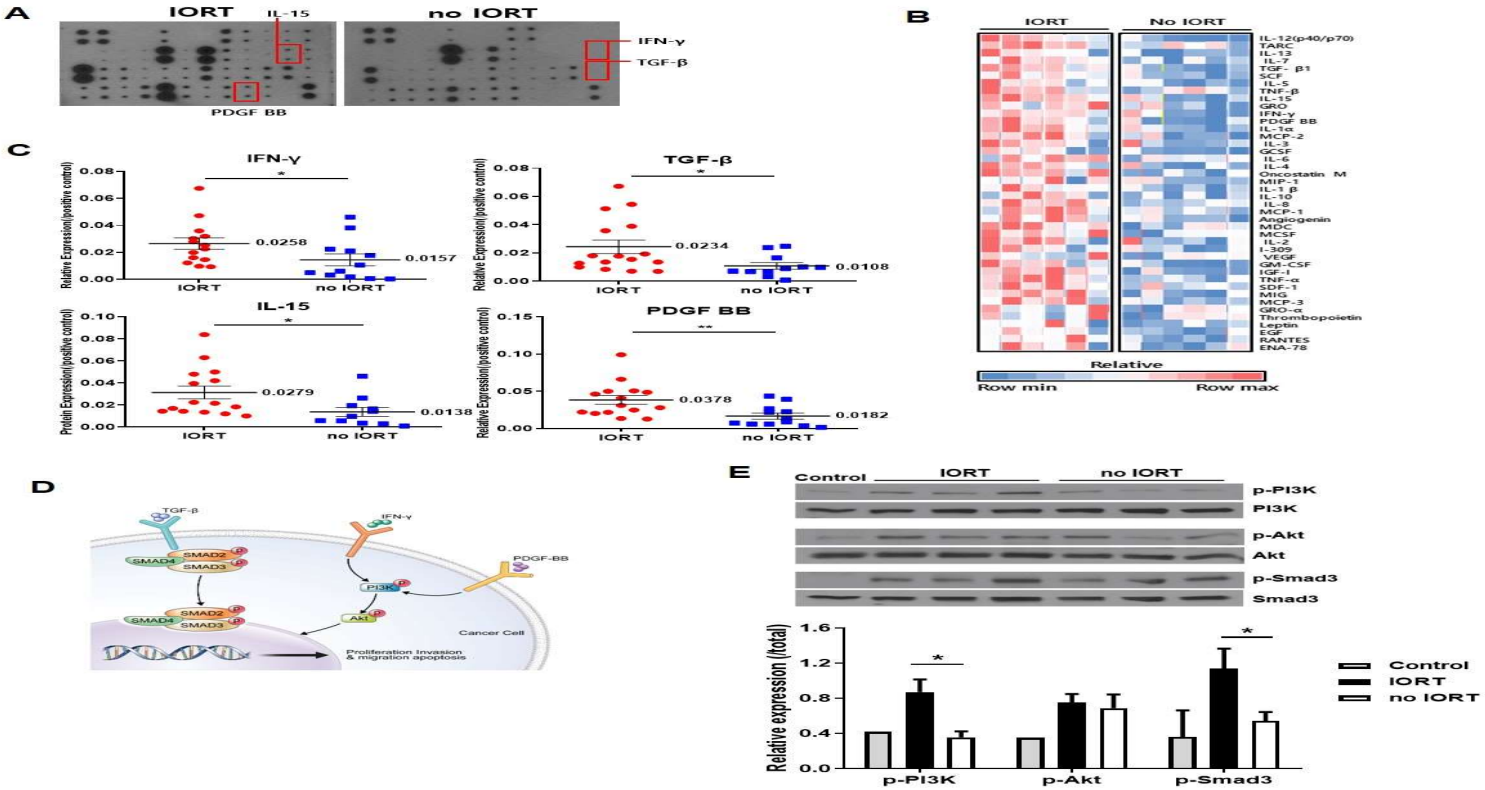
- **Bystander effect :**

  Effects of ionizing radiation at normal tissue induced inflammation and cytokine signals

RESEARCH Open Access

Intraoperative radiation therapy induces immune response activity after pancreatic surgery

Yun Sun Lee[1,2], Hyung Sun Kim[1], Yeona Cho[3], Ik Jae Lee[3], Hyo Jung Kim[1], Da Eun Lee[1,2], Hyeon Woong Kang[1,2] and Joon Seong Park[1*]



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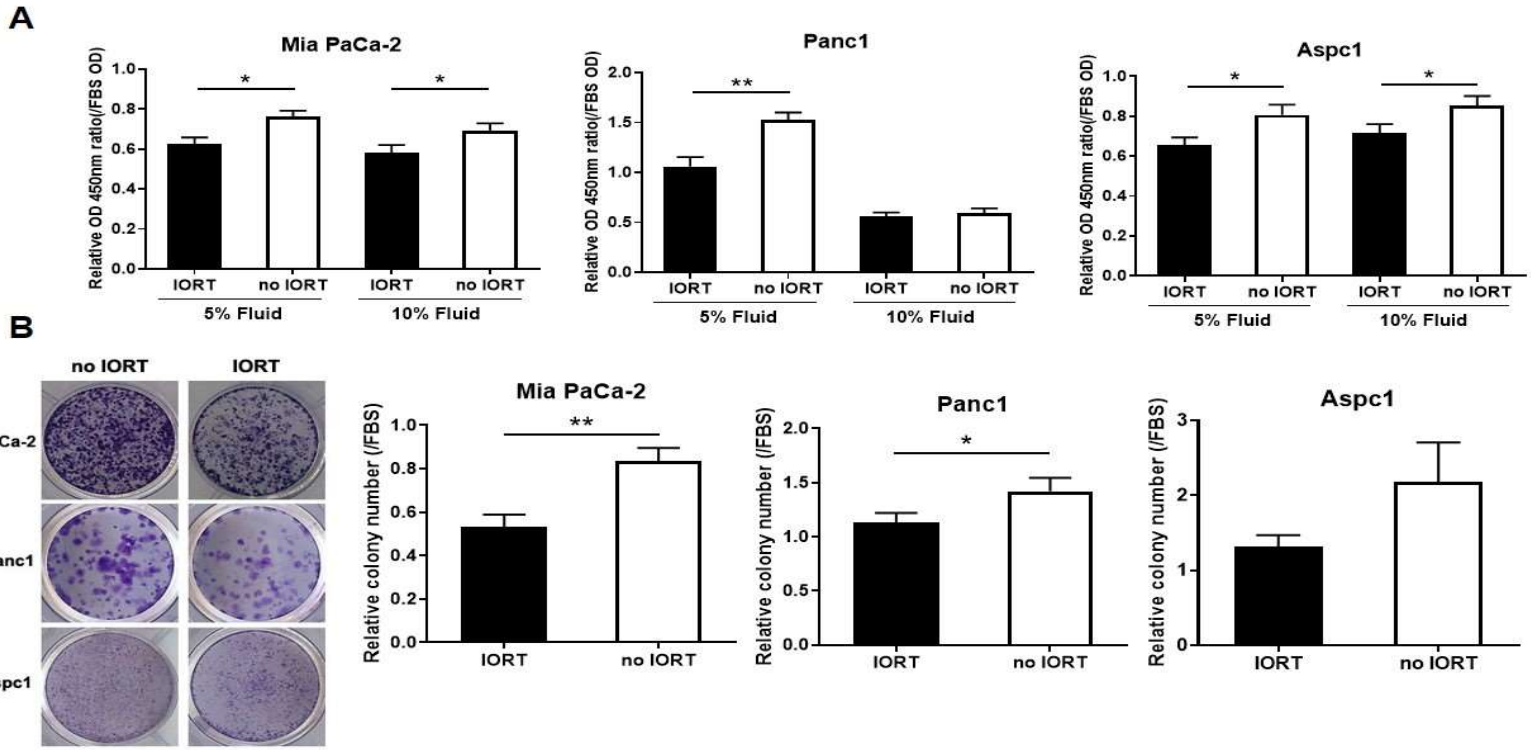

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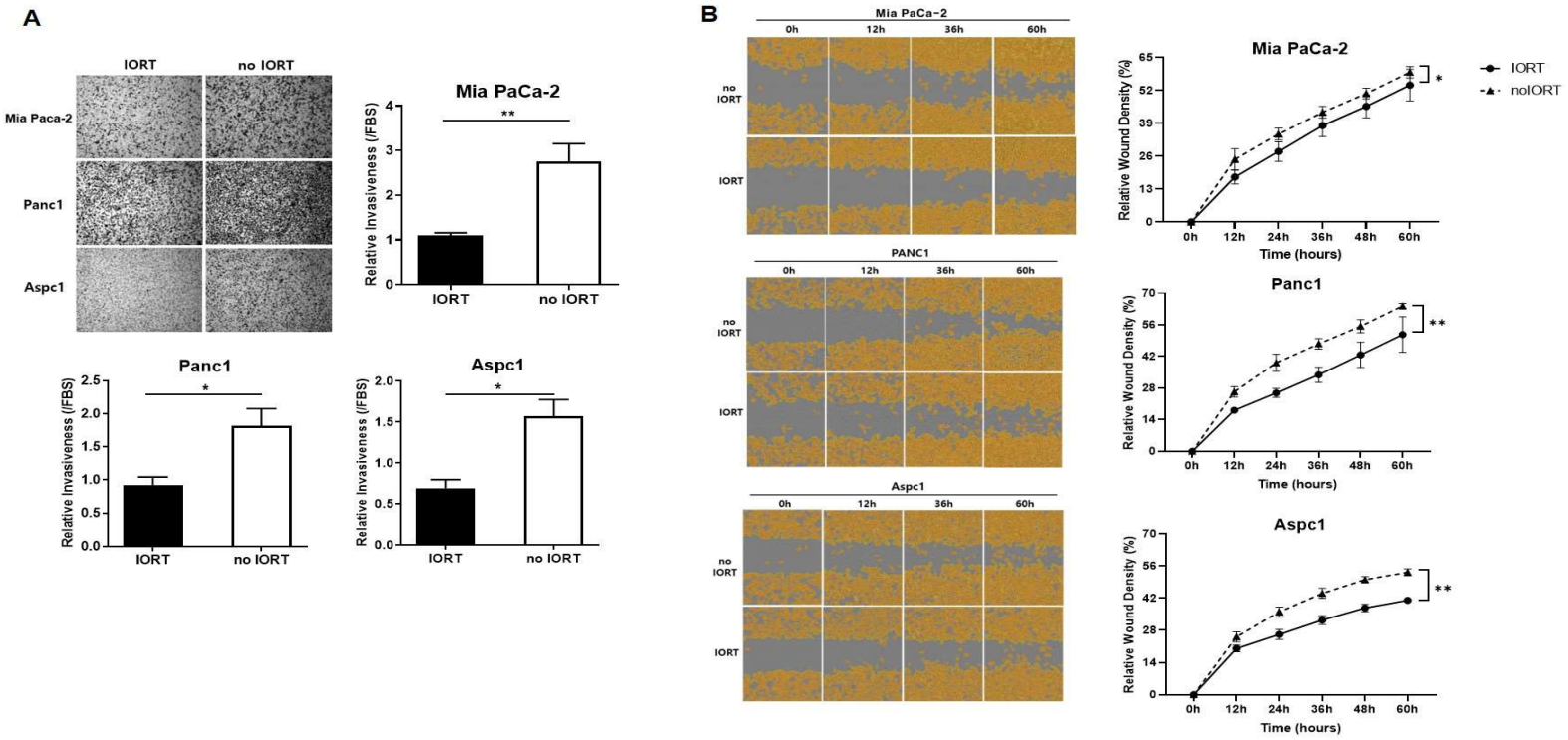

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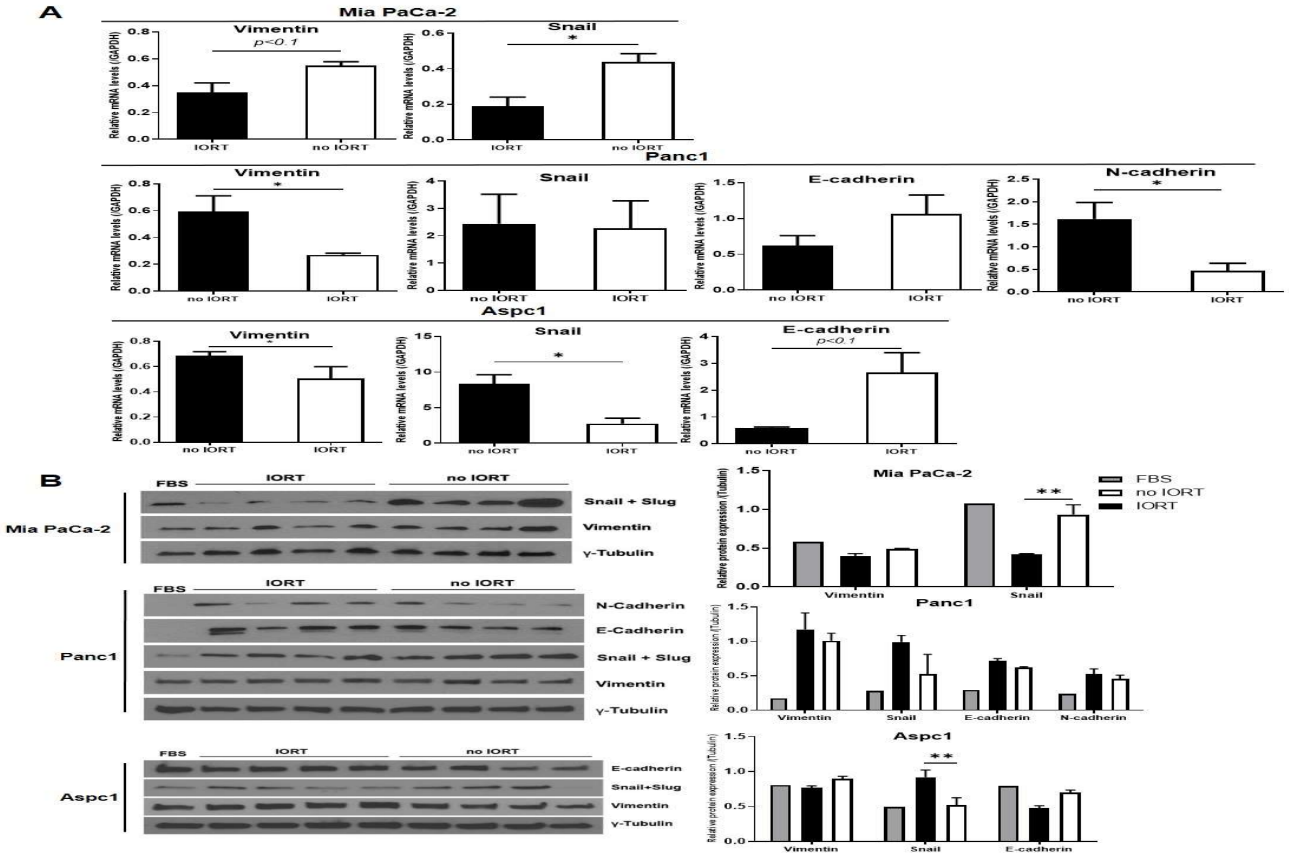

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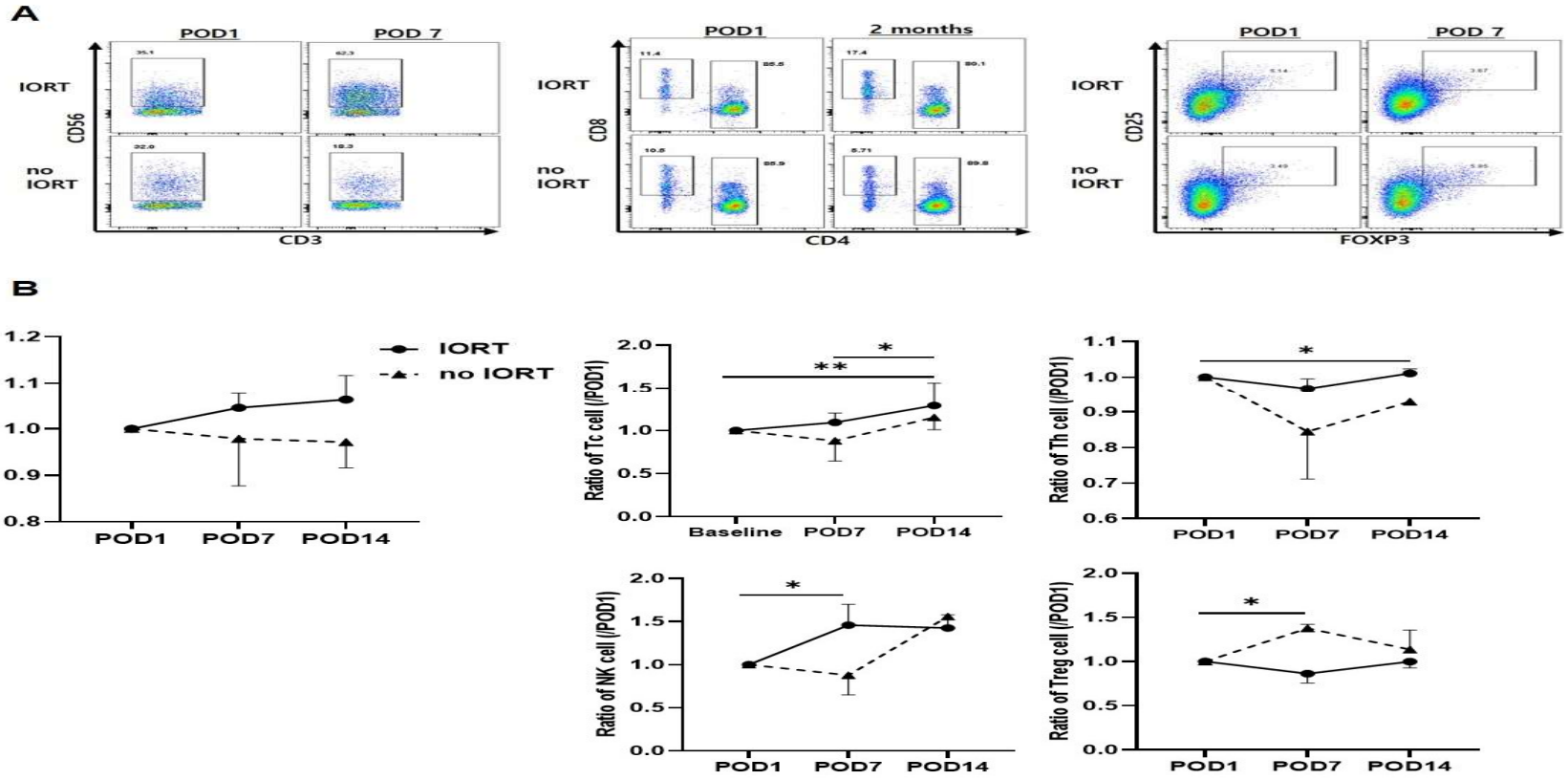

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Conclusions

IORT is safe and some immunologic advantages in PDAC

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