DEPARTMENT OF
ONCOLOGY
Medical Sciences Division

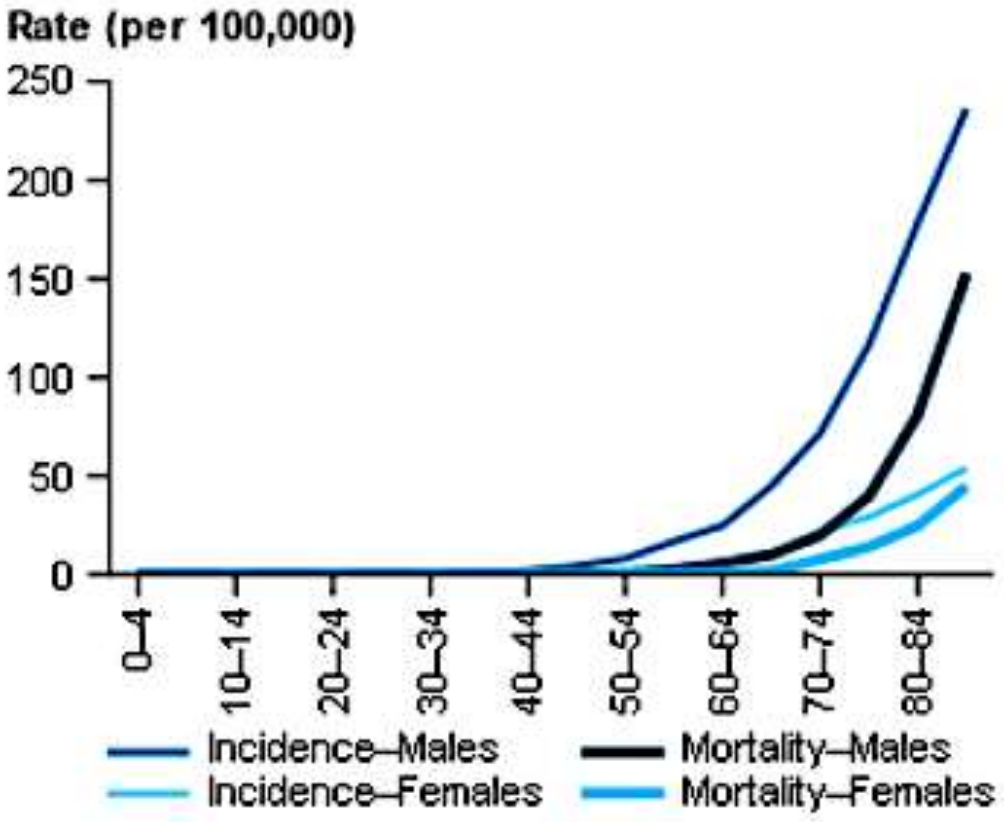
UNIVERSITY OF
OXFORD

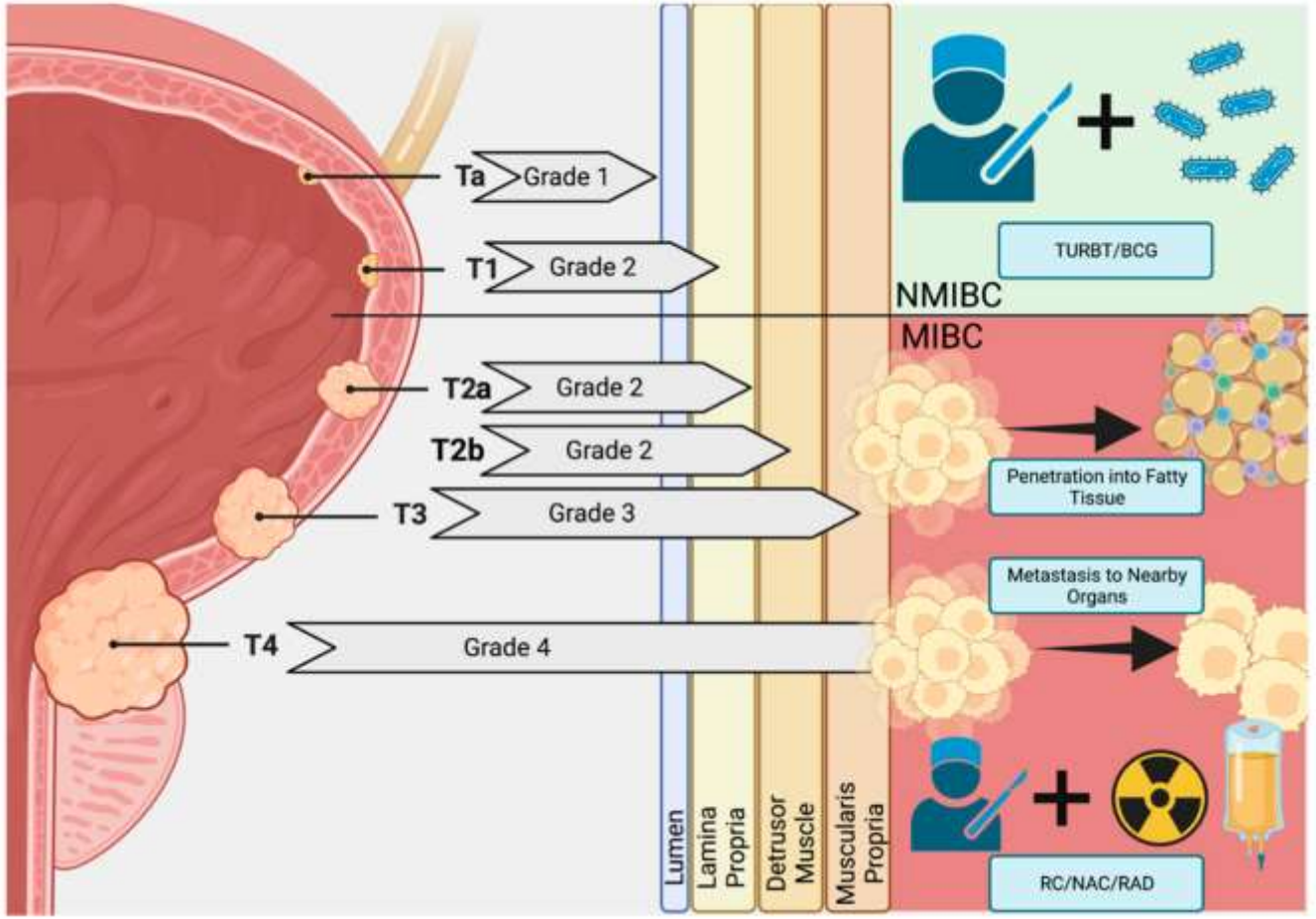
Improve chemo/radiotherapy of cancer through ultrasound-mediated drug delivery

Jia-Ling Ruan

2024.12.10

Muscle-Invasive Bladder Cancer (MIBC)

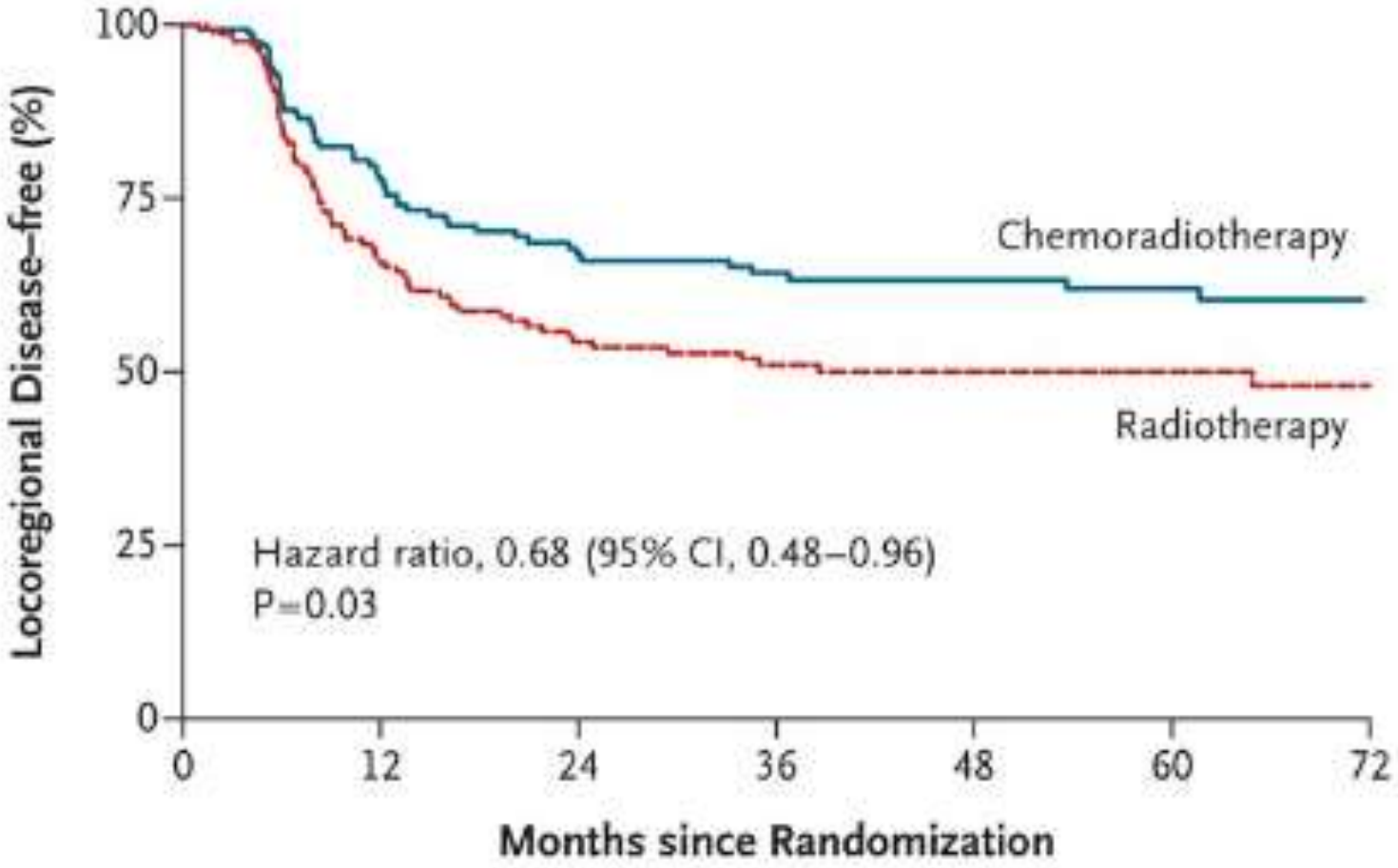




https://bladder-cancer.canceraustralia.gov.au/statistics

Biomedicines 2023, 11(2), 539;

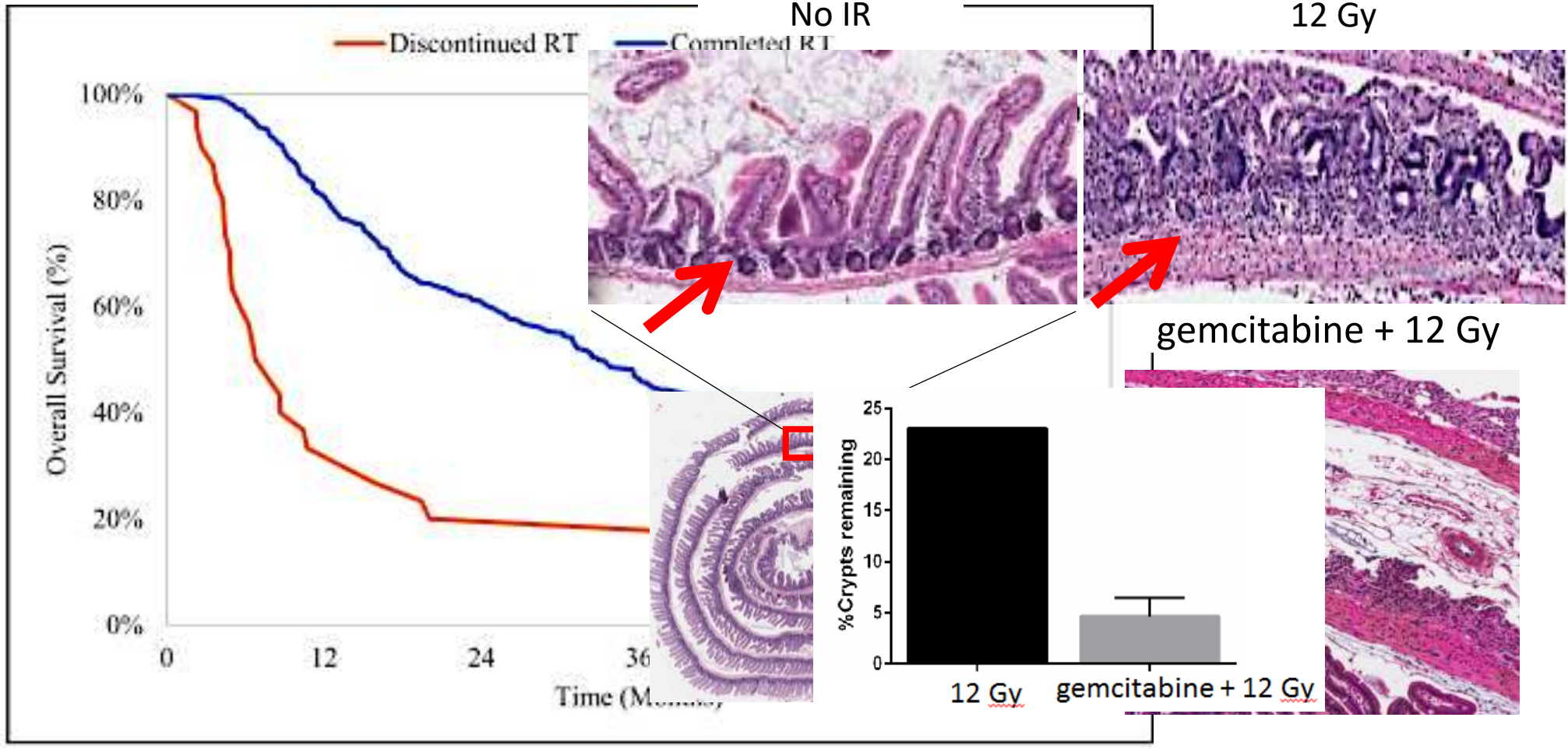
Muscle-Invasive Bladder Cancer and Chemoradiotherapy



N Engl J Med 2012; 366:1477-1488

Side effect from chemoradiotherapy

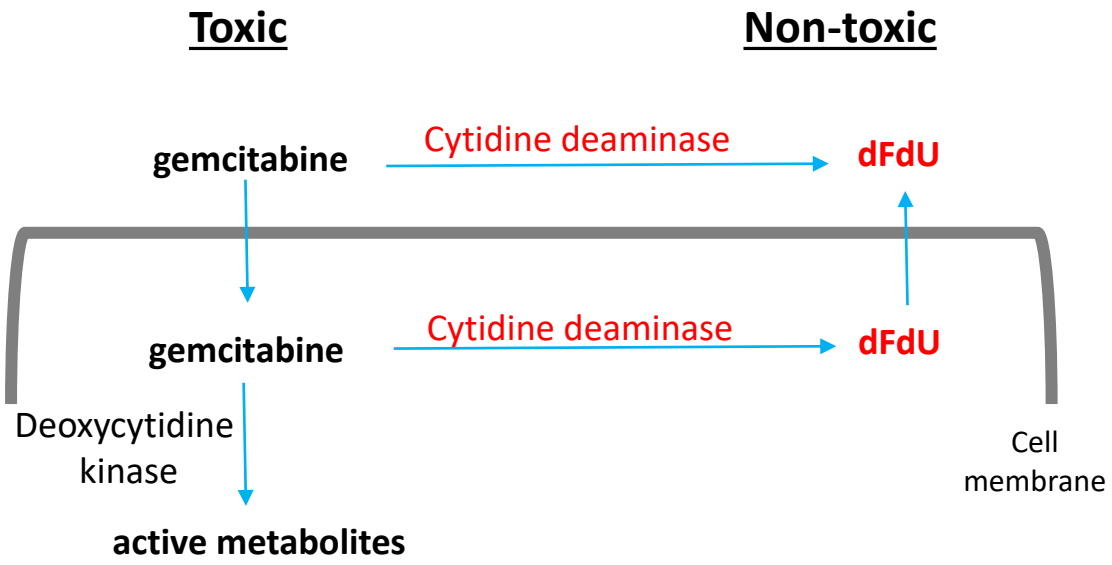
Chemorad
2016 Caff
2016 Thor
2011 Chou

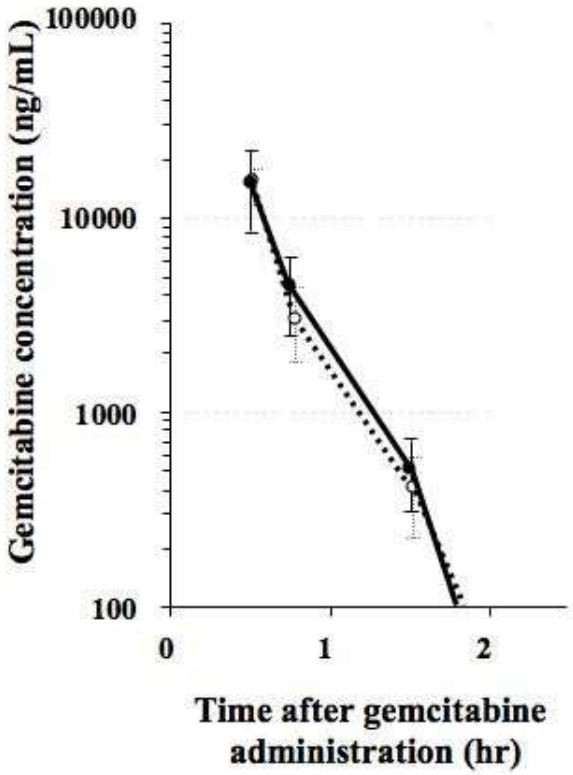


Adv Radiat Oncol. 2021 Oct 25;7(1):100836

Aim

- To improve chemoradiotherapy efficacy and reduce normal tissue toxicity via ultrasound

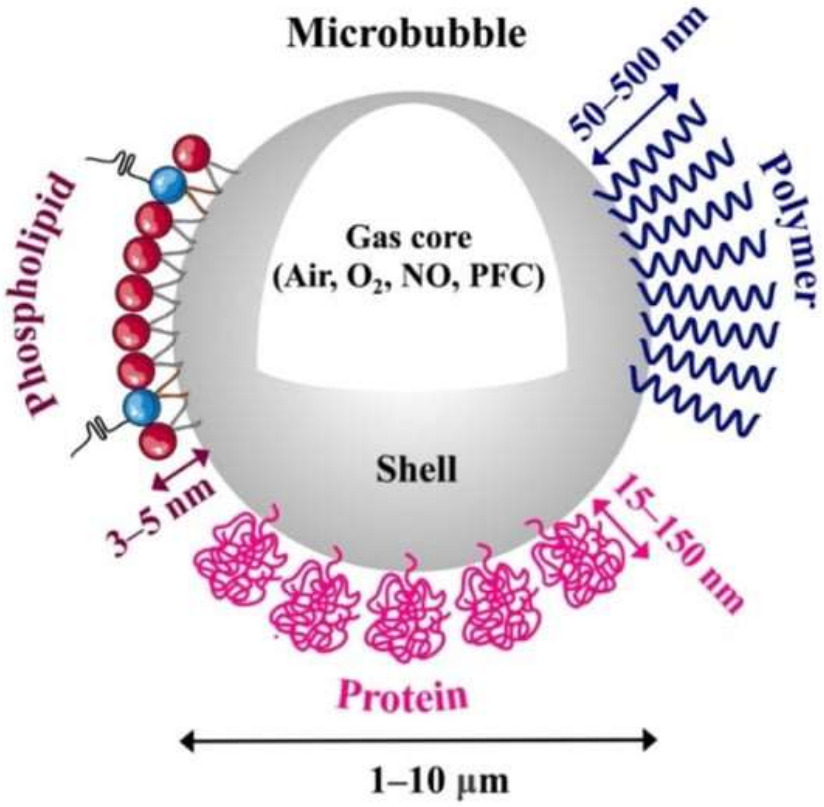


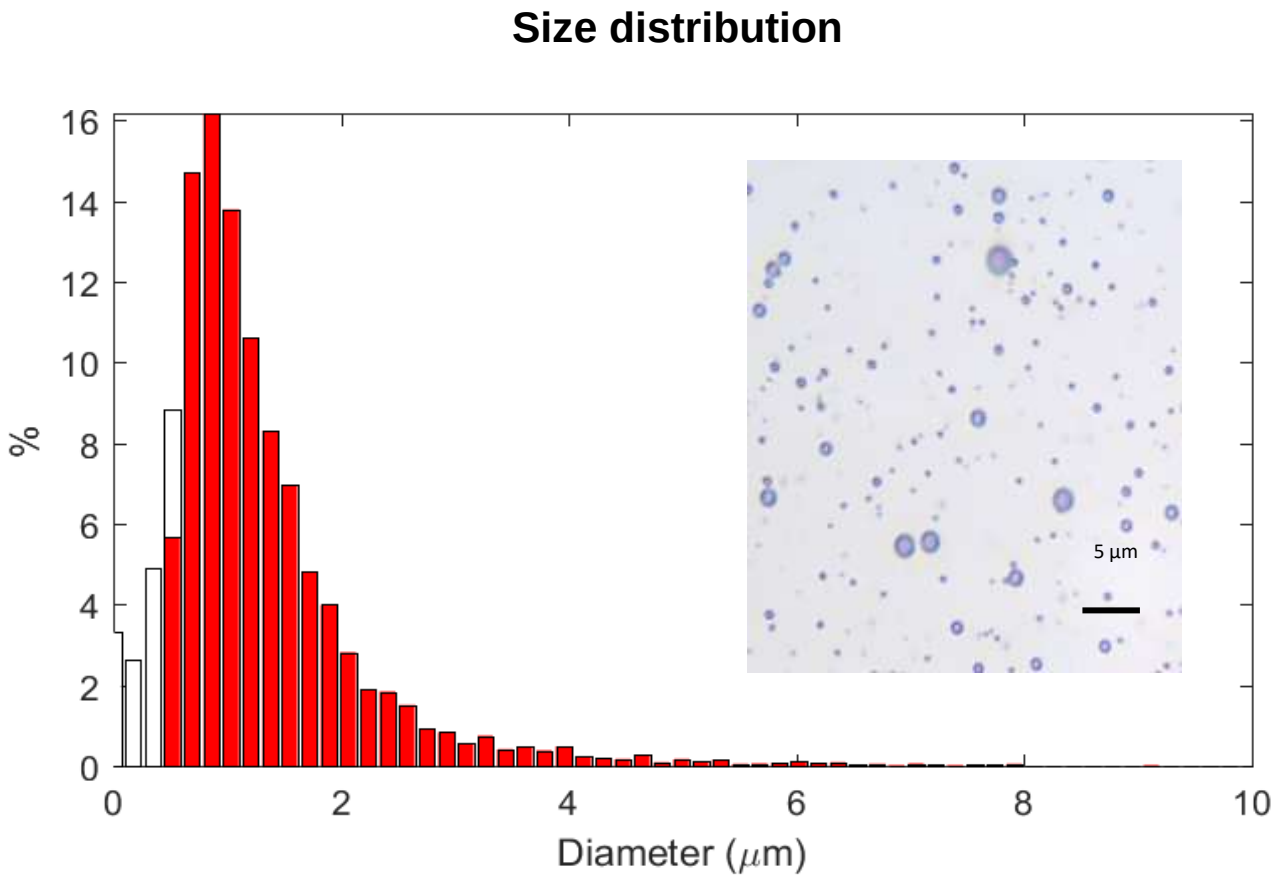


800 mg/m^2 iv

Journal of Experimental & Clinical Cancer Research2010 29:15

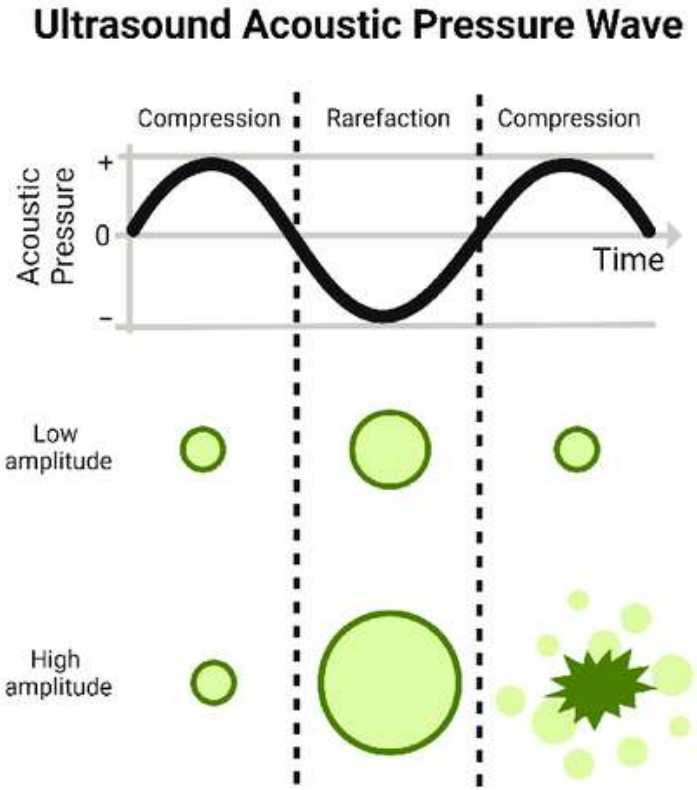
Ultrasound-mediated drug delivery: microbubbles (MB)



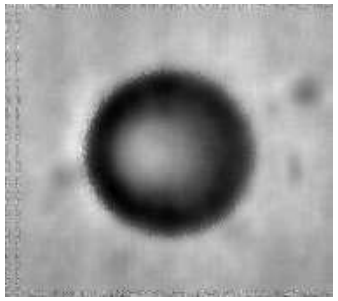


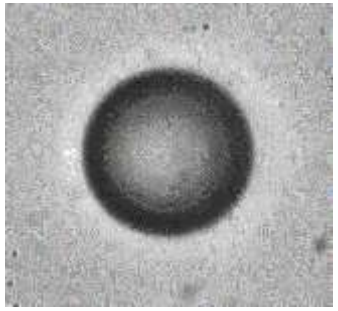
Pharmaceutics. 2023 May 30;15(6):1625

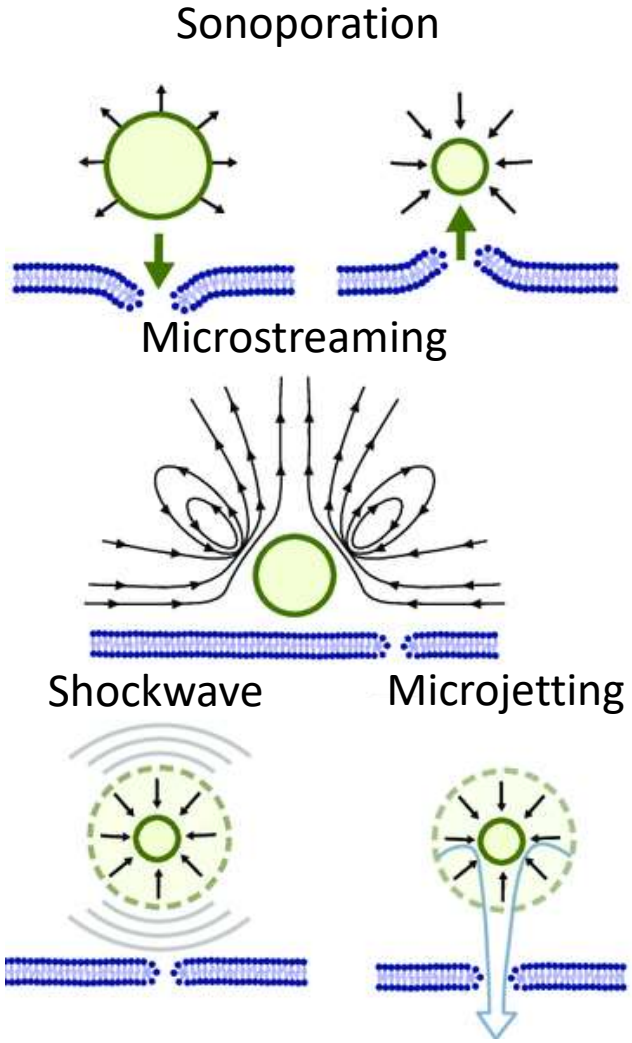
Ultrasound-mediated drug delivery: cavitation



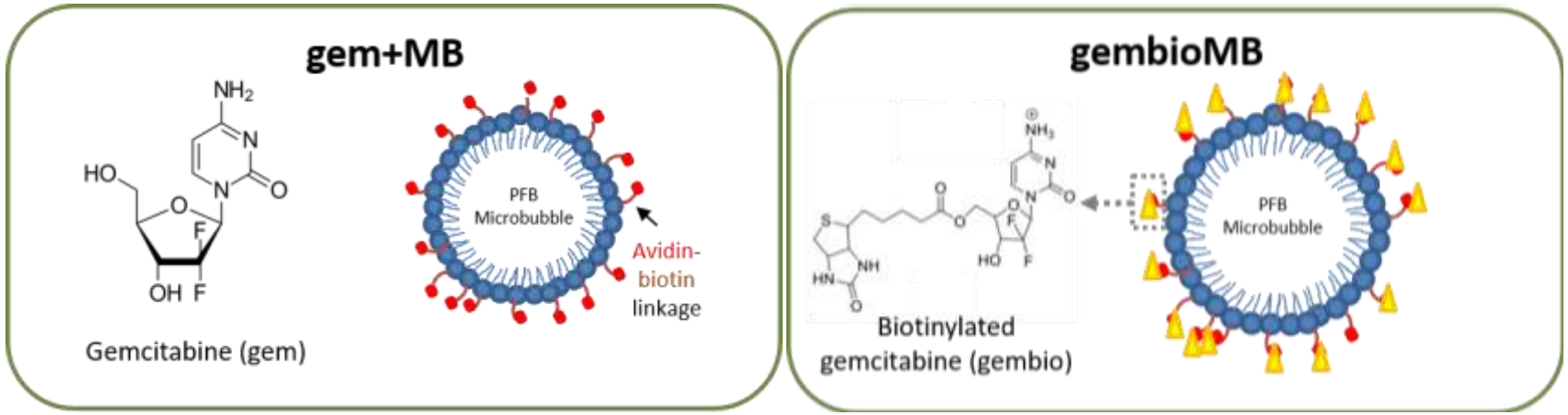
Pharmaceutics. 2022 Nov 7;14(11):2396.

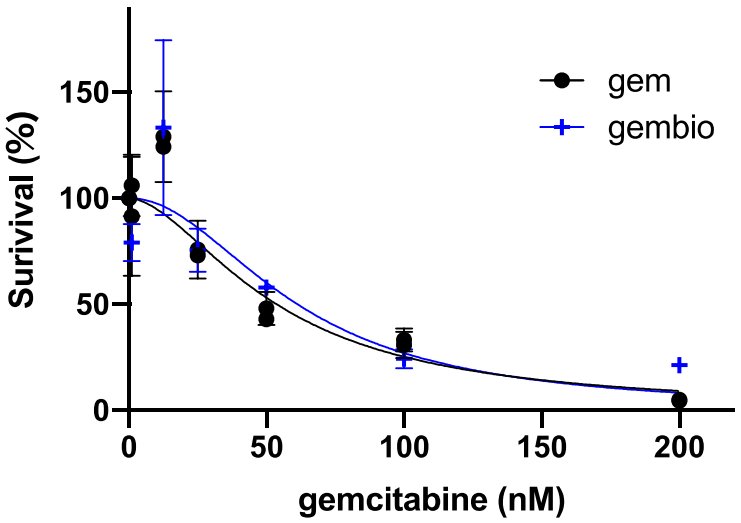


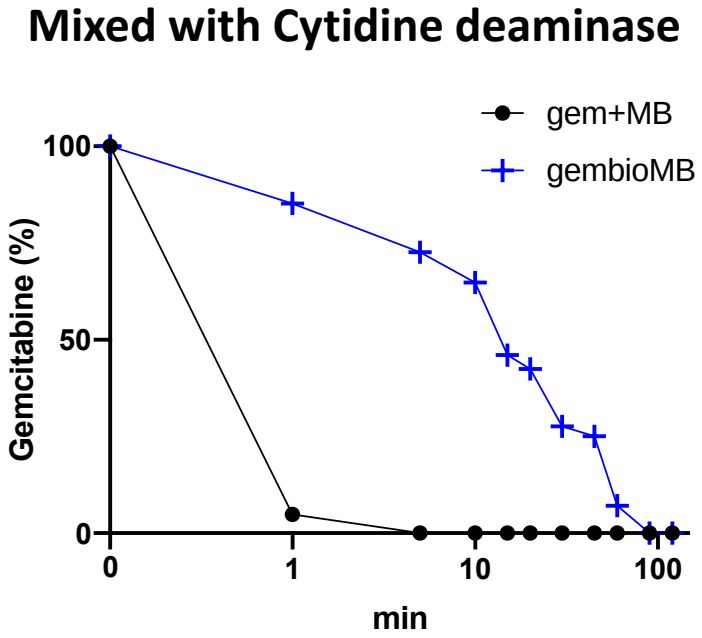


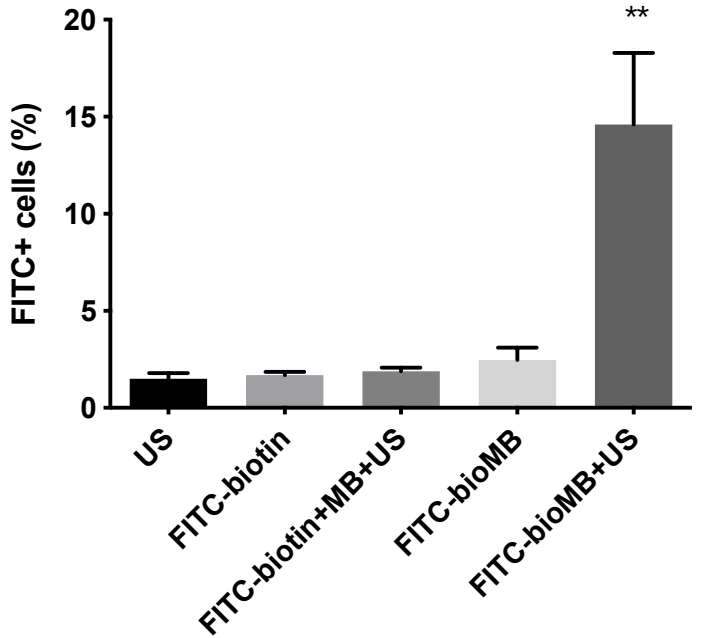


Strategies to deliver gemcitabine using microbubbles



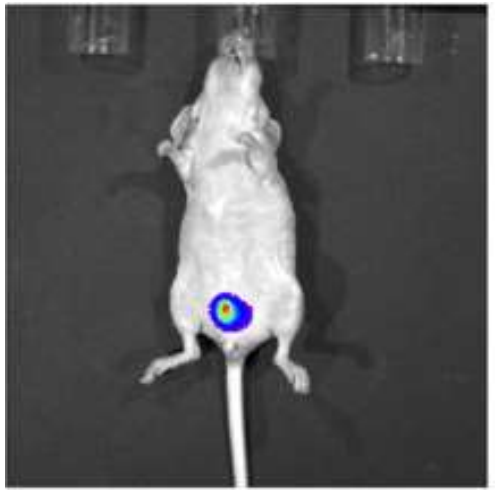


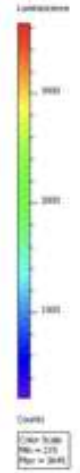


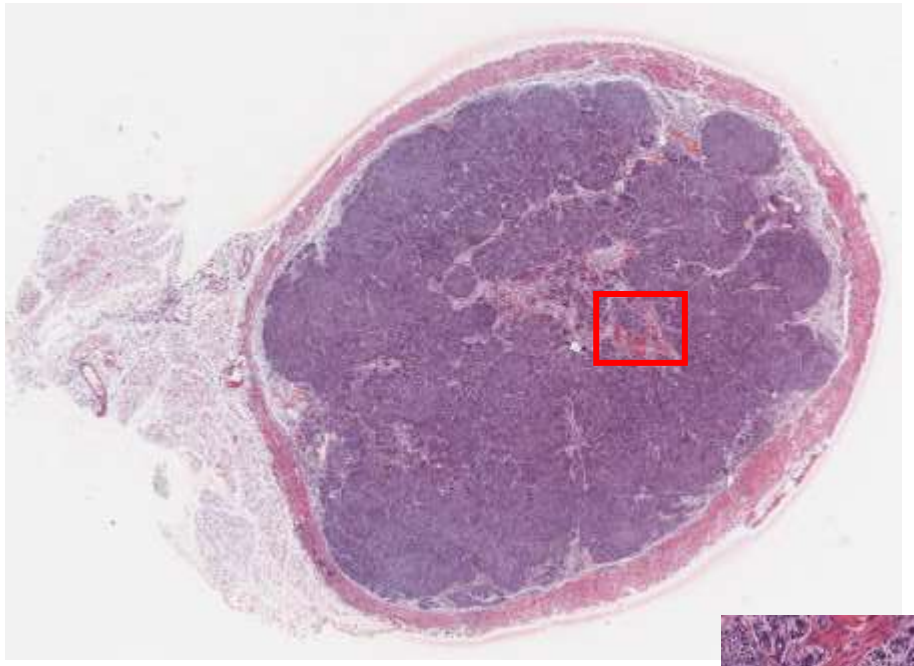


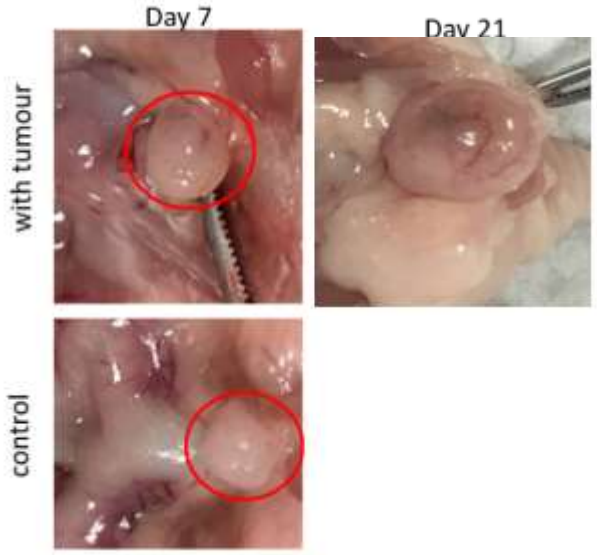
Ultrasound Med Biol. 2021;47(6):1596-1615.

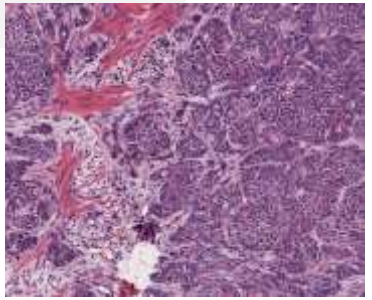
orthotopic MIBC model





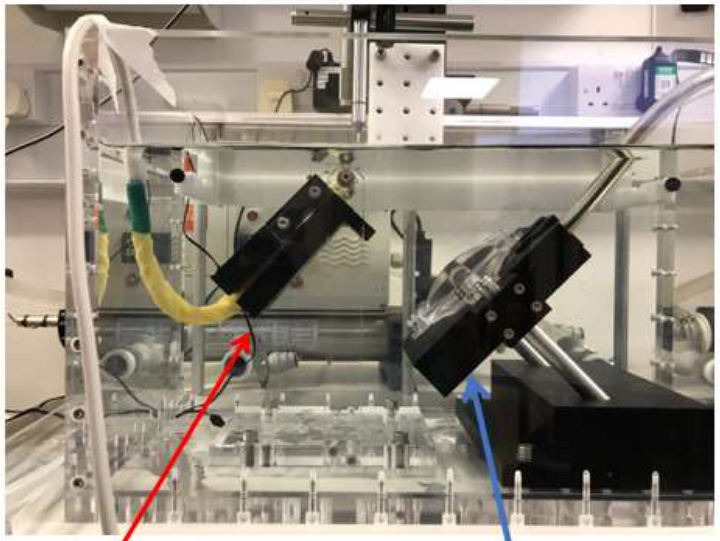




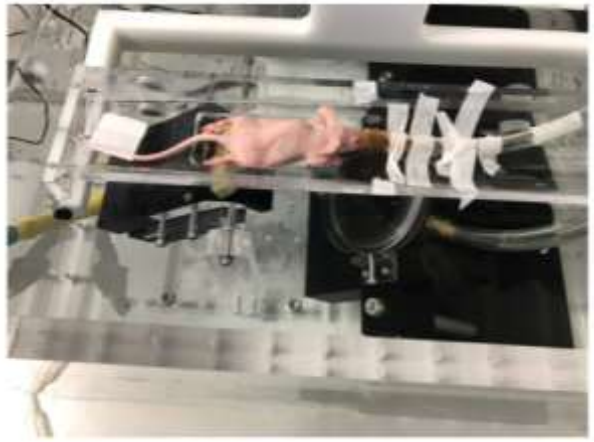


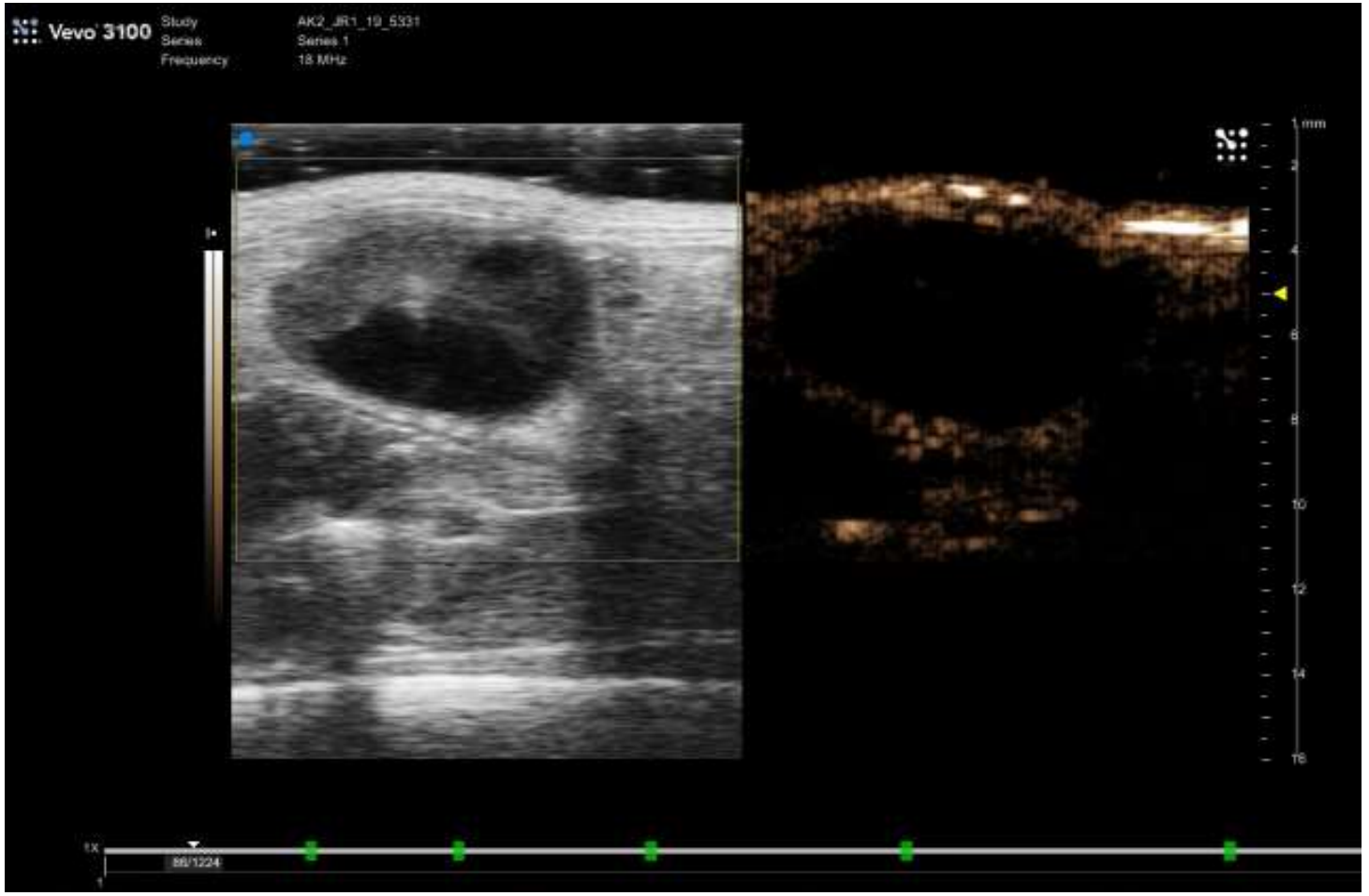
RT112 cells in CD1nude mice
End point:
Tumour > 450 mm^3 or weight loss >15% (severe hematuria)

Image-guided ultrasound-mediated drug delivery system



7.5 MHz Imaging probe 1.1 MHz Therapy probe

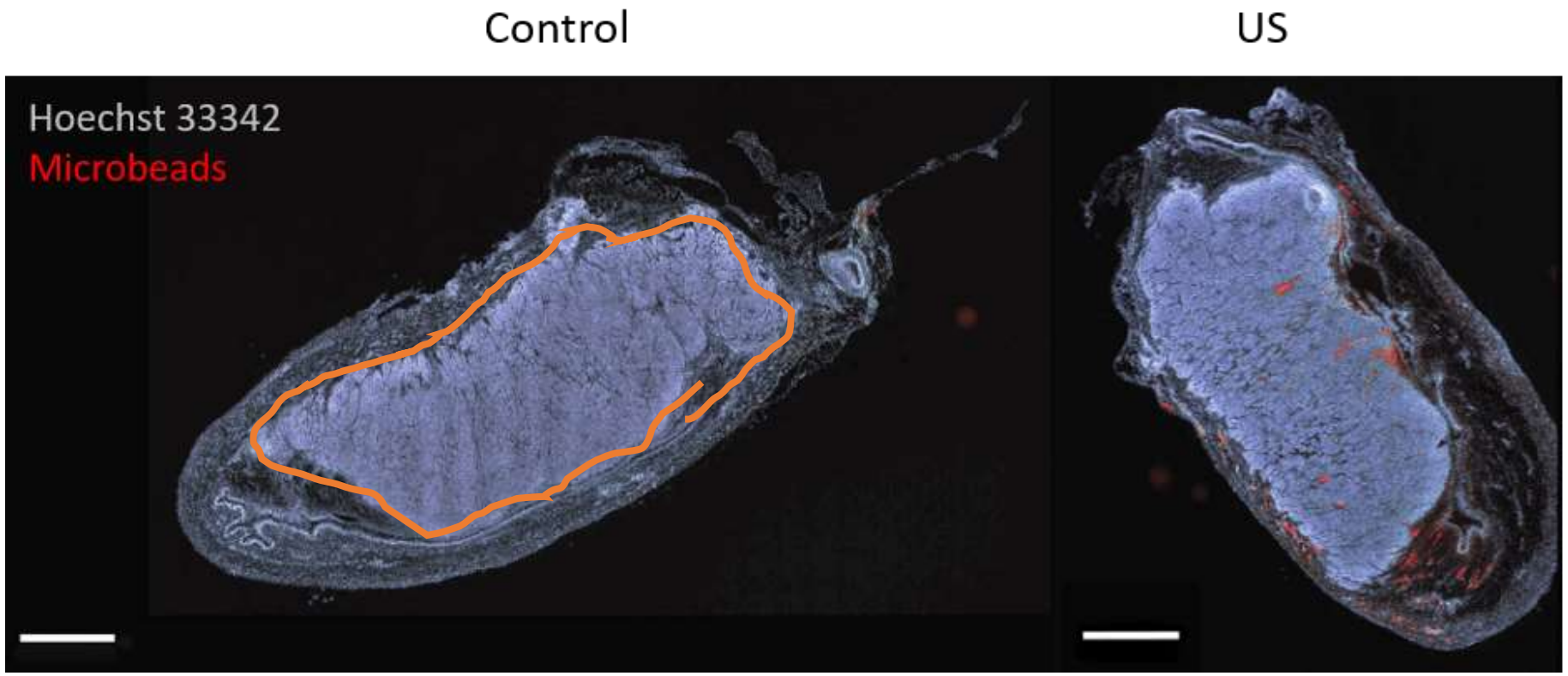


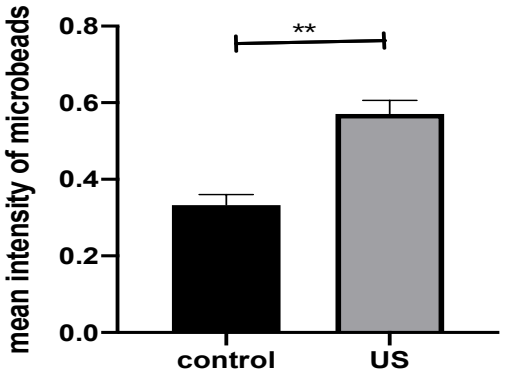


Therapy probe: 1.1 MHz centre frequency, 1 MPa PNP, 1% DC and 0.5 Hz PRF

Int J Radiat Oncol Biol Phys
. 2021 ;109(5):1472-1482.

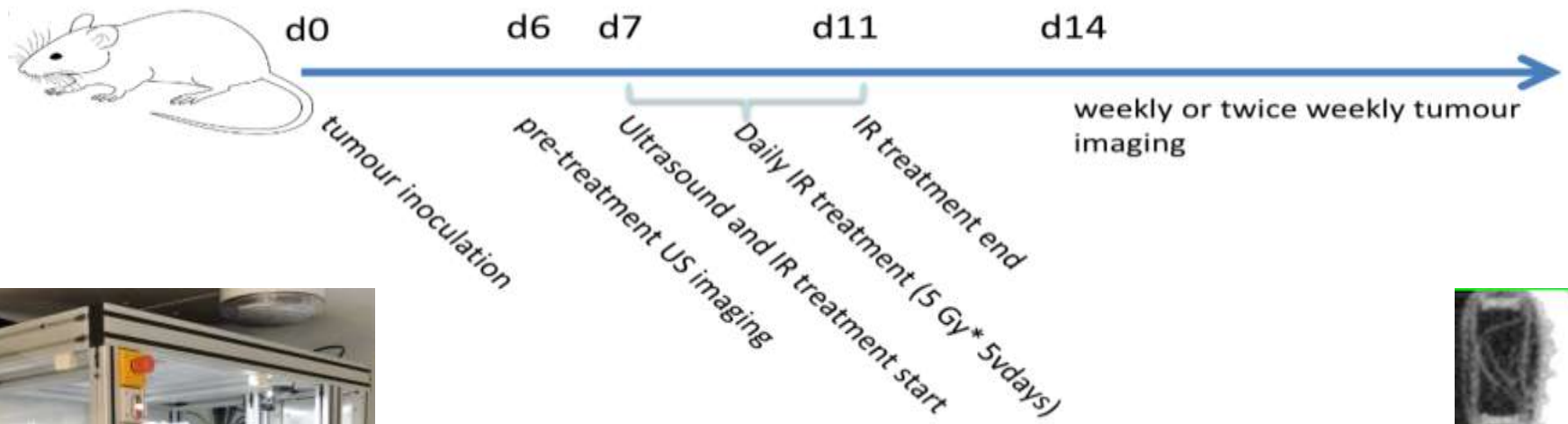
Ultrasound improves drug delivery

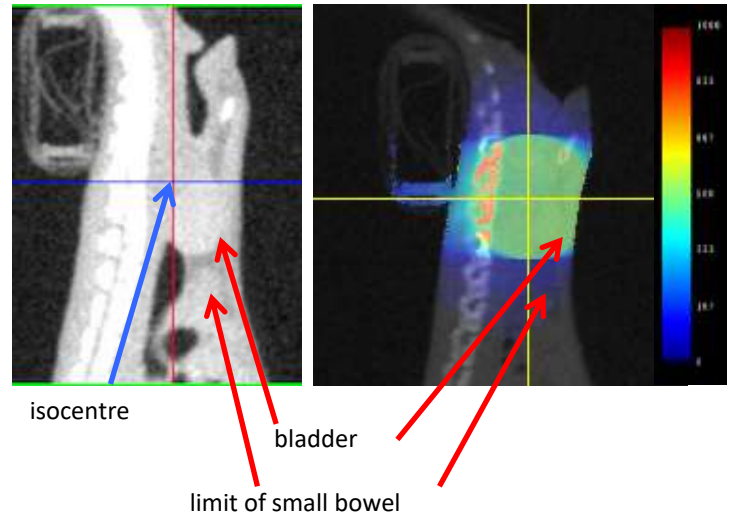




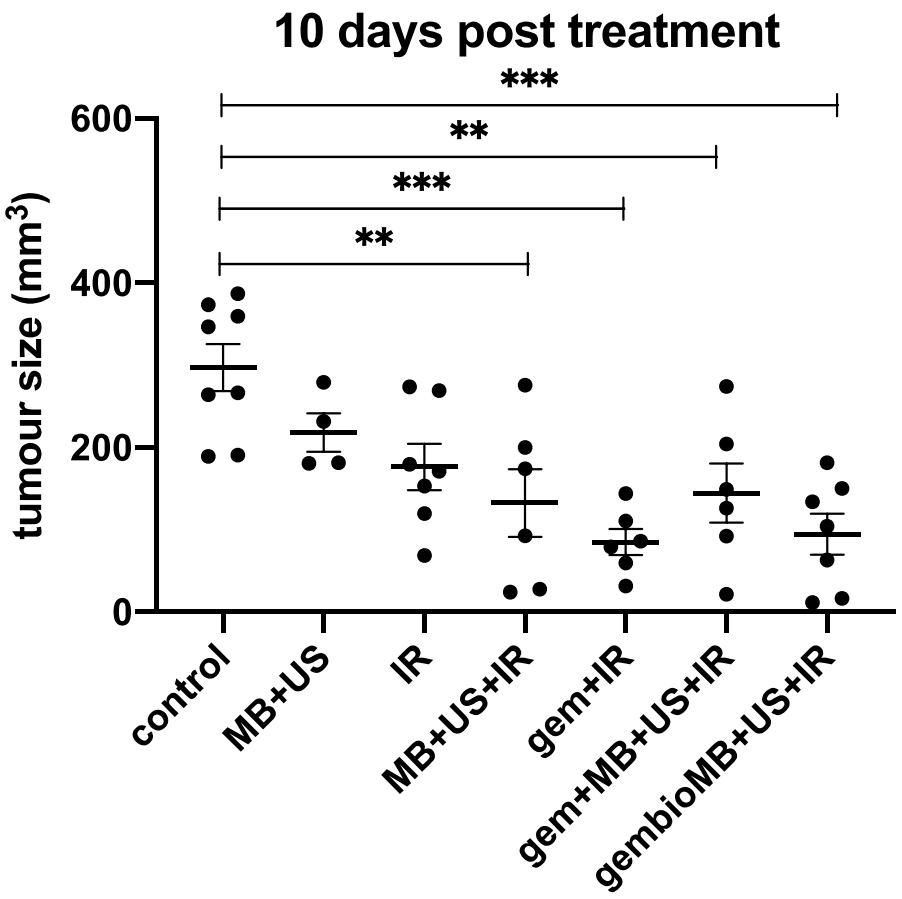
Int J Radiat Oncol Biol Phys
. 2021 ;109(5):1472-1482.

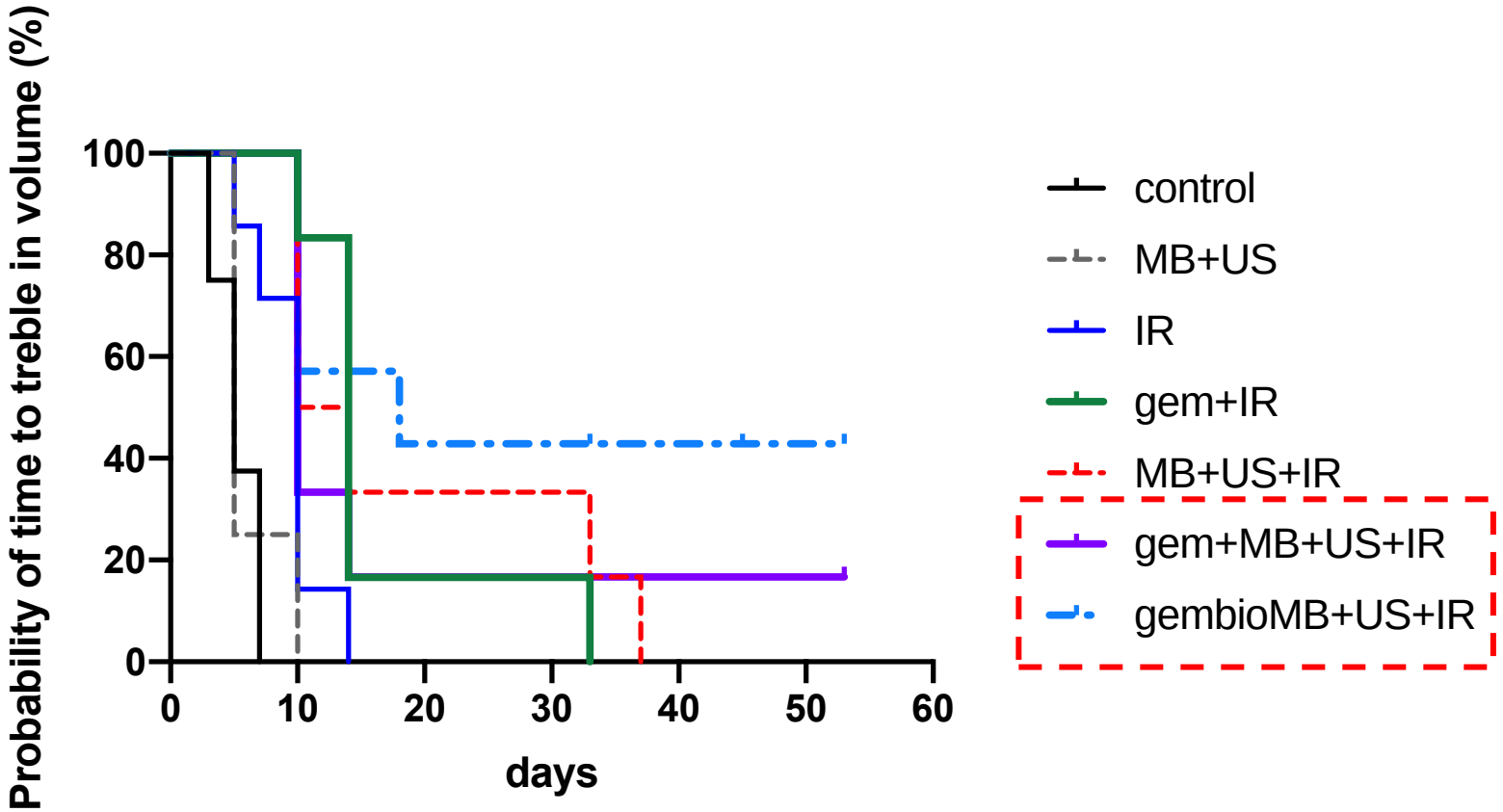
Combine with radiotherapy: SARRP





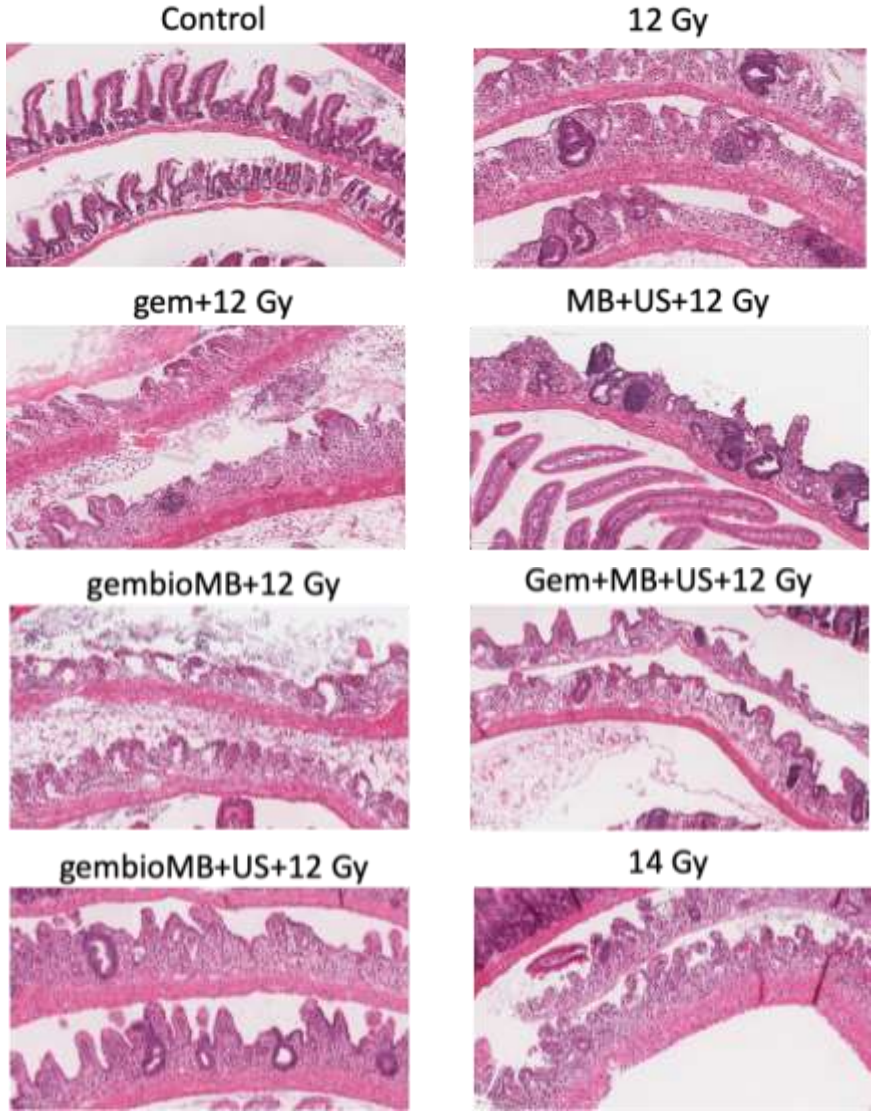
Ultrasound-mediated gemcitabine delivery improves tumour killing

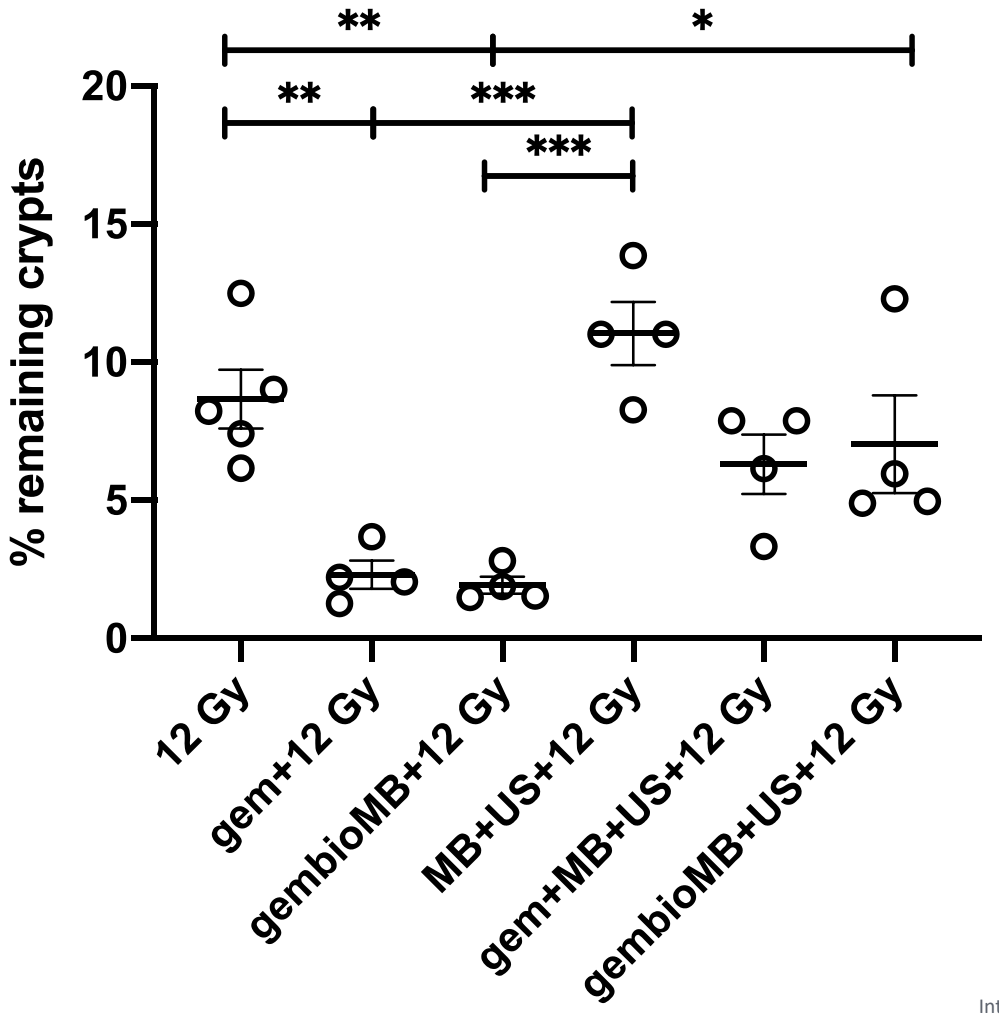




Int J Radiat Oncol Biol Phys
. 2021 ;109(5):1472-1482.

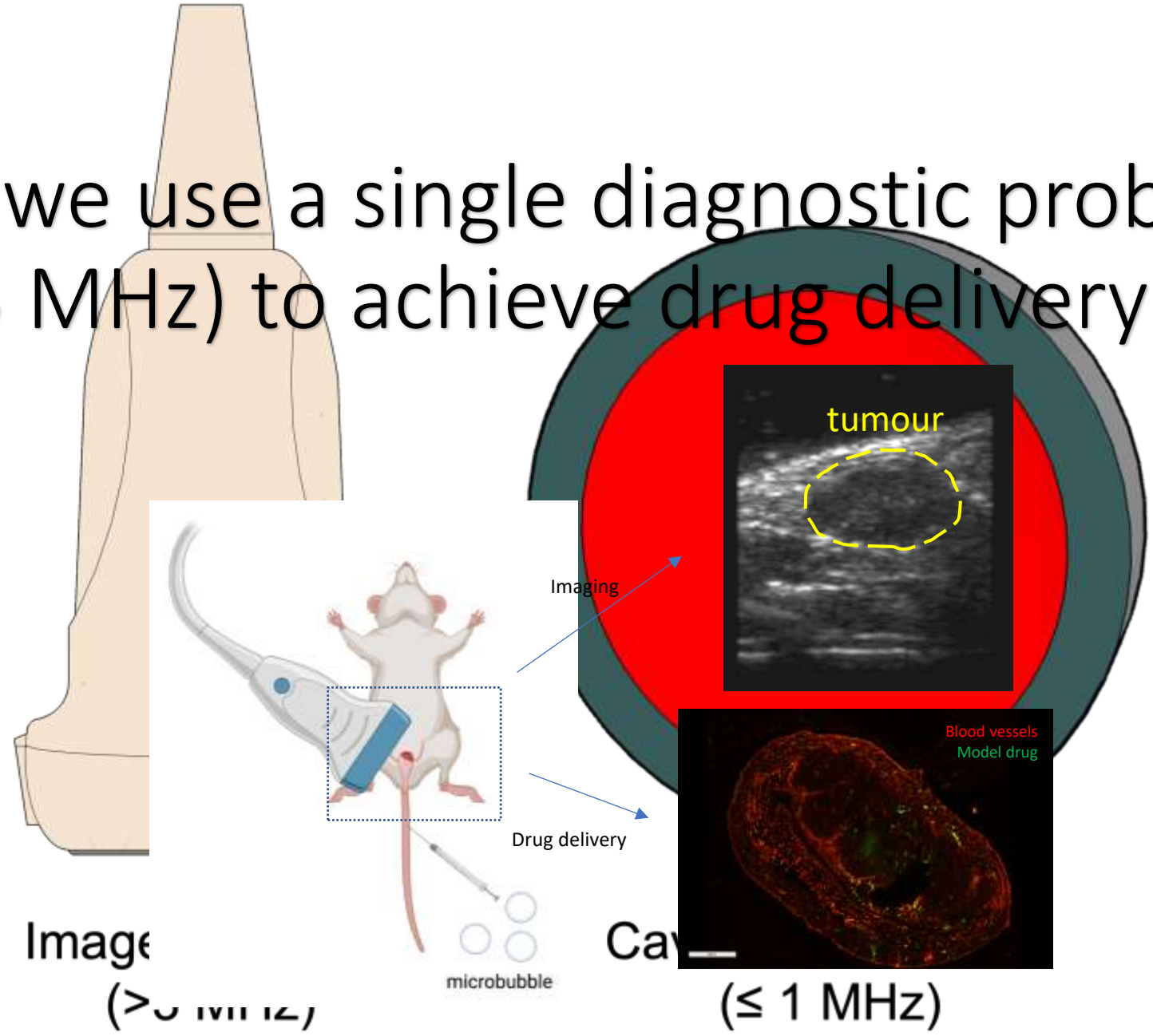
Ultrasound-mediated gemcitabine delivery for chemoradiotherapy



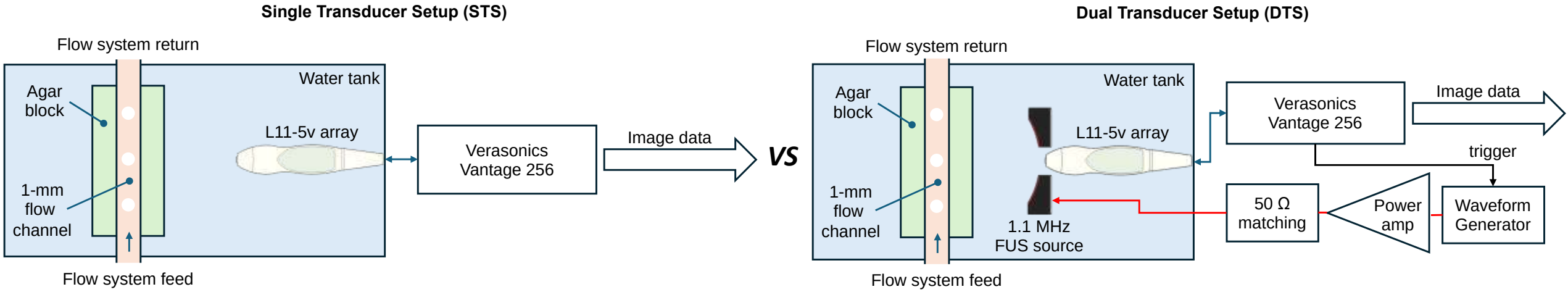


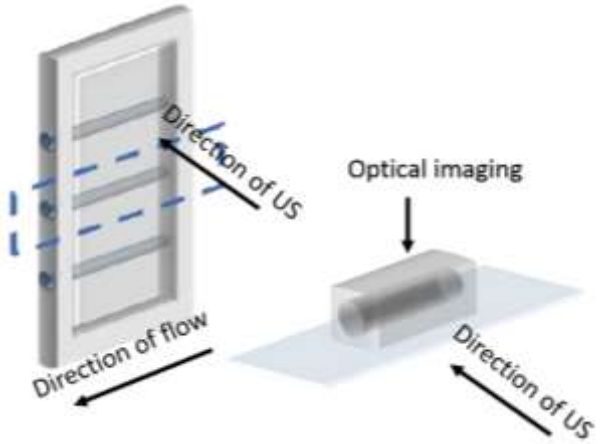
Int J Radiat Oncol Biol Phys . 2021 ;109(5):1472-1482.

Can we use a single diagnostic probe (> 3 MHz) to achieve drug delivery?



In vitro experiment to quantify delivery



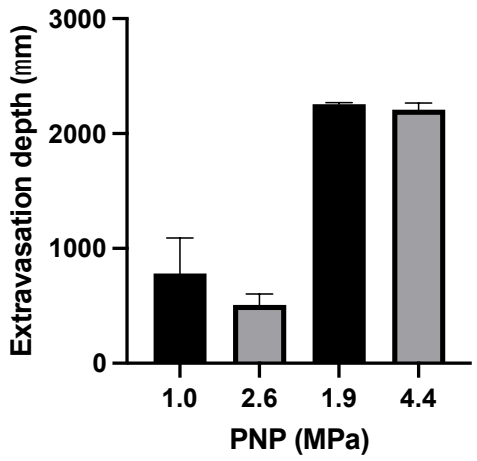


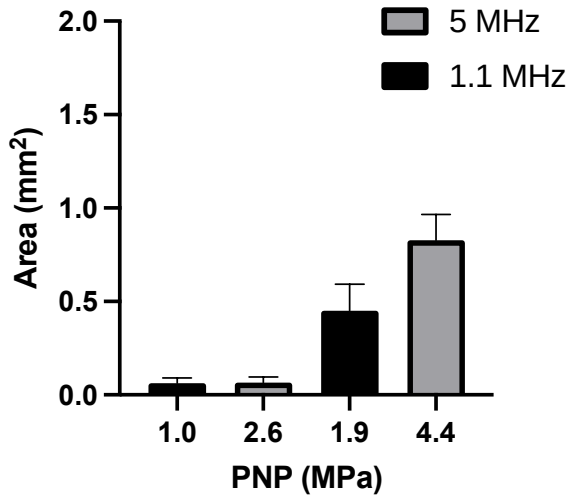
L11-5v	128 element linear array with Fc 7.5 MHz (6 MHz bandwidth)
STS	5 MHz transmit frequency

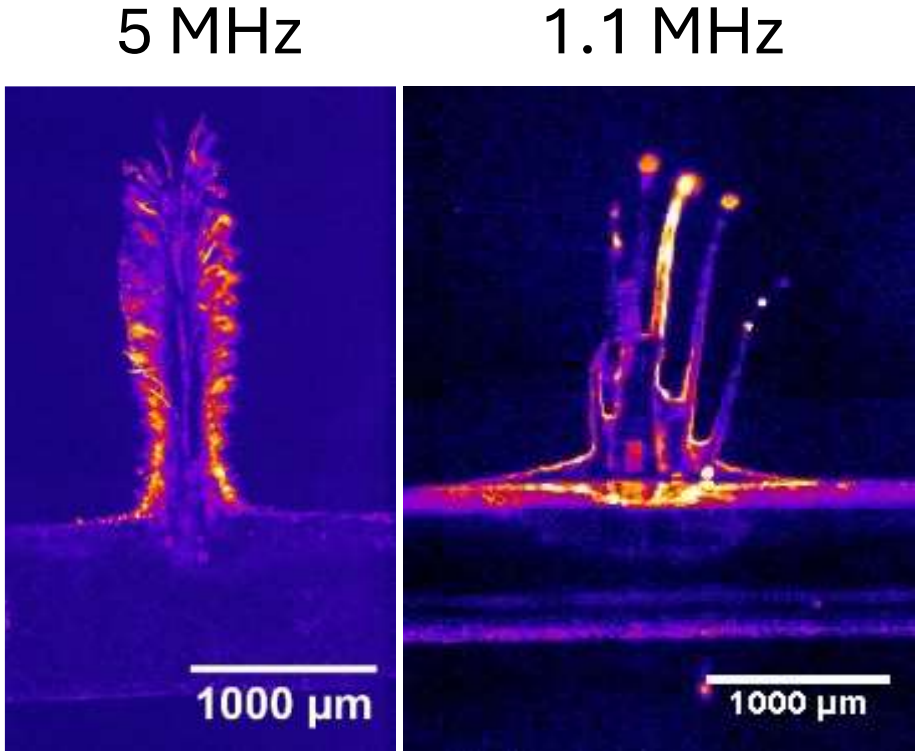
Int J Hyperthermia. 2024;41(1):2430330.

STS and DTS showed comparable extravasation

Frequency (MHz)	No. of cycles x 10^3	PRF (Hz)	Pressure (PNP, MPa)	I_{spta} (W/cm^2)
1.1 (DTS)	11	5	1.9	6.07
5.0 (STS)	10	5	5.1	8.67
1.1 (DTS)	11	5	1.0	1.67
5.0 (STS)	10	5	2.6	2.25

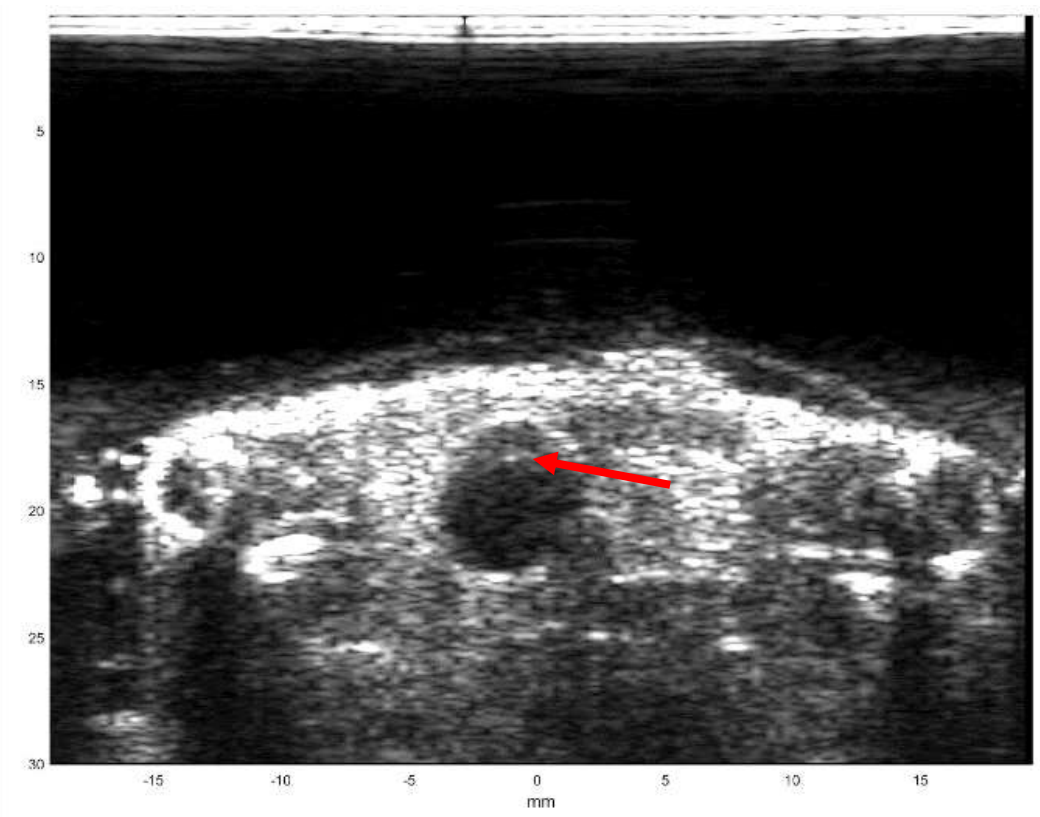




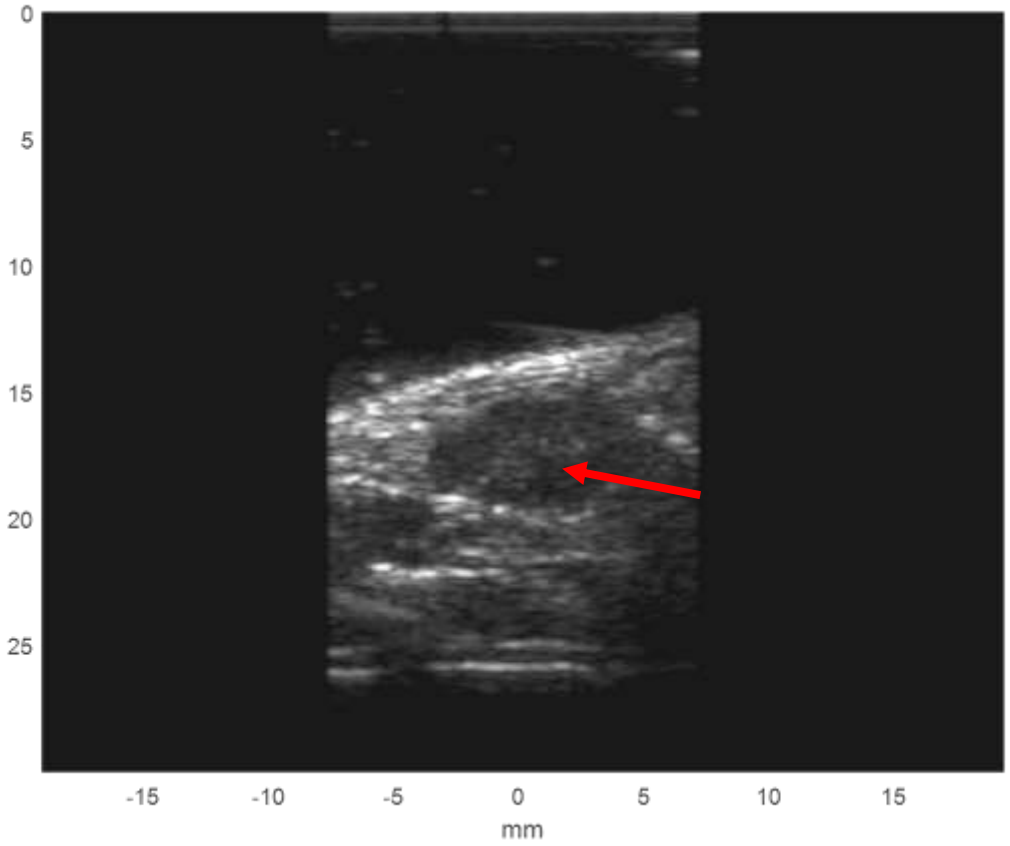


In vivo experiment: Imaging of orthotopic MIBC models

DTS

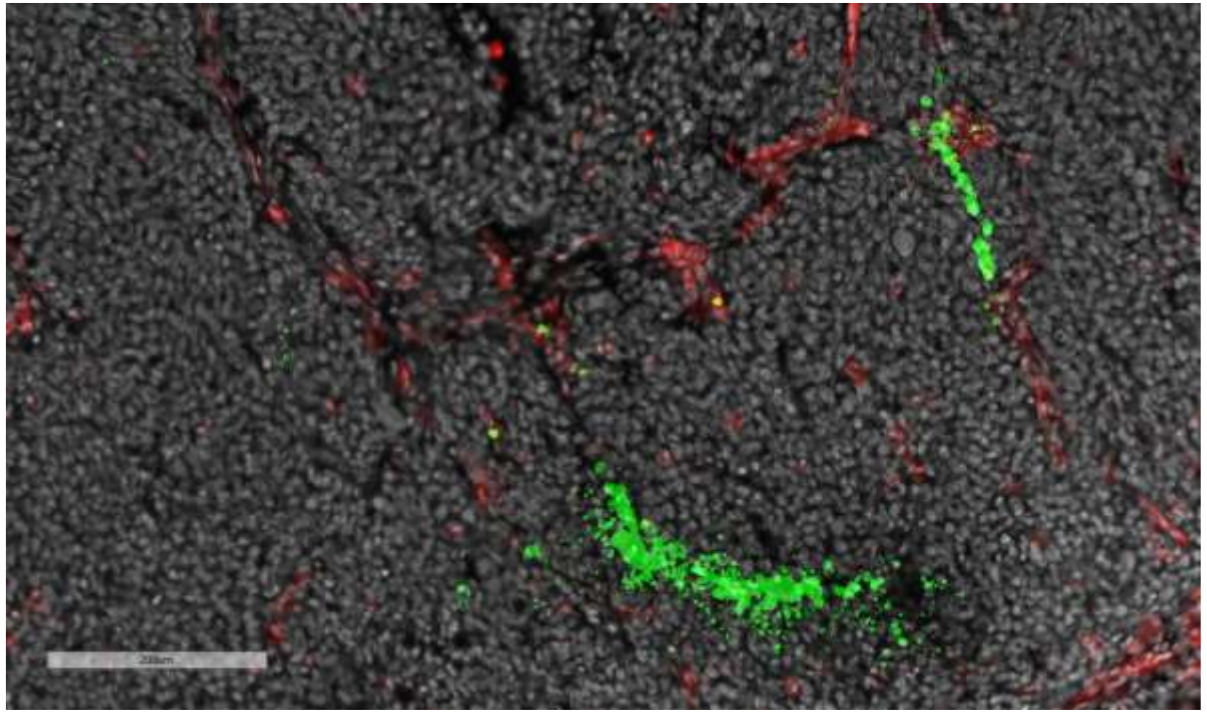


STS

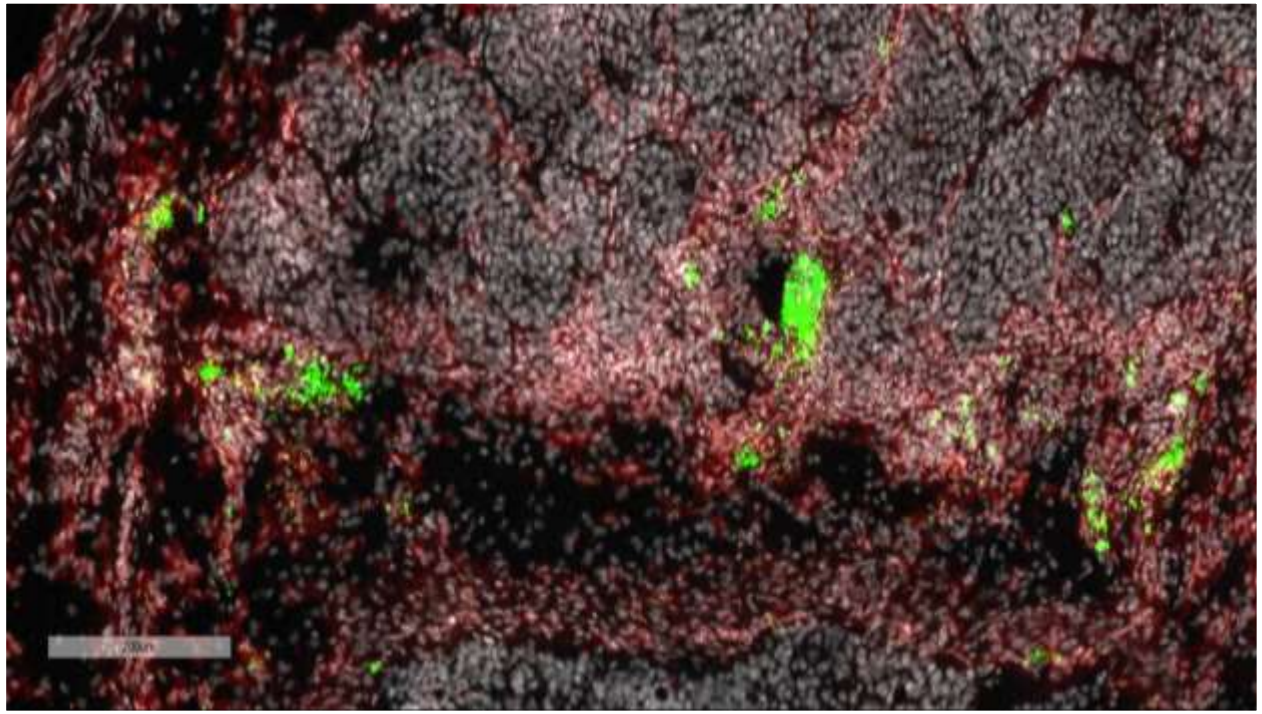


In vivo delivery on orthotopic MIBC model

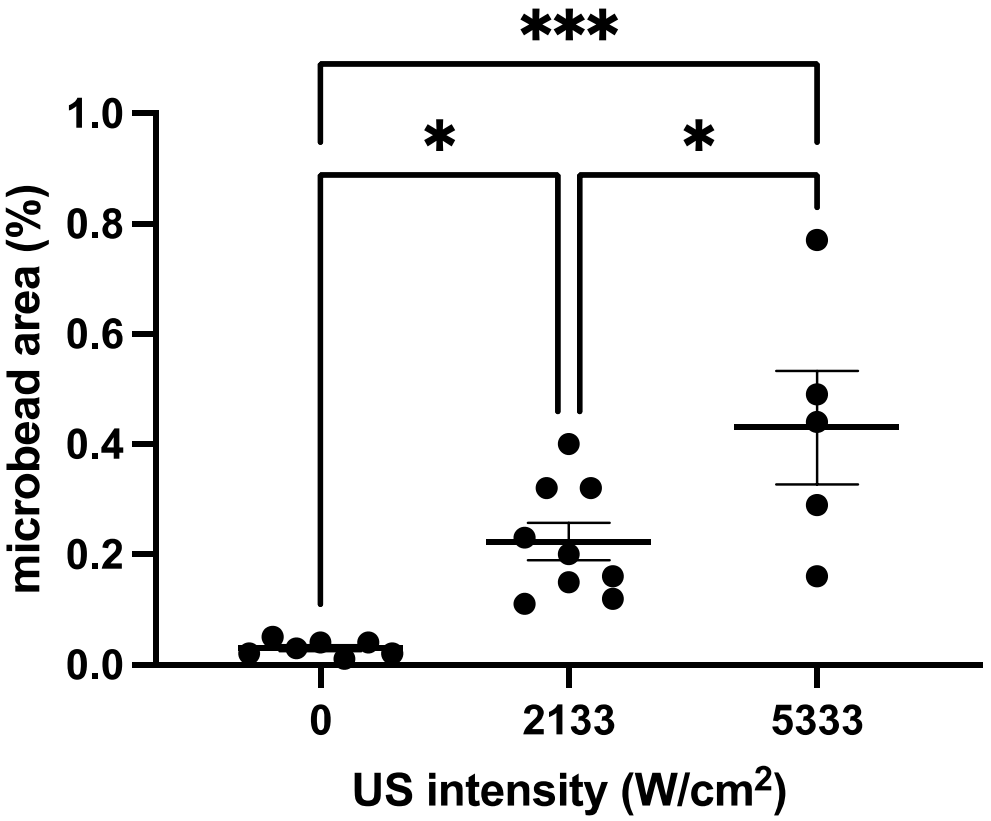
DTS



STS

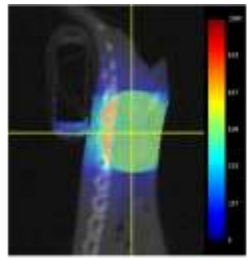


Increased drug delivery following increased ultrasound intensity

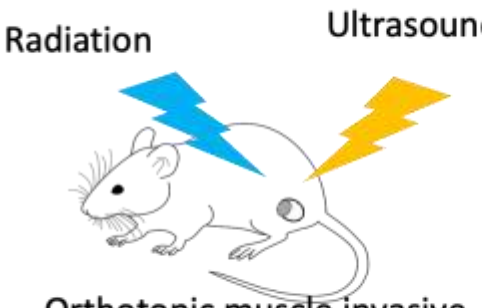


Summary

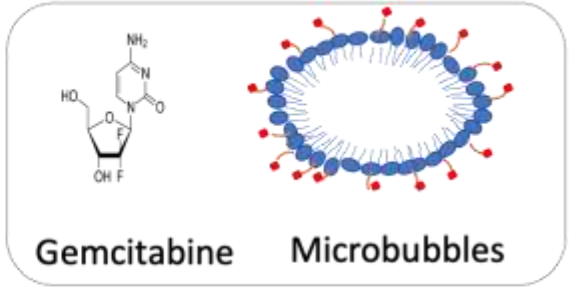
- Ultrasound-mediated gemcitabine delivery for chemoradiotherapy
  - Similar tumour growth delay to conventional chemoradiotherapy
  - Reduce acute gastrointestinal toxicity



Radiotherapy planning on SARRP

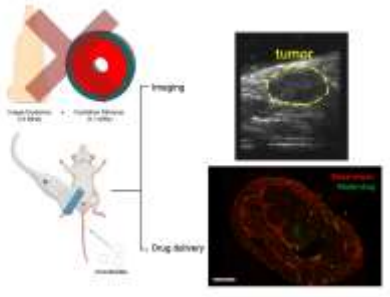


Orthotopic muscle invasive bladder cancer model



Microbubble-based gemcitabine delivery

- Ultrasound-mediated drug delivery using a single higher frequency(> 3 MHz) probe is achievable.



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- Dr. Michael Gray

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- Magdalena Hutchins

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- Dr. Jamie Thompson
- Ms. Amy Elliot

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