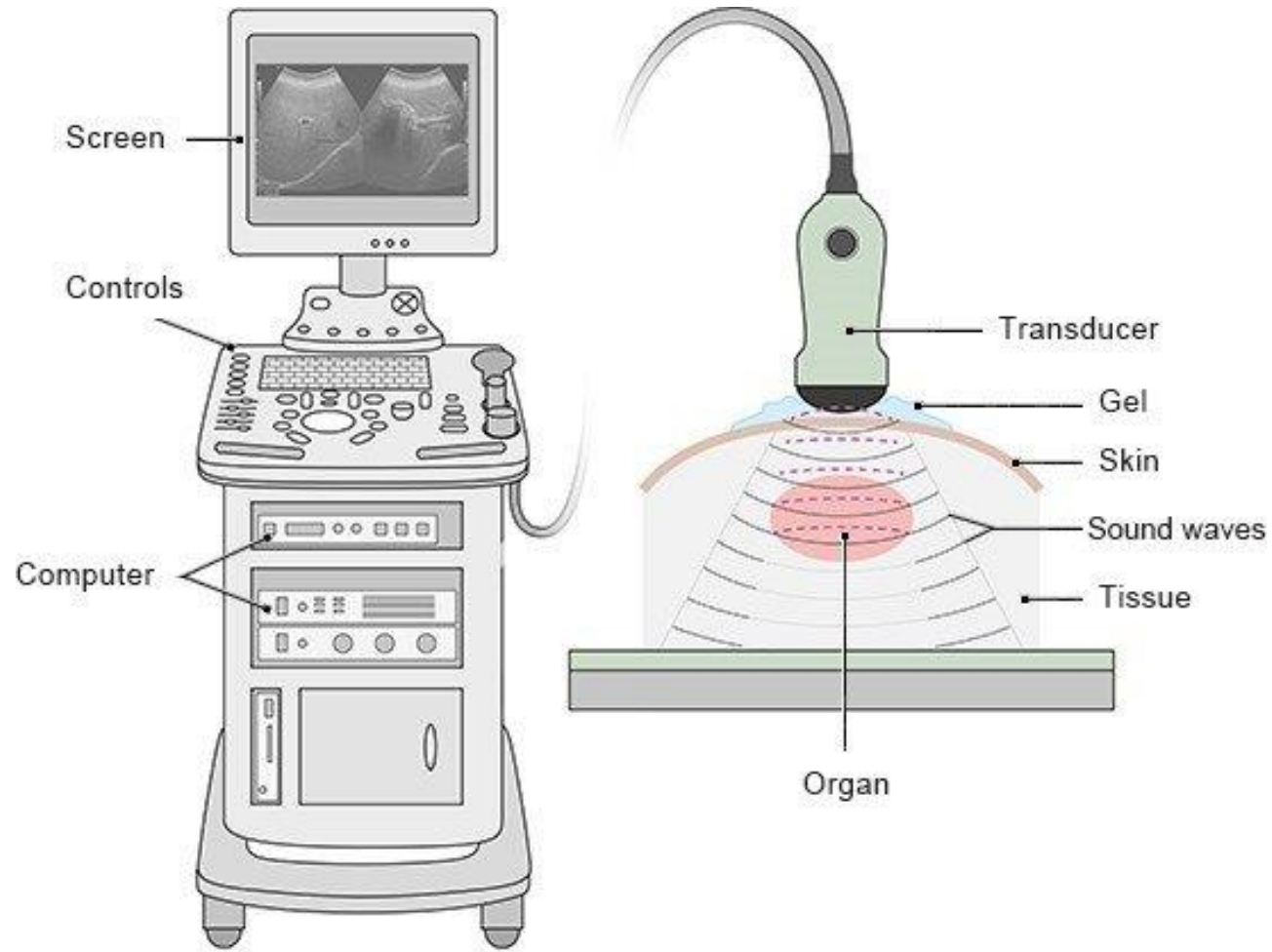


# High Intensity Focused Ultrasound (HIFU) for Pancreatic Cancer

**Keaton Jones - HPB**  
**Nuffield Department of Surgical Sciences**  
**University of Oxford**

Have you heard of HIFU?

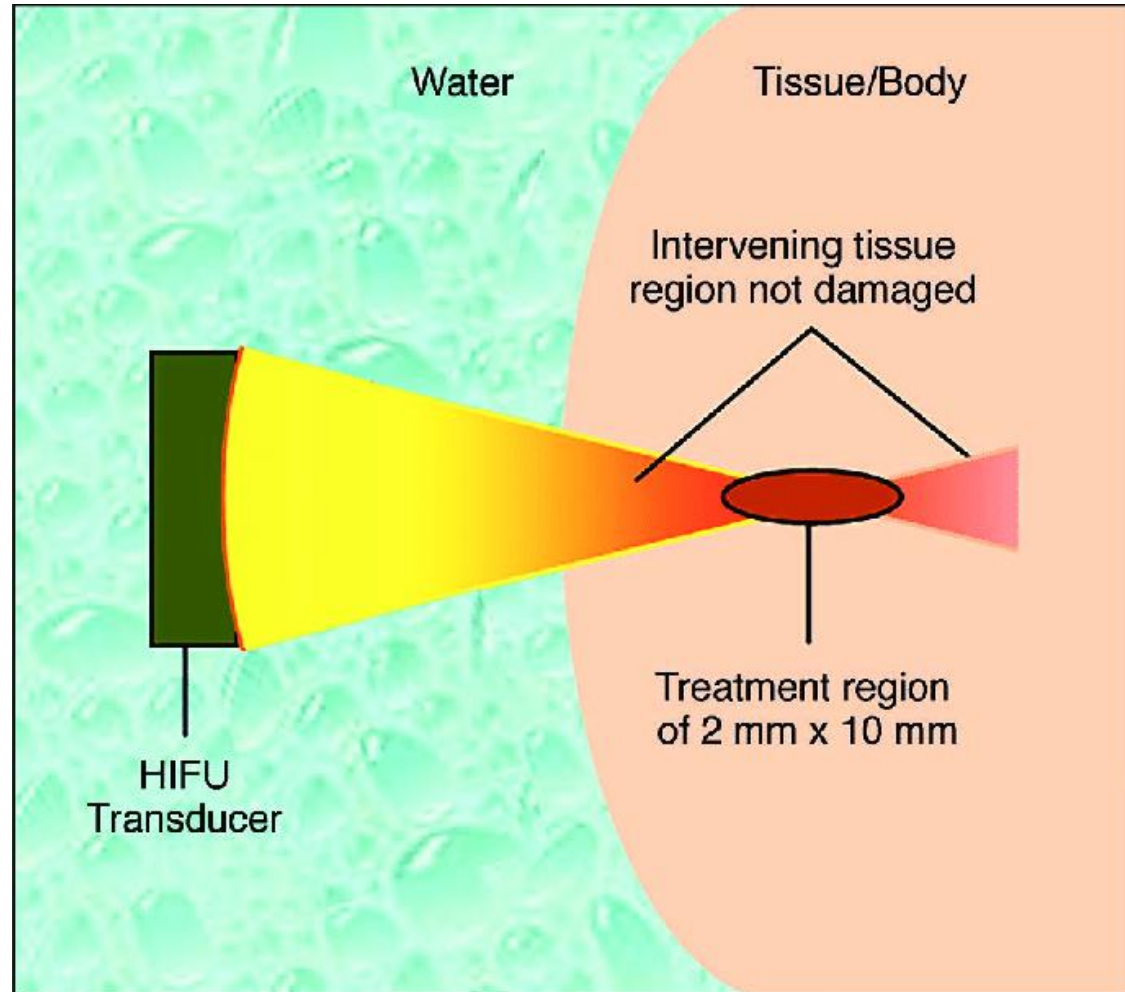
# What is HIFU?



- Low energy
- Sound waves
- Imaging only
- No effect on tissues

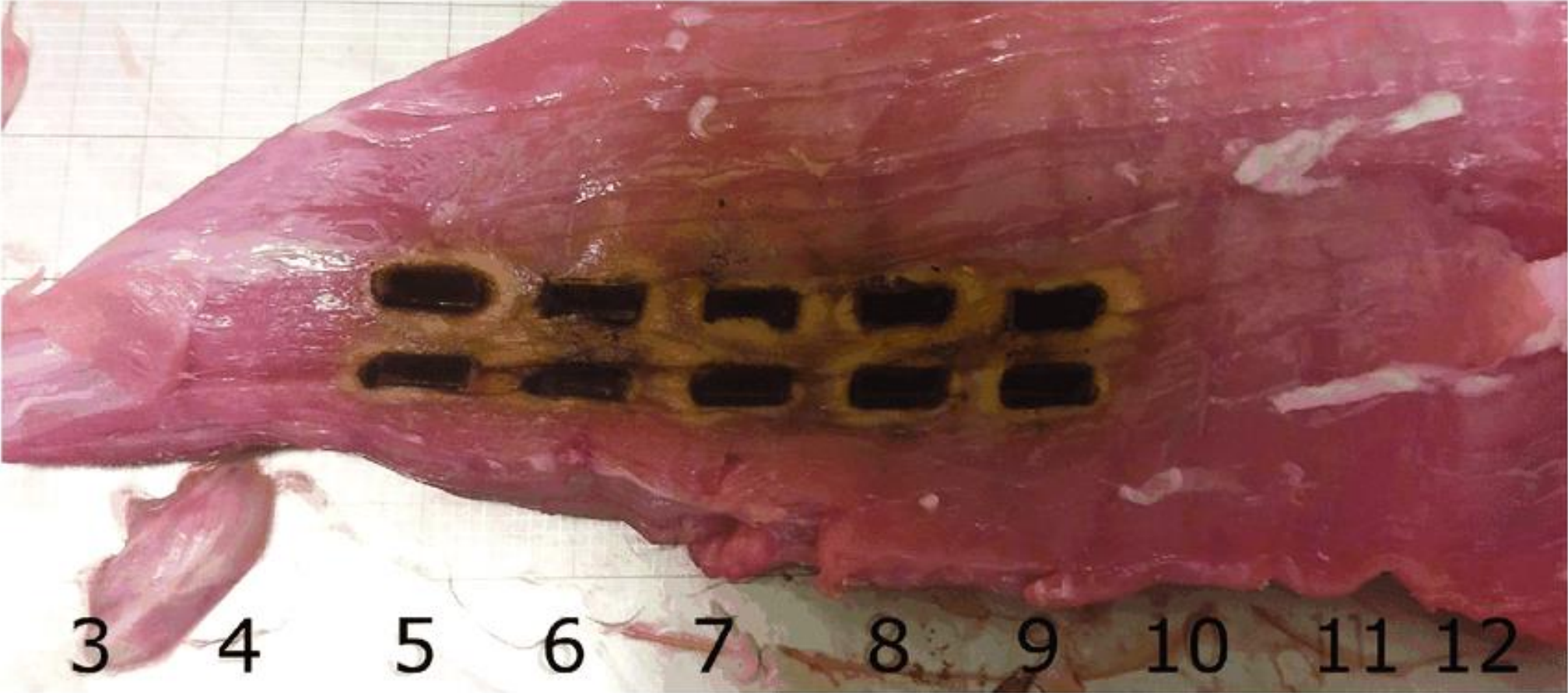
**Conventional diagnostic ultrasound**

# What is HIFU?



- Focused energy
- Exposures over seconds
- Tissue heats to  $\sim 80^{\circ}\text{C}$
- Tissue dies due to necrosis

# What is HIFU?



# Success in other fields

Research Article

## Survival and quality of life outcomes of high-intensity focused ultrasound treatment of localized prostate cancer



Peter L. Royce <sup>a, b, \*, ☆</sup>, James J.Y. Ooi <sup>a, ☆</sup>, Selva Sothilingam <sup>c</sup>, Henry H. Yao <sup>a</sup>

<sup>a</sup> Department of Urology, Alfred Health, Melbourne, Victoria, Australia

<sup>b</sup> Urology Associates, Cabrini Health, Malvern, Victoria, Australia

<sup>c</sup> University of Malaya, Kuala Lumpur, Malaysia

ORIGINAL ARTICLE

## Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease

Raúl Martínez-Fernández, M.D., Ph.D., Jorge U. Máñez-Miró, M.D., Rafael Rodríguez-Rojas, Ph.D., Marta del Álamo, M.D., Binit B. Shah, M.D., Frida Hernández-Fernández, M.Sc., José A. Pineda-Pardo, Ph.D., Mariana H.G. Monje, M.D., Ph.D., Beatriz Fernández-Rodríguez, M.D., Scott A. Sperling, Psy.D., David Mata-Marín, M.Sc., Pasqualina Guida, M.Sc., [et al.](#)

ORIGINAL ARTICLE BRIEF REPORT

## Ultrasound Blood–Brain Barrier Opening and Aducanumab in Alzheimer's Disease

Ali R. Rezai, M.D., Pierre-Francois D'Haese, Ph.D., Victor Finomore, Ph.D., Jeffrey Carpenter, M.D., Manish Ranjan, M.B., B.S., Kirk Wilhelmsen, M.D., Rashi I. Mehta, M.D., Peng Wang, Ph.D., Umer Najib, M.D., Camila Vieira Ligo Teixeira, Ph.D., Tasneem Arsiwala, Ph.D., Abdul Tarabishy, M.D., [et al.](#)



# HIFU for pancreatic cancer is not new...

*Review Article*

## **High-Intensity Focused Ultrasound Treatment for Advanced Pancreatic Cancer**

**Yufeng Zhou**

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Pancreatic cancer is under high mortality but has few effective treatment modalities. High-intensity focused ultrasound (HIFU) is becoming an emerging approach of noninvasively ablating solid tumor in clinics. A variety of solid tumors have been tried on thousands of patients in the last fifteen years with great success. The principle, mechanism, and clinical outcome of HIFU were introduced first. All 3022 clinical cases of HIFU treatment for the advanced pancreatic cancer alone or in combination with chemotherapy or radiotherapy in 241 published papers were reviewed and summarized for its efficacy, pain relief, clinical benefit rate, survival, Karnofsky performance scale (KPS) score, changes in tumor size, occurrence of echogenicity, serum level, diagnostic assessment of outcome, and associated complications. Immune response induced by HIFU ablation may become an effective way of cancer treatment. Comments for a better outcome and current challenges of HIFU technology are also covered.

- 2014
- 3022 patients!
- Pain relief
- No definitive improvement in survival
- **All studies in Asia**

# The Oxford Experience

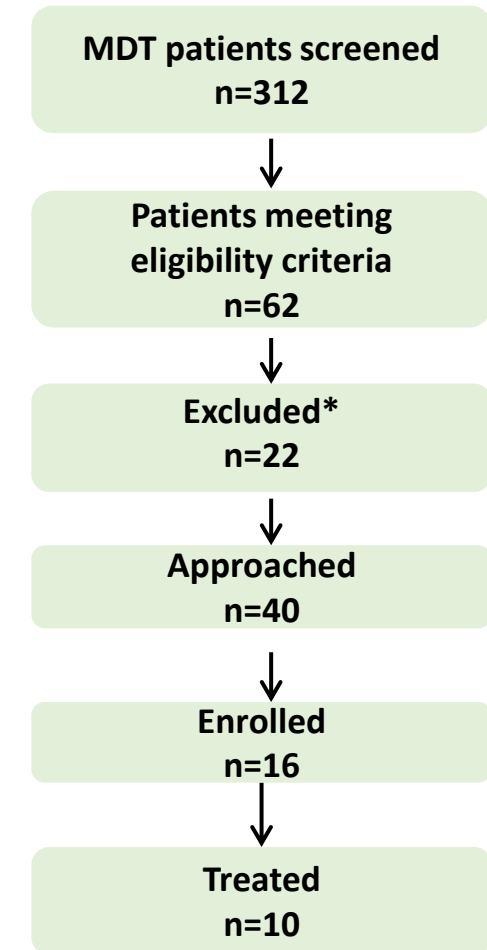
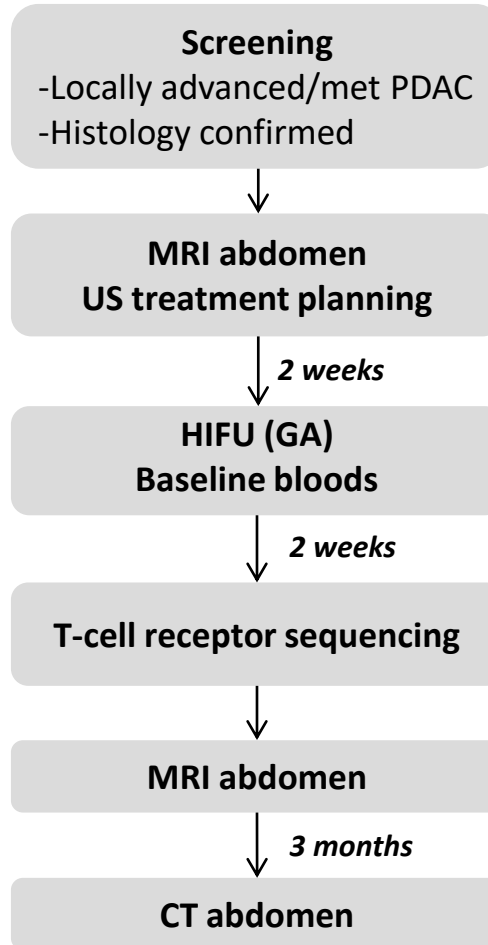
## Phase I Trial

### Primary Endpoint:

1. Safety

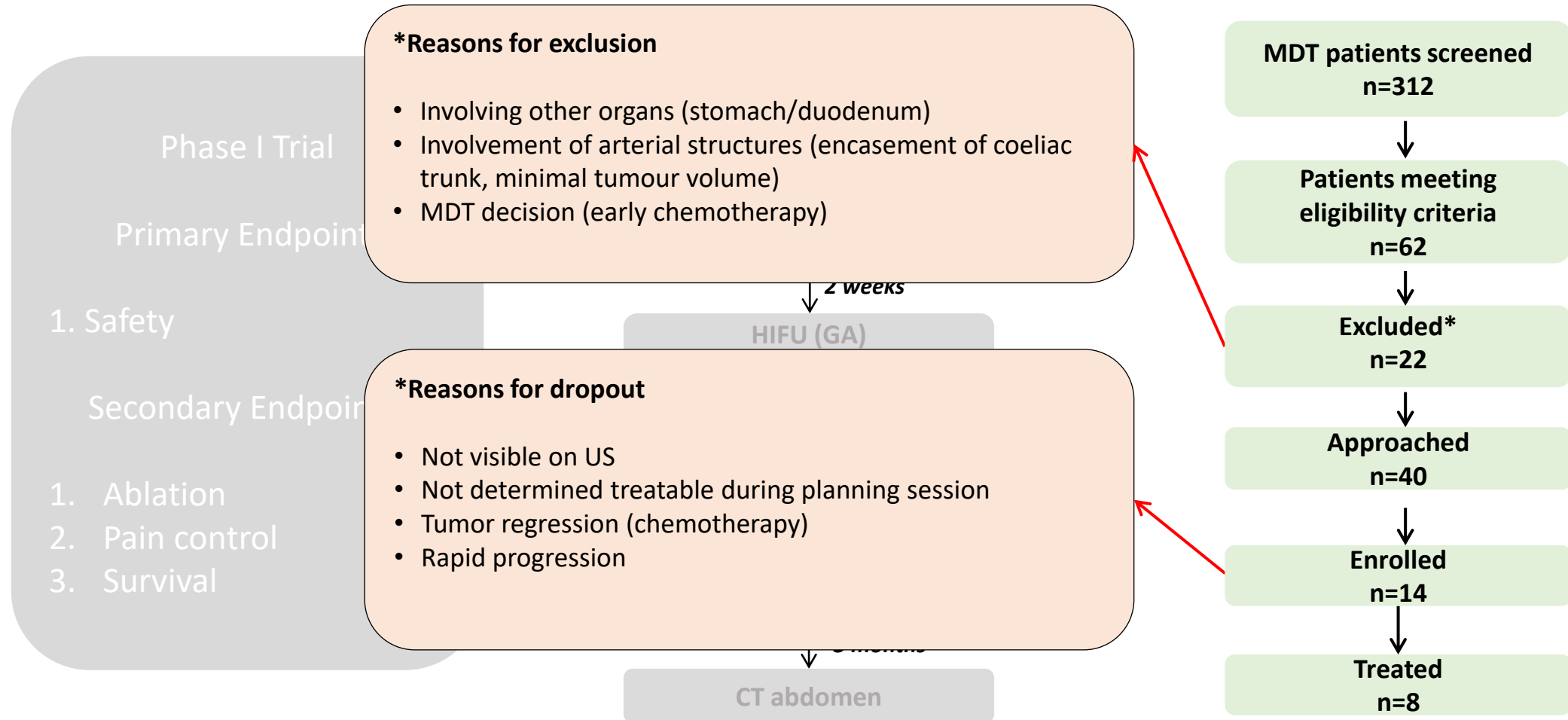
### Secondary Endpoints:

1. Ablation
2. Pain control
3. Immune priming





# The Oxford Experience



# Clinicopathological data

Patient	Age	Site	Tumour location	Stage	Chemo naïve?	Pre-HIFU rx	PS	CA 19.9	HIFU date
1	80	BIR	Body	T4NxM0	No	Gemcitabine	1	17700	06.12.2019
2	80	OXF	Body	T4NxM1	No	Gem-abraxane	1	2270	14.2.2020
3	66	OXF	Neck	T4NxM1	No	mFolfinirox	1	5210	30.04.2021
4	53	OXF	Tail	T4NxM1	No	Folfinirox	1	9102	11.05.2021
5	64	OXF	Head	T4NxM0	No	Folfinirox + Nivolumab	0	9083	12.11.2021
6	55	OXF	Body	T3N2M1	Yes	NA	0	3033	28.3.2023
7	57	GWH	Body	T3N1M1	No	Folfinirox	0	2303	01.09.2023
8	69	DHT	Head	T2N1M1	No	Gem-abraxane	0	100	15.09.2023
9	75	OXF	Body	T4NxM0	No	Folfinirox	0	280	16.01.2024
10	80	GWH	Head	T4NxM0	No	Folfinirox	1	2300	14.02.2024

# Patient 2

Pre-treatment

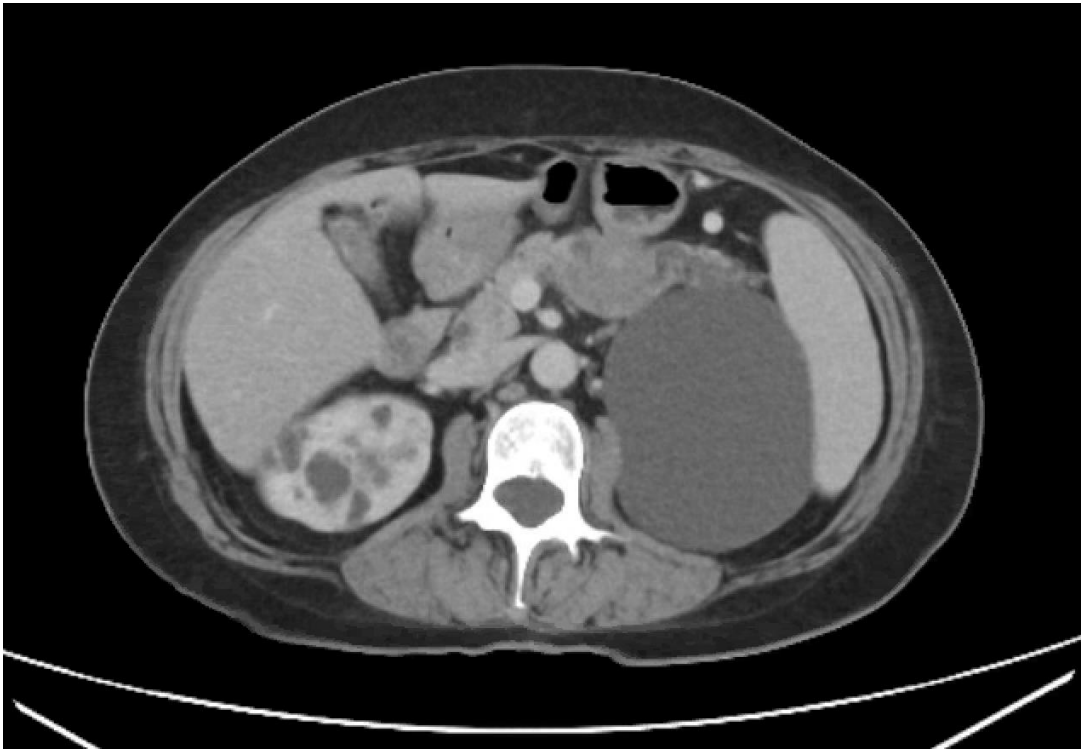


3 months post-HIFU

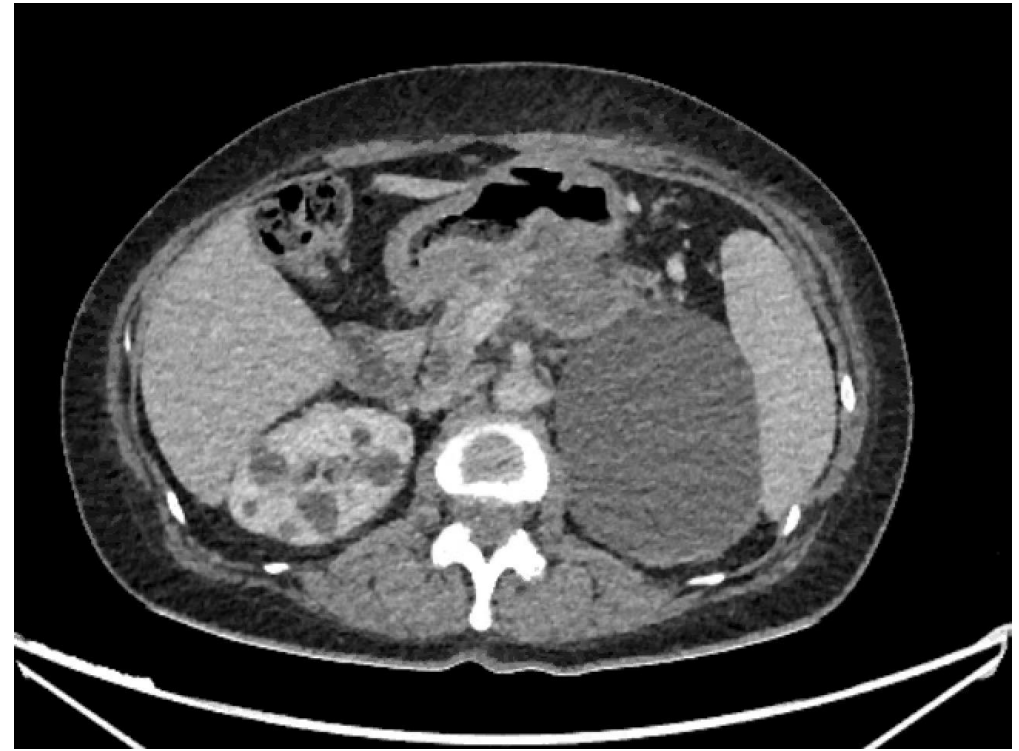


# Patient 8

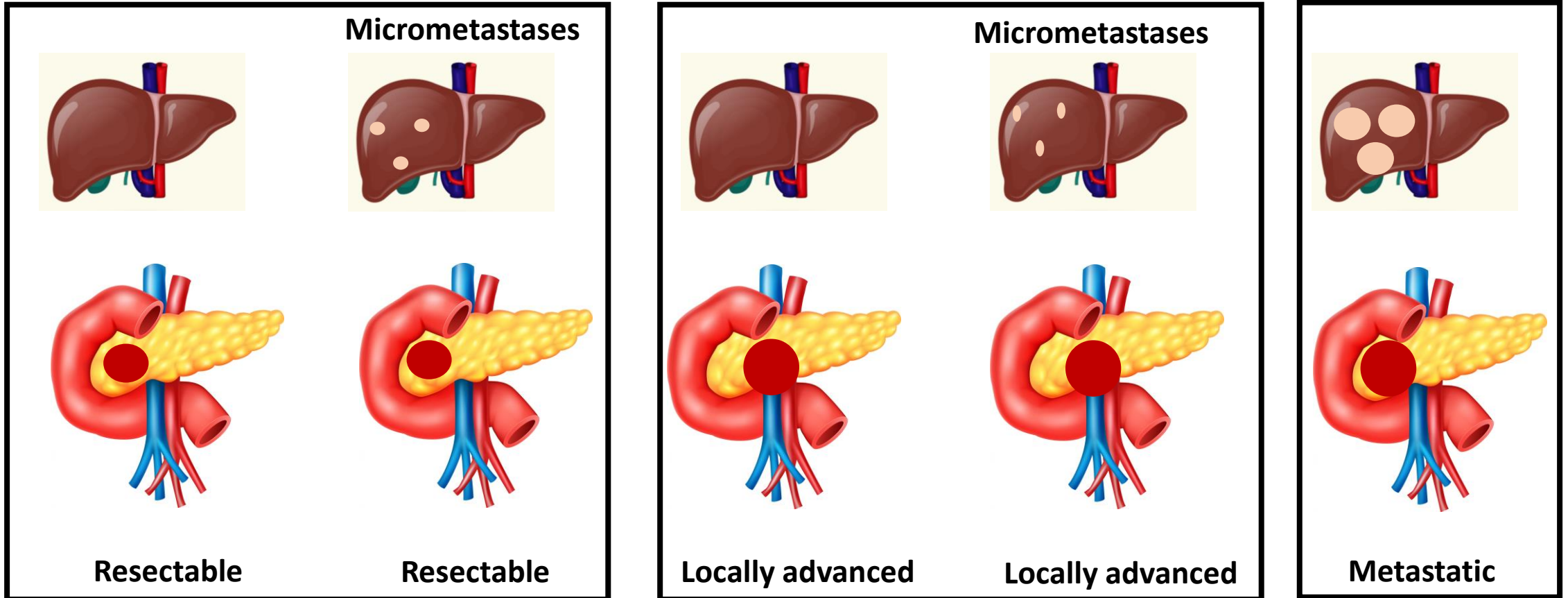
Pre-treatment



2 weeks post HIFU



# Future directions



Months



# Future directions



**Micrometastases**

**Resectable**      **Resectable**

**Micrometastases**

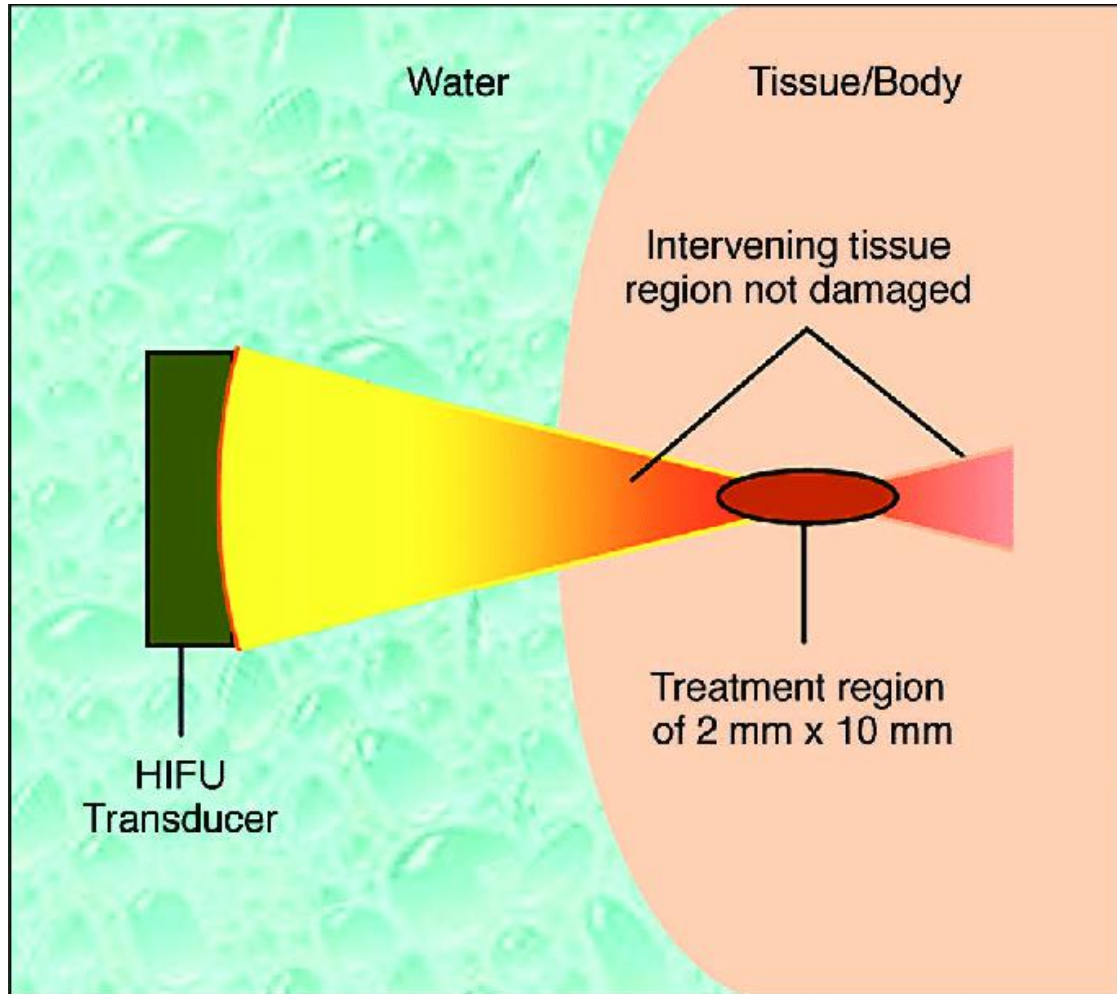
**Locally advanced**      **Locally advanced**

**Metastatic**





# Final note on histotripsy



- Focused energy
- Exposures over **milliseconds**
- No tissue heating
- Cells burst due to pressure
- Safer next to blood vessels/stomach
- Leaves proteins behind for recognition by the **immune system**


# Final note on histotripsy

## Pulsed focused ultrasound can improve the anti-cancer effects of immune checkpoint inhibitors in murine pancreatic cancer

Petros X. E. Mouratidis<sup>1</sup>, Marcia Costa<sup>1</sup>, Ian Rivens<sup>1</sup>, Elizabeth E. Repasky<sup>2</sup> and Gail ter Haar<sup>1</sup>

<sup>1</sup>Joint Department of Physics, Division of Radiotherapy and Imaging, The Institute of Cancer Research—Royal Marsden Hospital, Sutton SM2 5NG, UK

<sup>2</sup>Department of Immunology, Roswell Park Comprehensive Cancer Centre, Buffalo, NY 14263, USA

 PXEM, 0000-0002-7248-6076

Open access

Original research



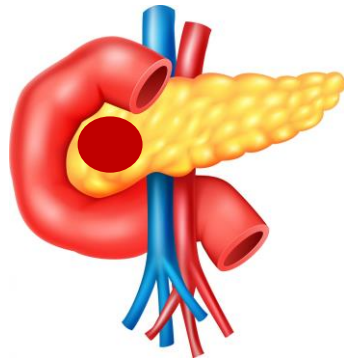
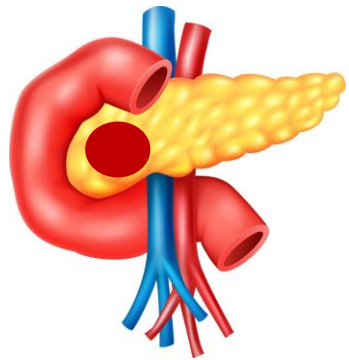
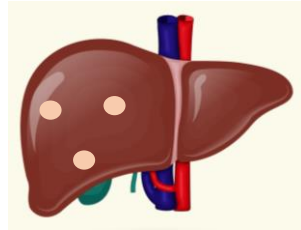
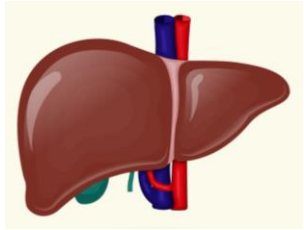
## Non-thermal histotripsy tumor ablation promotes abscopal immune responses that enhance cancer immunotherapy

Shibin Qu,<sup>1,2</sup> Tejaswi Worlikar,<sup>3</sup> Amy E Felsted,<sup>1</sup> Anutosh Ganguly,<sup>1,4</sup> Megan V Beems,<sup>1</sup> Ryan Hubbard,<sup>3</sup> Ashley L Pepple,<sup>1</sup> Alicia A Kevelin,<sup>1</sup> Hannah Garavaglia,<sup>1</sup> Joe Dib,<sup>1</sup> Mariam Toma,<sup>1</sup> Hai Huang,<sup>5</sup> Allan Tsung,<sup>5</sup> Zhen Xu,<sup>3</sup> Clifford Suhyun Cho<sup>1,4</sup>

# HIFU + immunotherapy



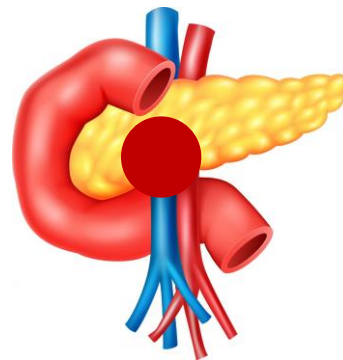
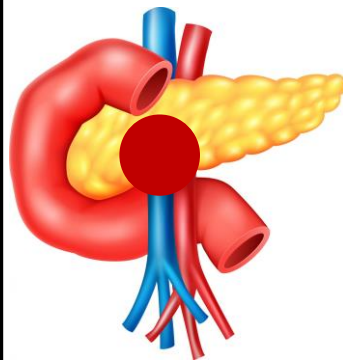
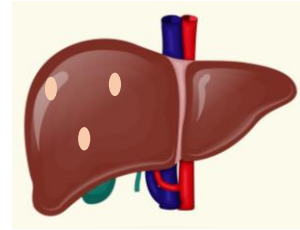
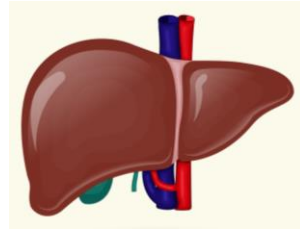
Micrometastases



Resectable

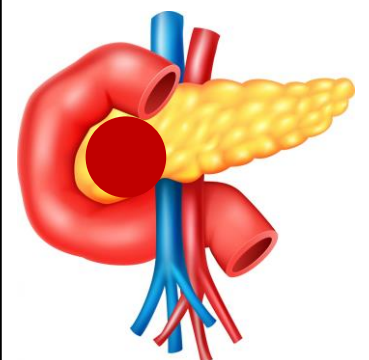
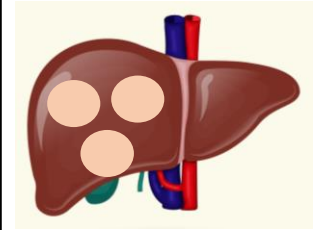
Resectable

Micrometastases



Locally advanced

Locally advanced



Metastatic

Months



# Summary

- HIFU is safe for pancreatic cancer
- Highly selected group
- Evidence for pain relief but not improved survival
- Future appears to lie with combination treatments

Do you feel more familiar with  
how HIFU may be used for  
pancreatic cancer?