Molecular Imaging for Lung Cancer

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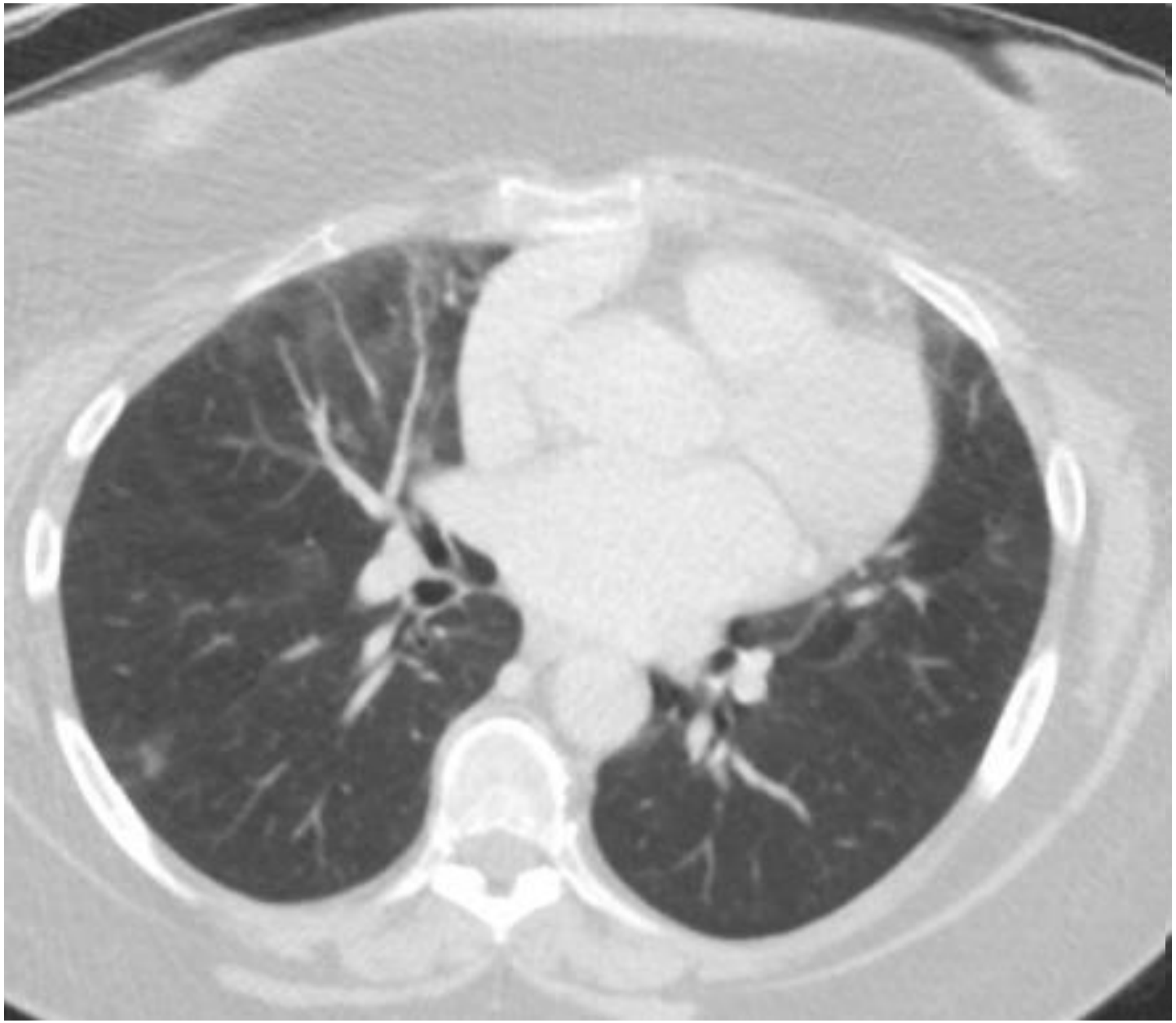
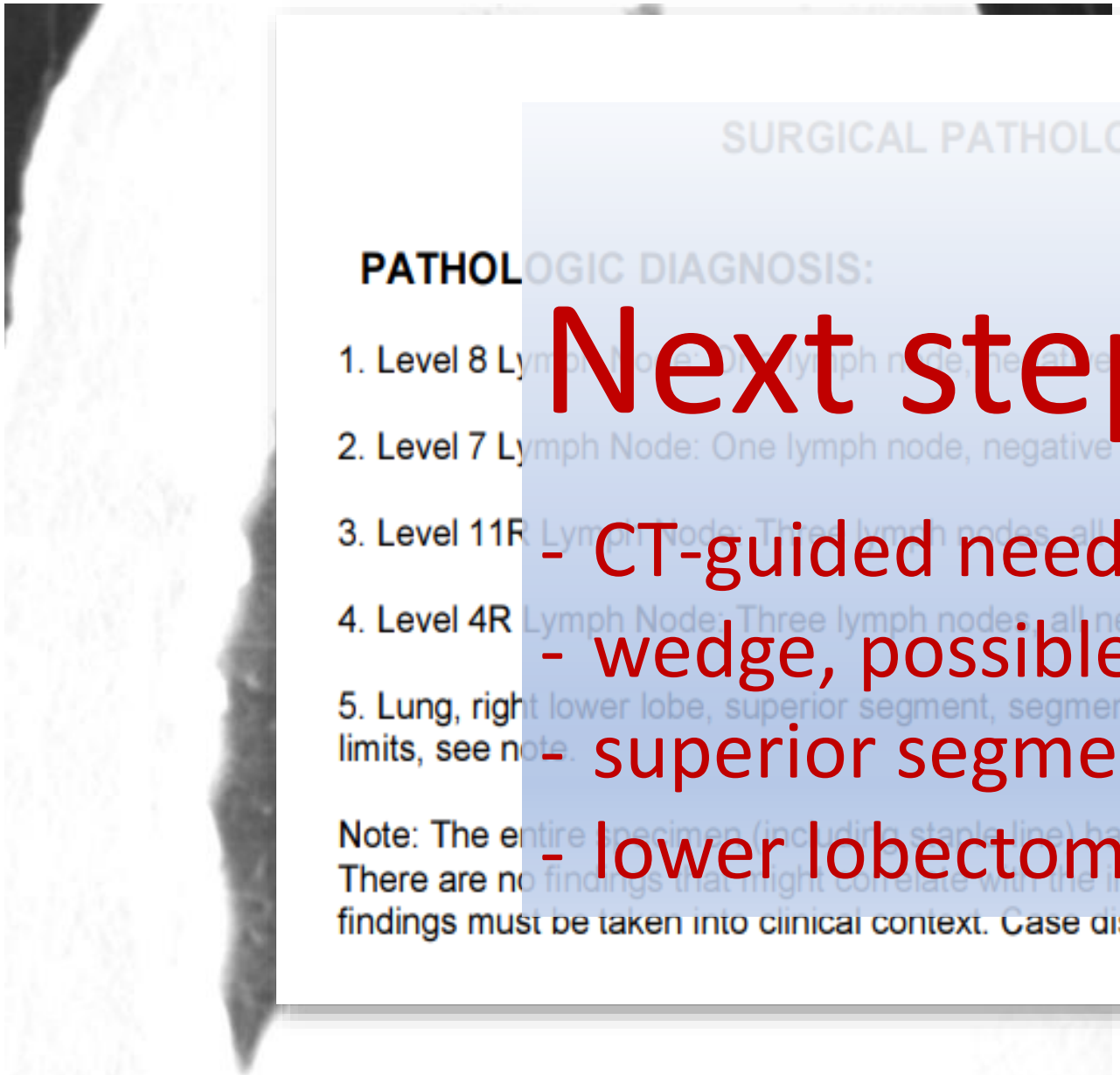
Boston, MA





SURGICAL PATHOLOGY REPORT - Final

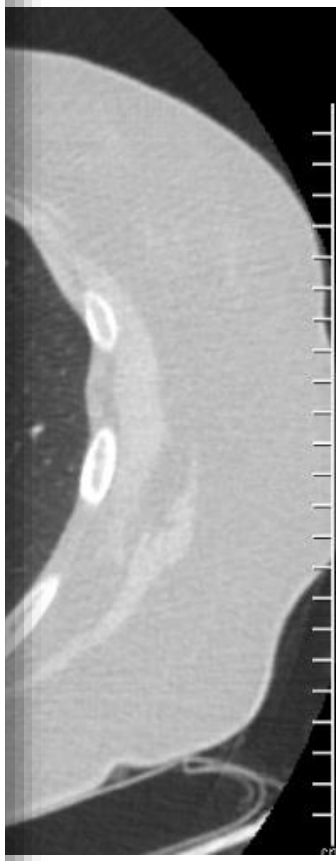
PATHOLOGIC DIAGNOSIS:

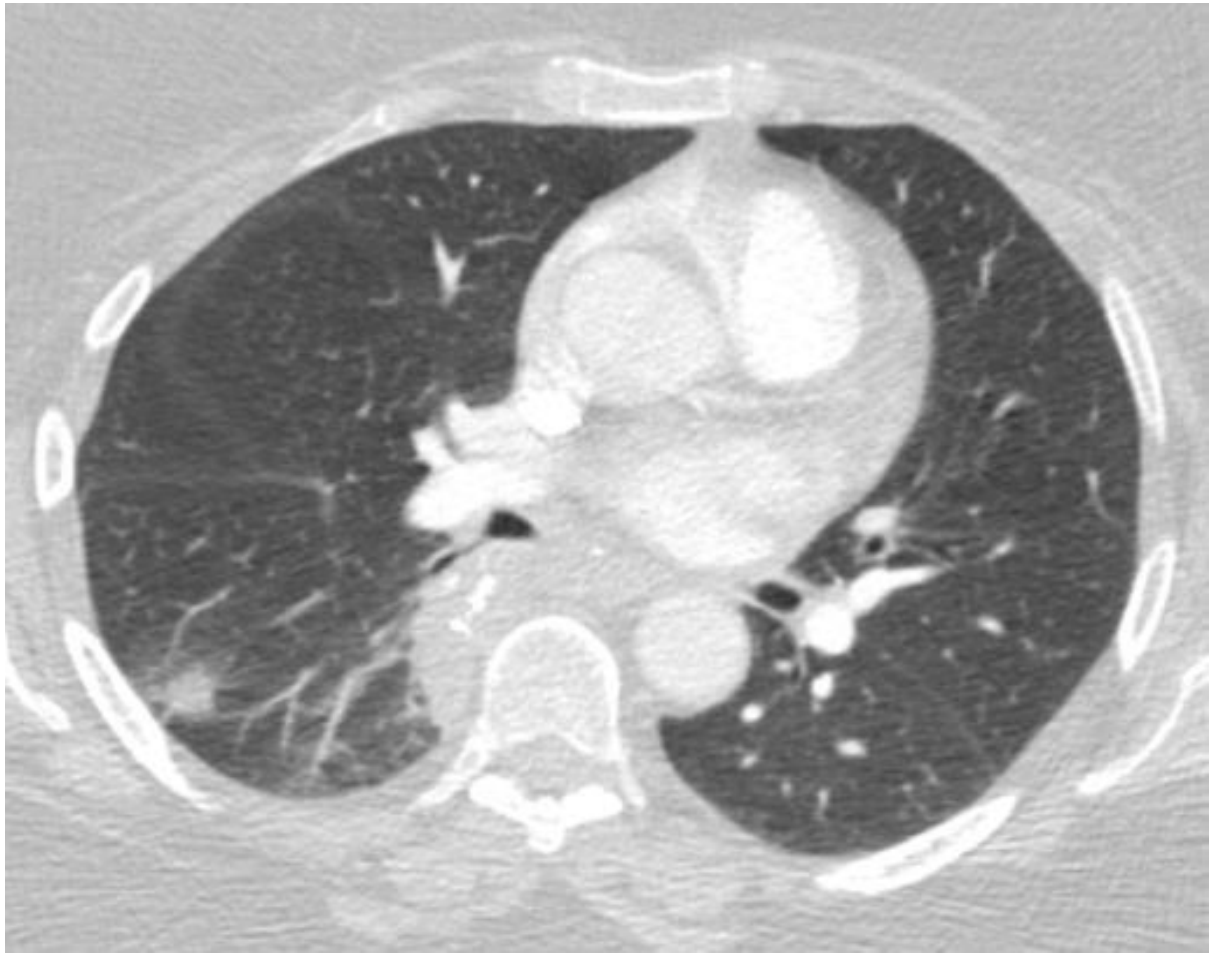
1. Level 8 Lymph Node: One lymph node, negative for malignancy (0/1).
2. Level 7 Lymph Node: One lymph node, negative for malignancy (0/1).
3. Level 11R Lymph Node: Three lymph nodes, all negative for malignancy (0/3).
4. Level 4R Lymph Node: Three lymph nodes, all negative for malignancy (0/3).
5. Lung, right lower lobe, superior segment, segmentectomy: Pulmonary parenchyma, within normal limits, see note.

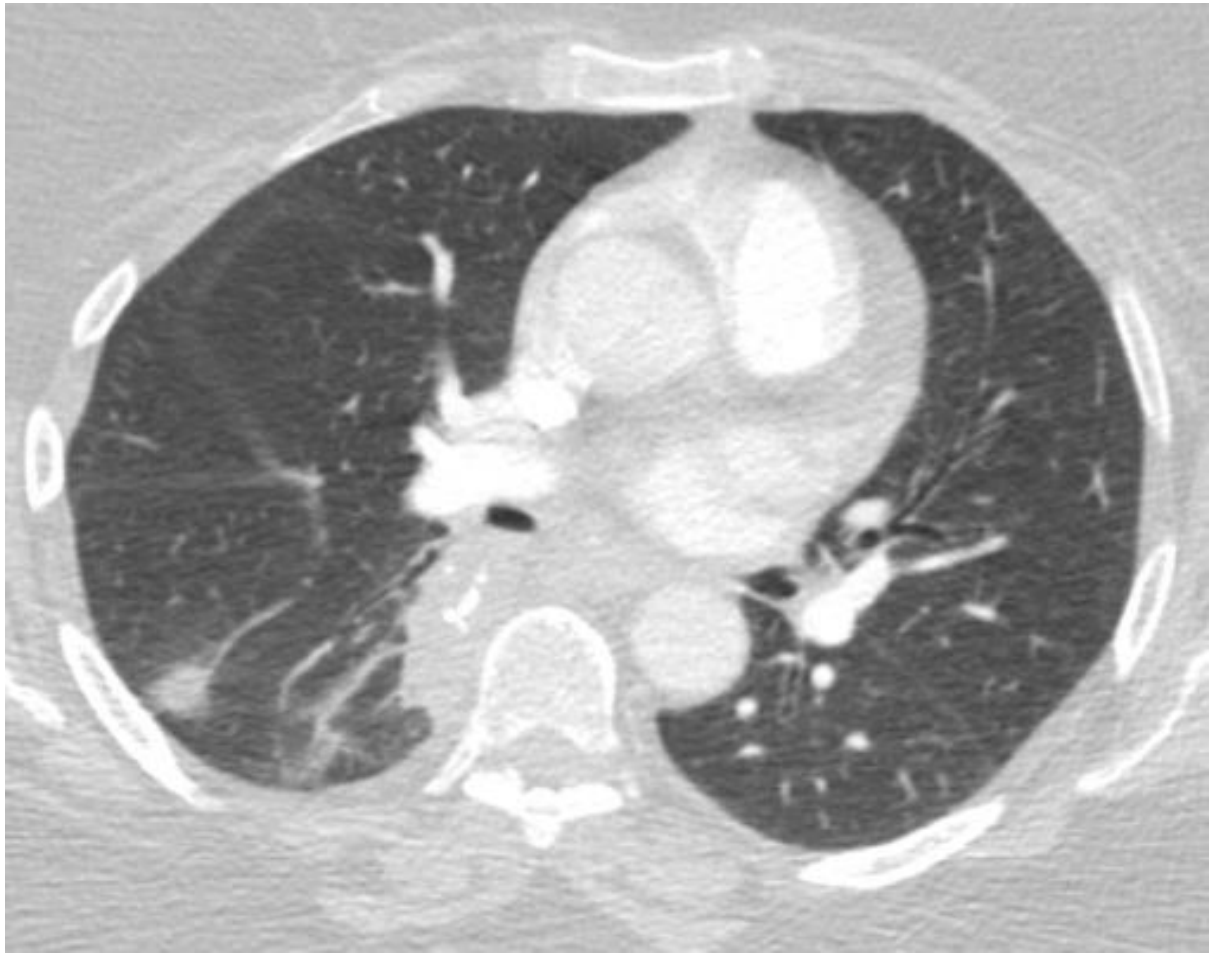
Note: The entire specimen (including staple line) has been submitted for histologic examination. There are no findings that might correlate with the imaging findings of a 1.1 CM lesion. These findings must be taken into clinical context. Case discussed with [redacted] on 10/27/21.

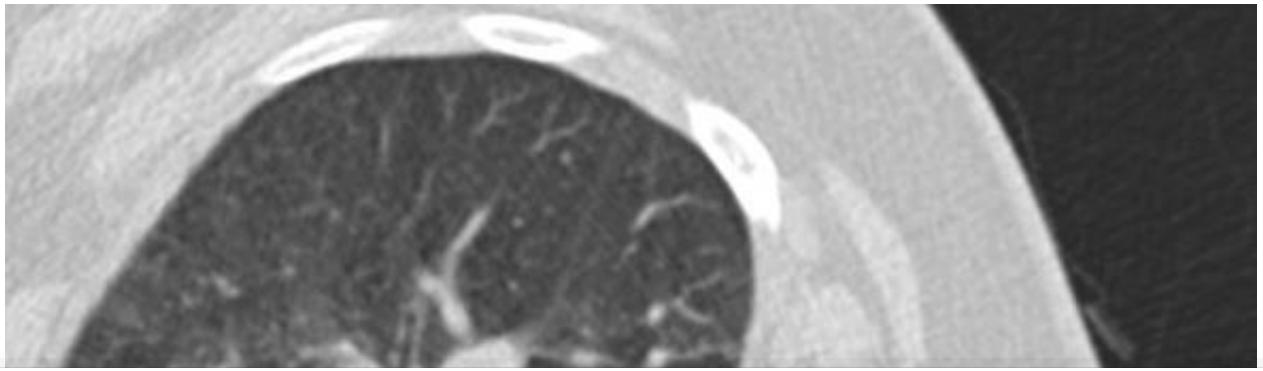
Next steps?

- CT-guided needle biopsy
- wedge, possible anatomic
- superior segmentectomy
- lower lobectomy









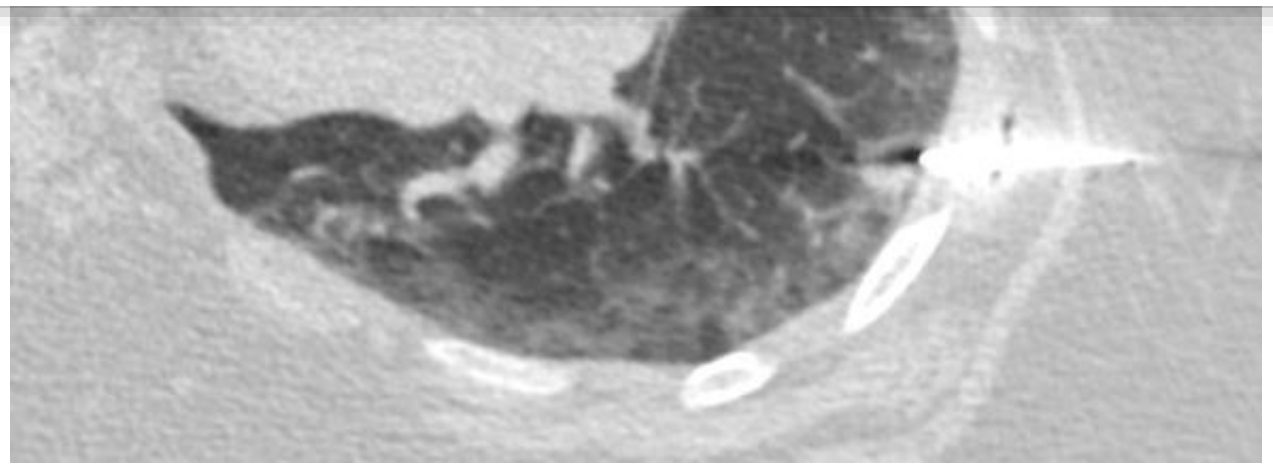
SURGICAL PATHOLOGY REPORT - Final

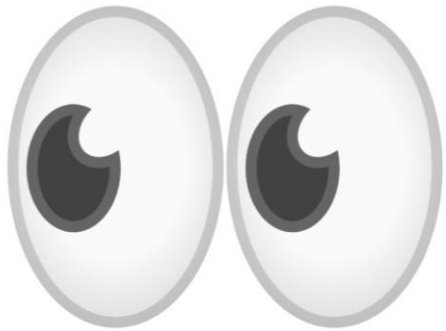
PATHOLOGIC DIAGNOSIS:

1. Right lower lobe lung biopsy #1: Well differentiated adenocarcinoma consistent with lung origin.

2. Right lower lobe lung biopsy #2: Well differentiated adenocarcinoma, consistent with lung origin, see note.

Note: Tumor cells are positive for TTF-1 and Napsin.

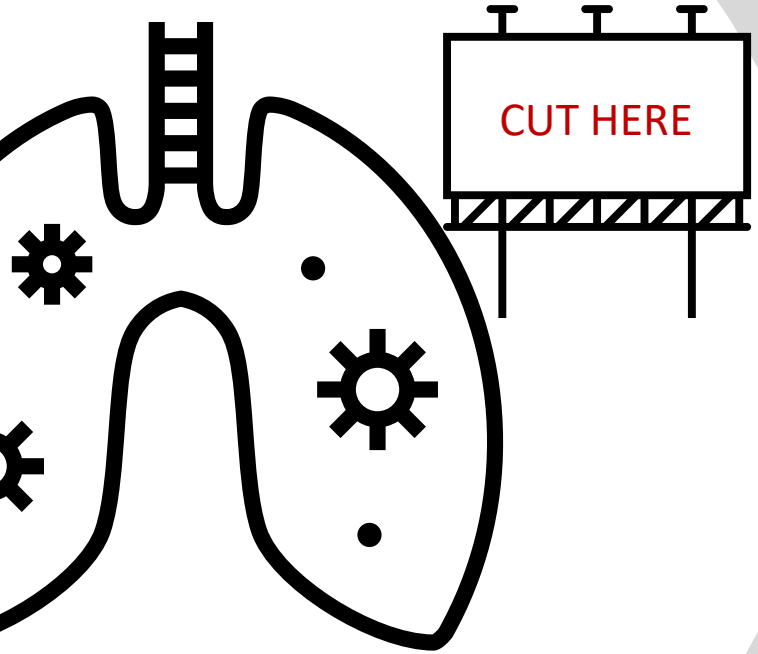


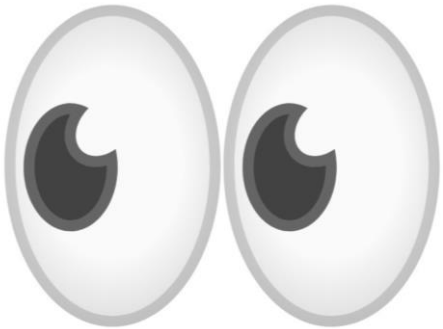


Nodule localization

Nodule localization

Gill RR. J Surg Oncol. 2020 Jun;121(8):1225-1232.

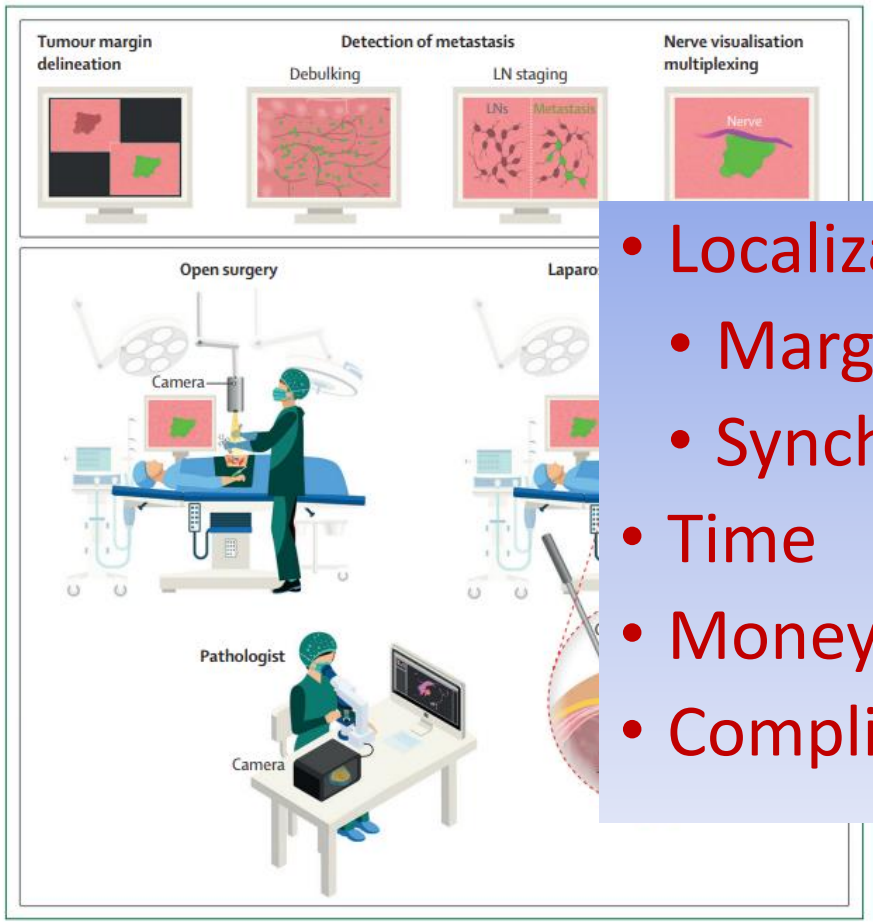




Nodule localization

Limitations

- Localization needed
  - Margins
  - Synchronous lesions
- Time
- Money
- Complications



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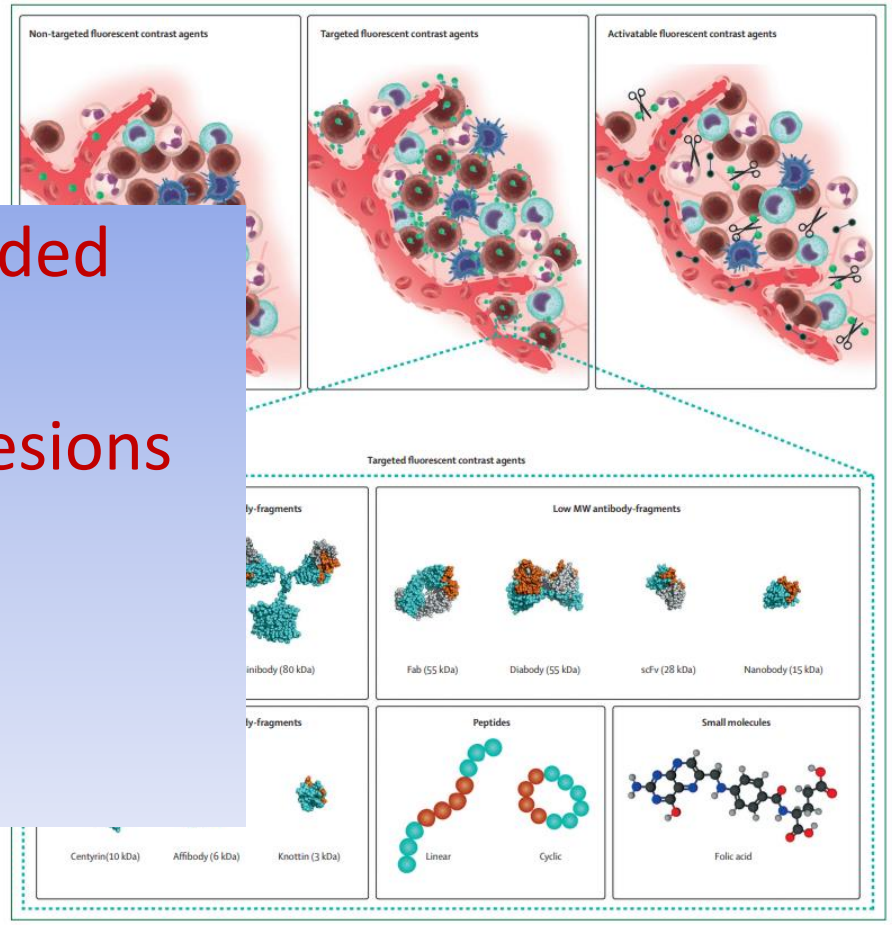

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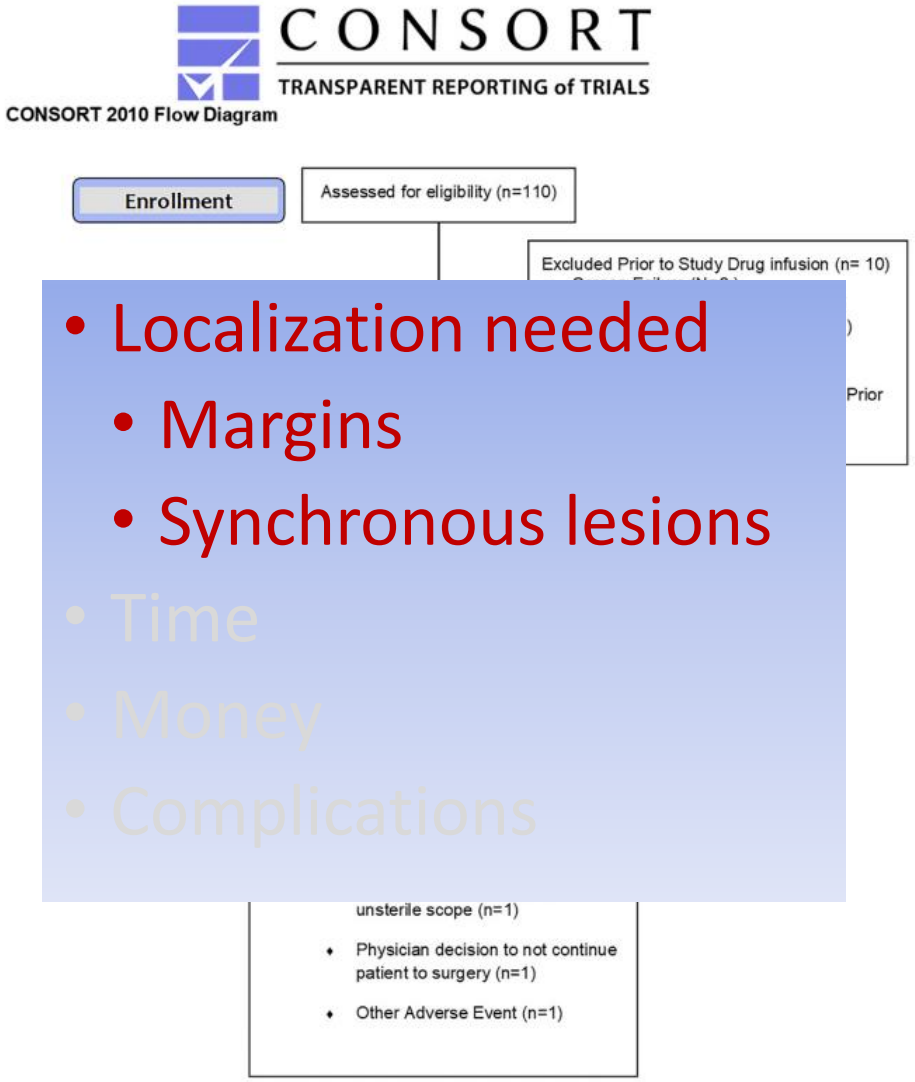

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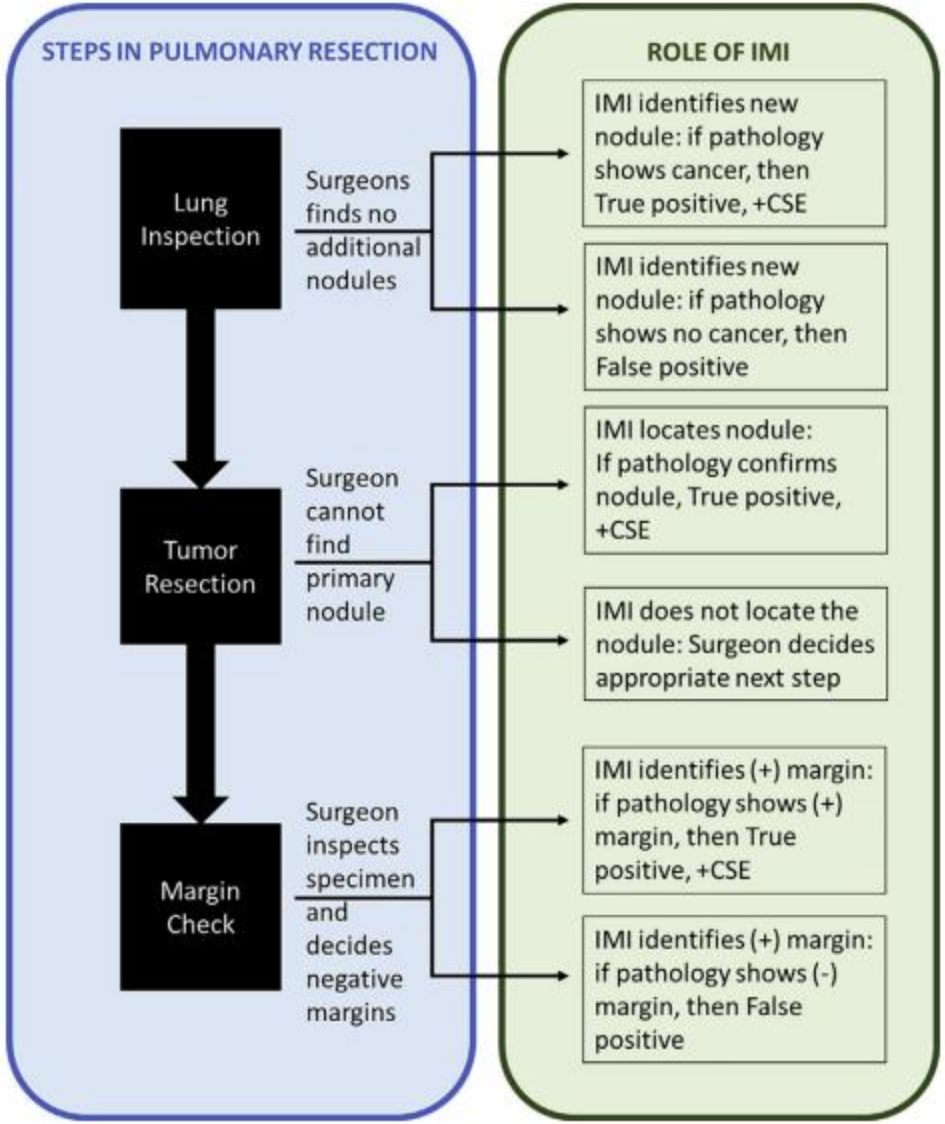
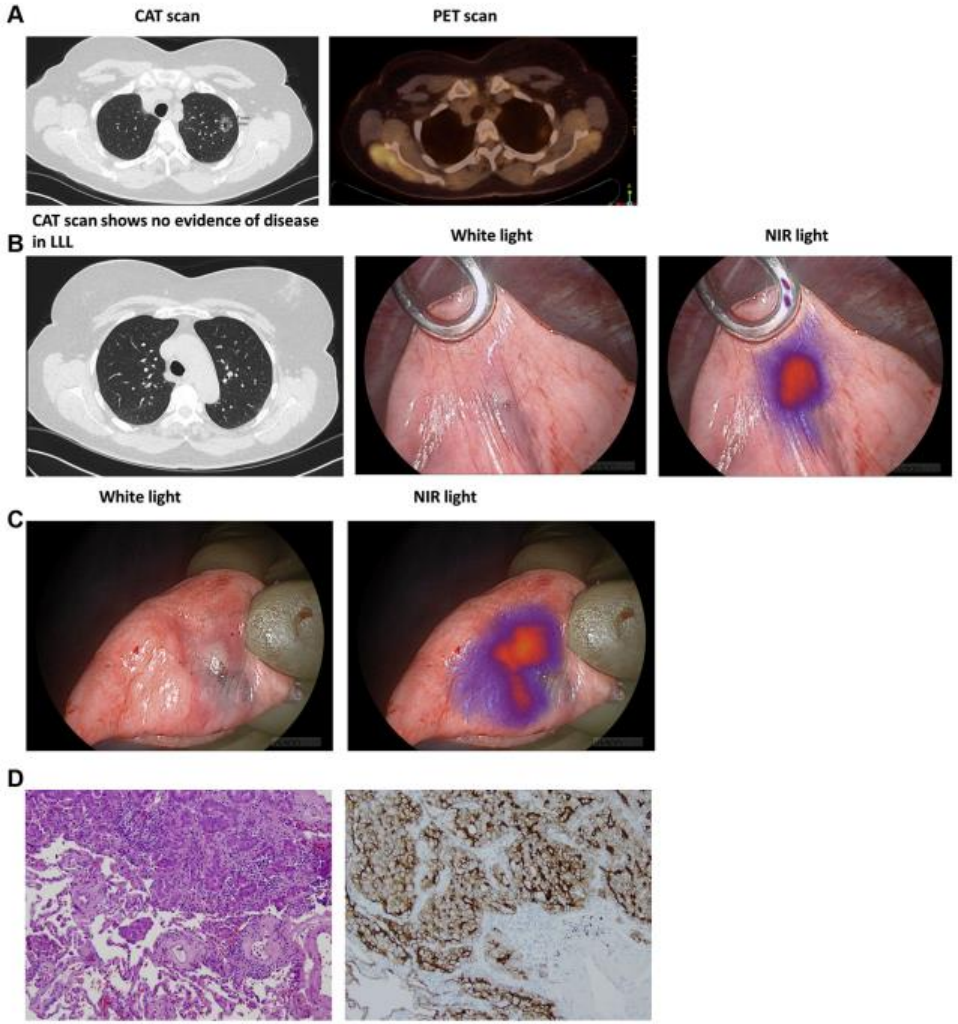


Gangadharan S. Ann Thorac Surg. 2021 Oct;112(4):1150-1159.

Table 2. Clinically Significant Events

Events	Data
Total number of patients analyzed	92 patients
Synchronous nodules	
Synchronous nodules identified only by IMI	24 nodules
Cancerous synchronous nodules identified only by IMI	9 nodules
Number of patients with synchronous nodules identified only IMI	7 patients
Number of patients with change in clinical stage because of IMI	7 patients
Additional cancers discovered by IMI	
Stage IA adenocarcinoma	6 patients
Adenoid cystic carcinoma	1 patient
Stage IV papillary thyroid cancer	1 patient
Total number of patients with clinically significant events	24 patients
Percent of patients with clinically significant events	26%

IMI, intraoperative molecular imaging.



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Tumor localization	
Localization of primary pulmonary nodule only by IMI	11 patients
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Margin identification	
Close margins (<5 mm) detected by IMI	16 patients
True positive margin	9 patients
Summary of clinically significant events	
Total number of clinically significant events	28 events
Number of patients with change in clinical stage because of IMI	7 patients
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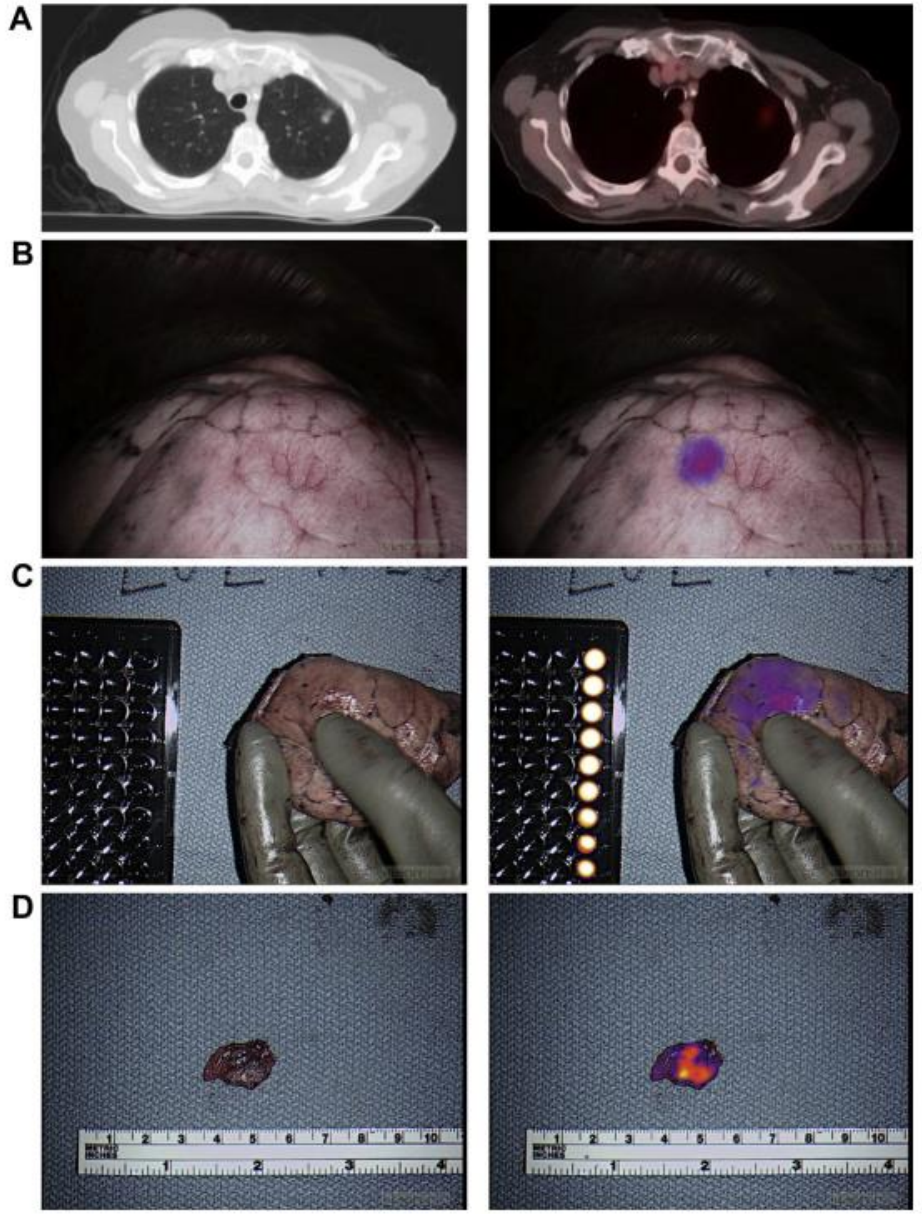

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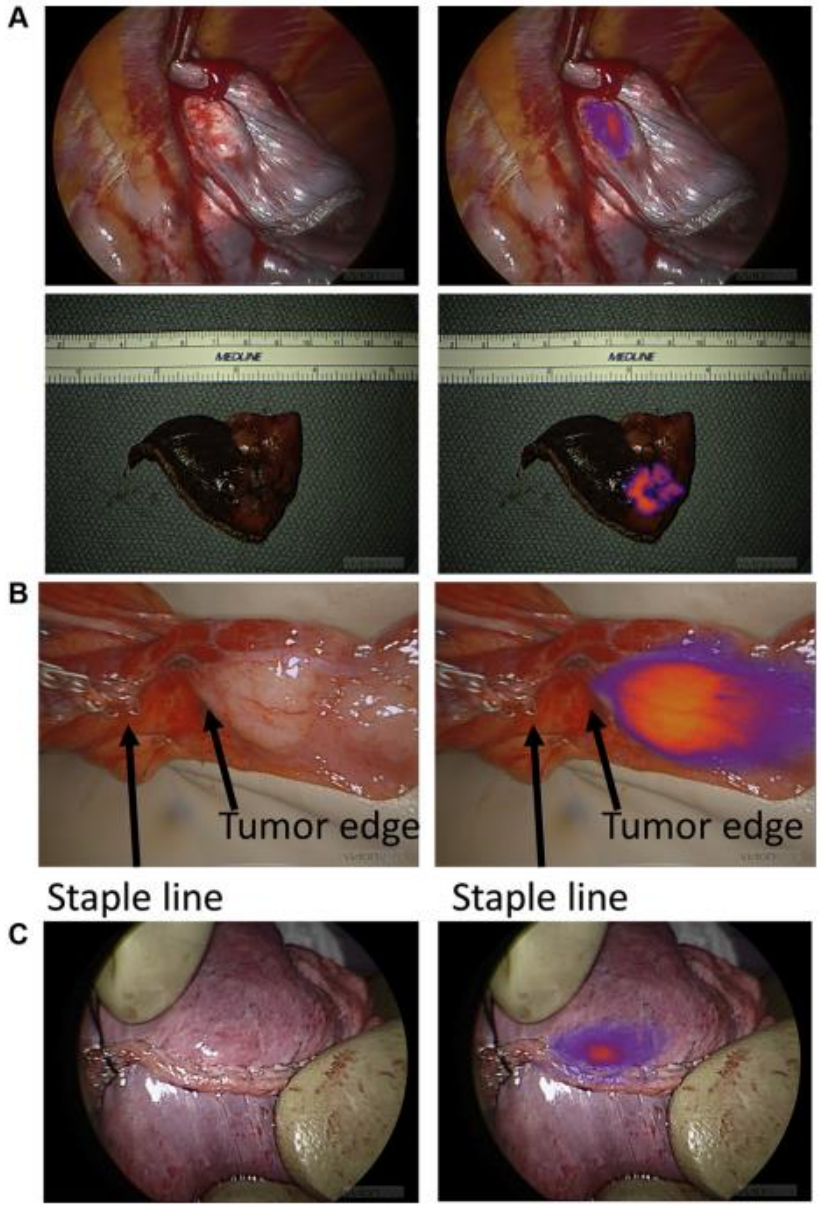

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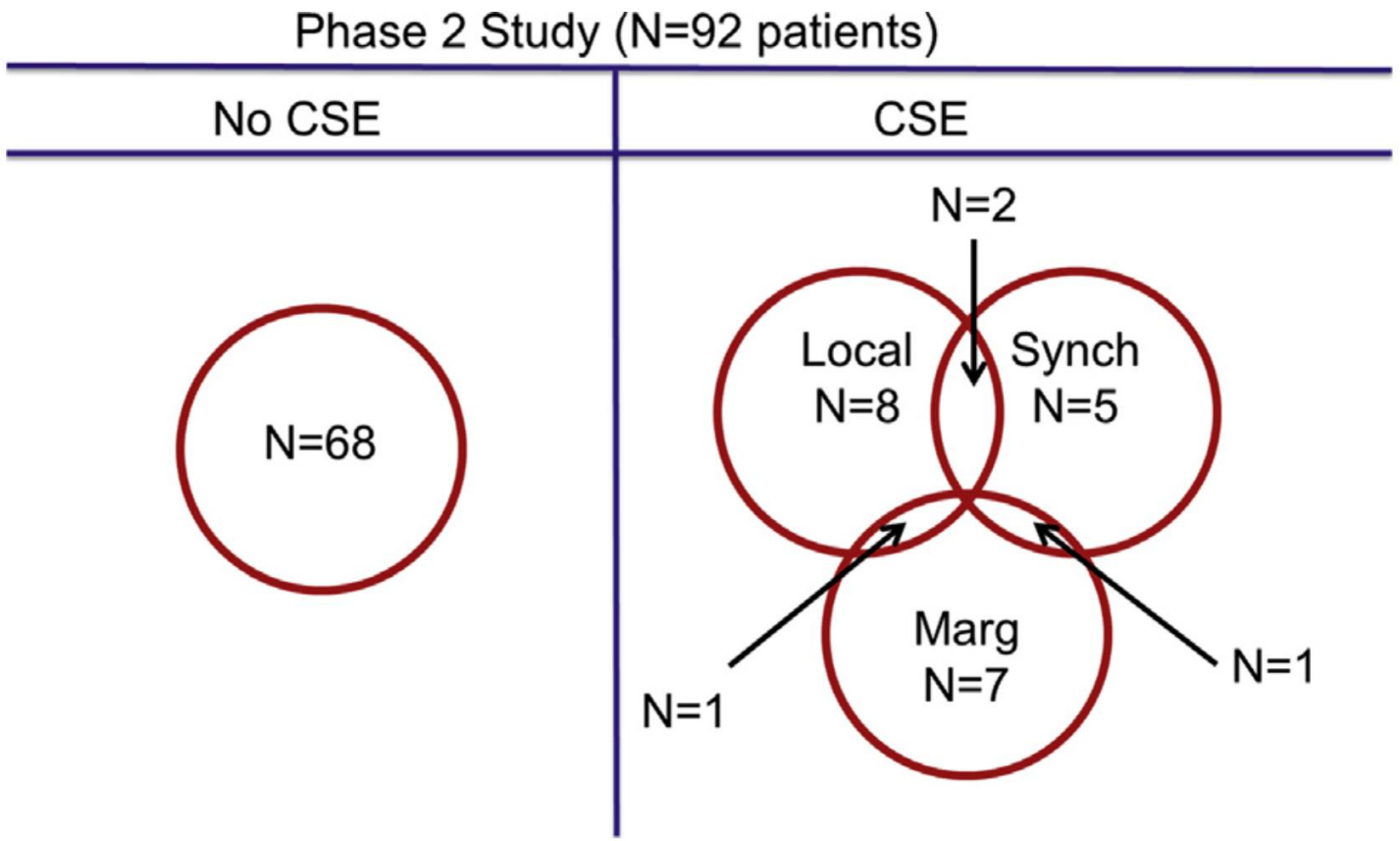

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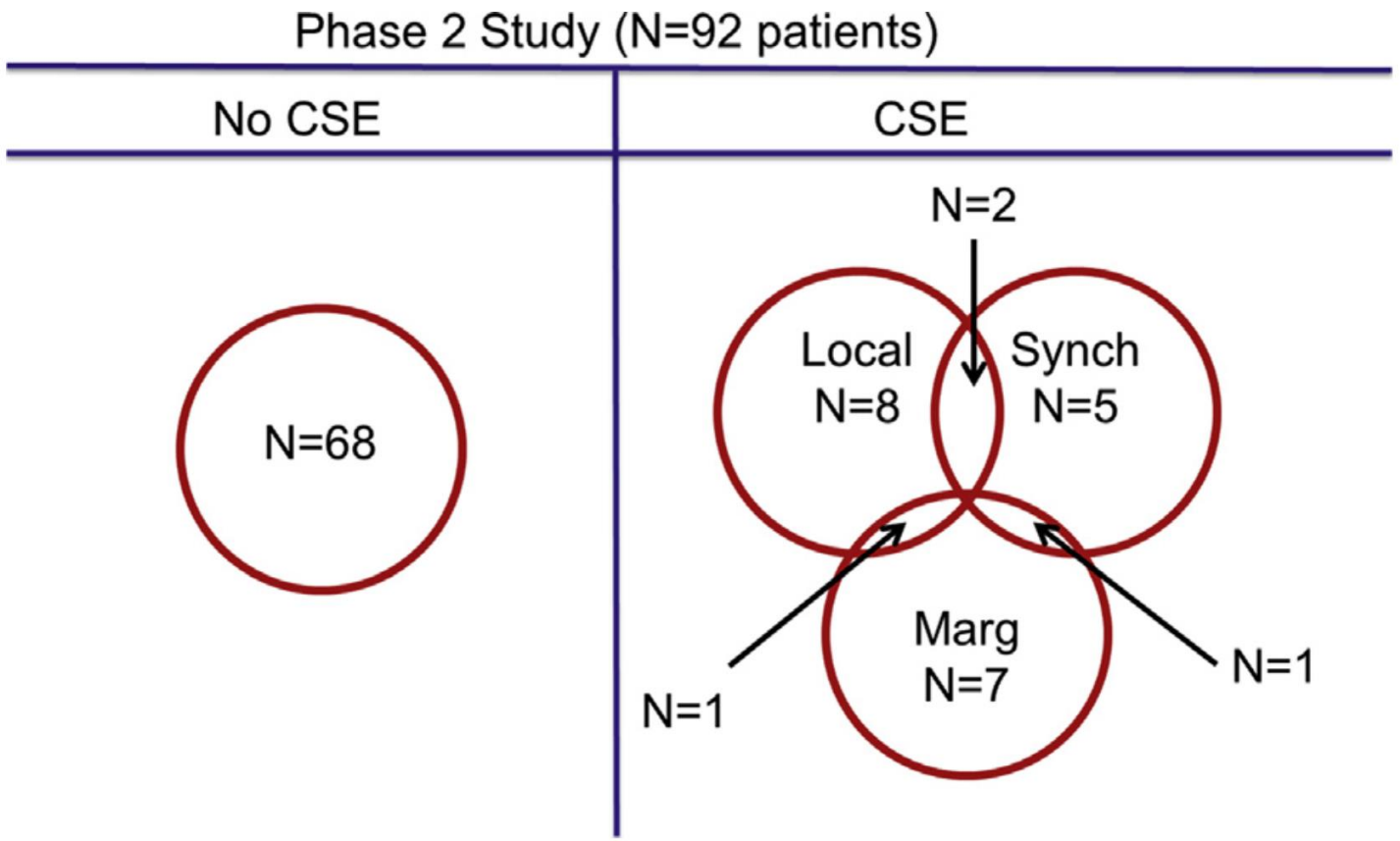

- 13 of 92 not able to be found
- 1.54 cm vs 2.27 cm
- 6 of 11 found only by IMI were GGO
- Avg 6 mm from visceral pleura surface

- Why was SOC only able to localize 85%?
- What is the applicable depth and size?
- Was localization really needed (i.e. was surgery really needed)?

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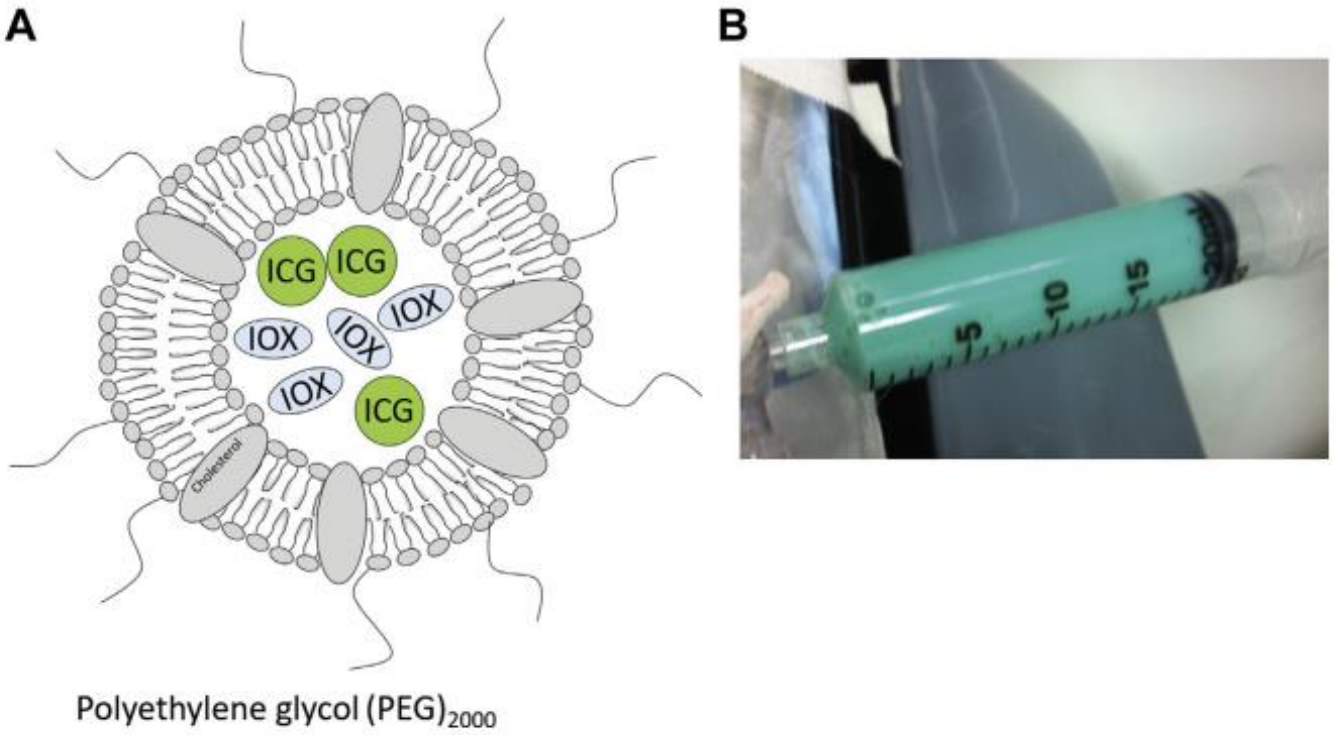
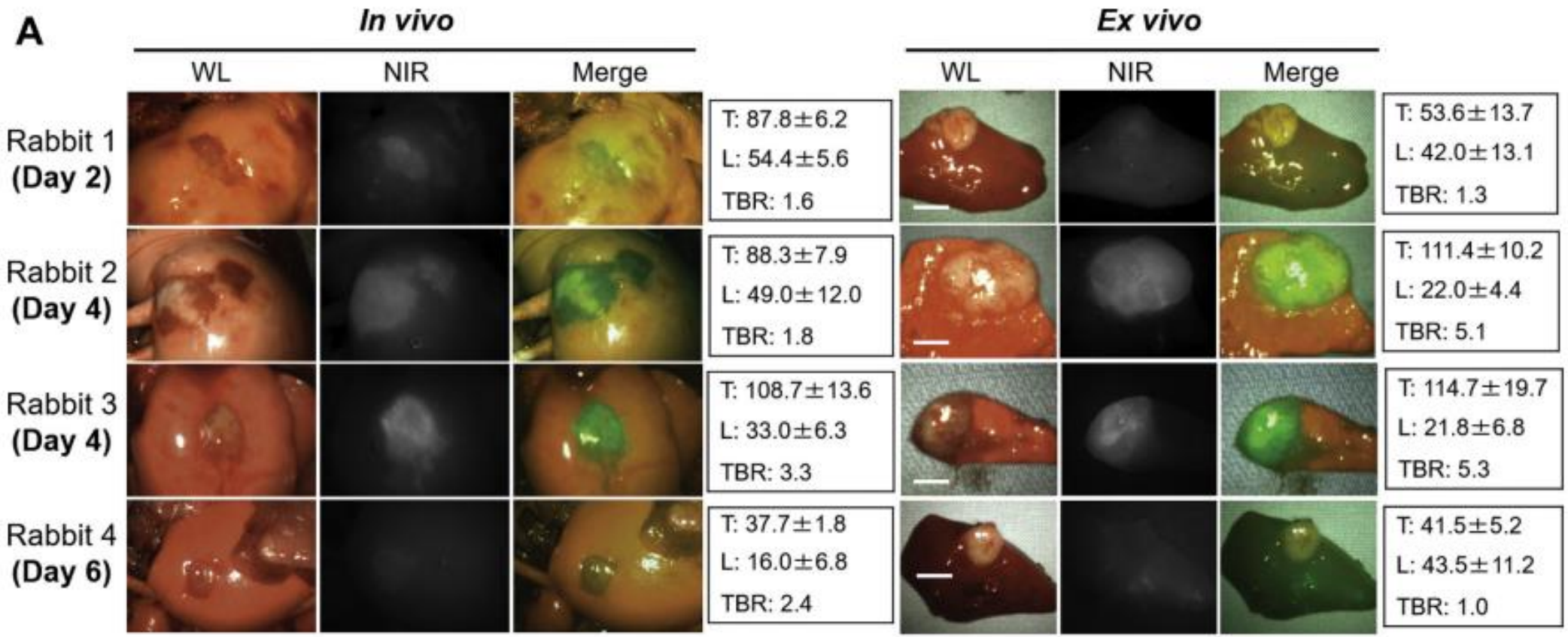


Wada H. Ann Thorac Surg. 2019 Jan;107(1):248-256.



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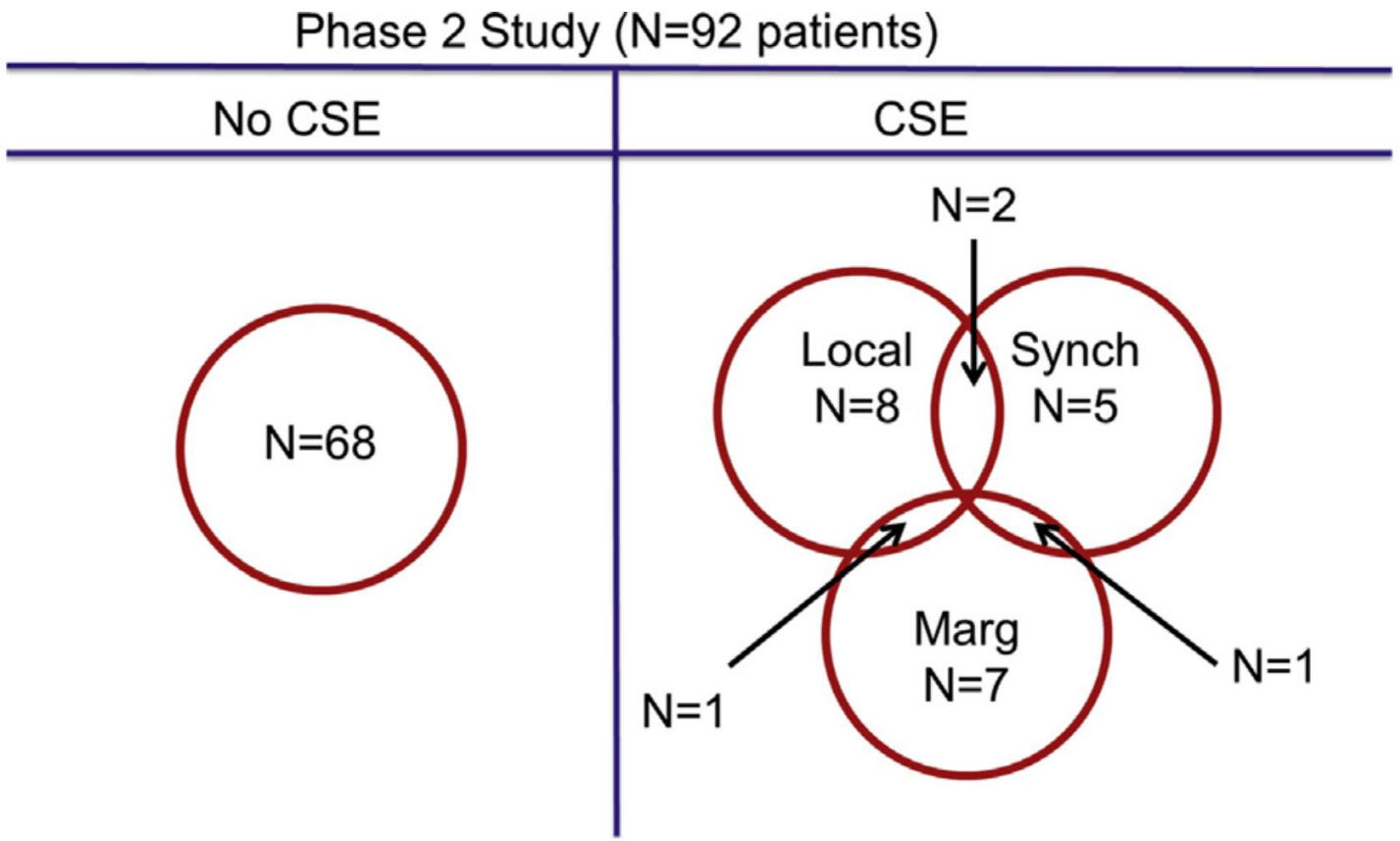

- 16 had fluorescence < 5 mm from staple line
- 9 were positive pathologically

- What was the gross evaluation and would that have led to additional resection?
- Is a PPV of 56% adequate?

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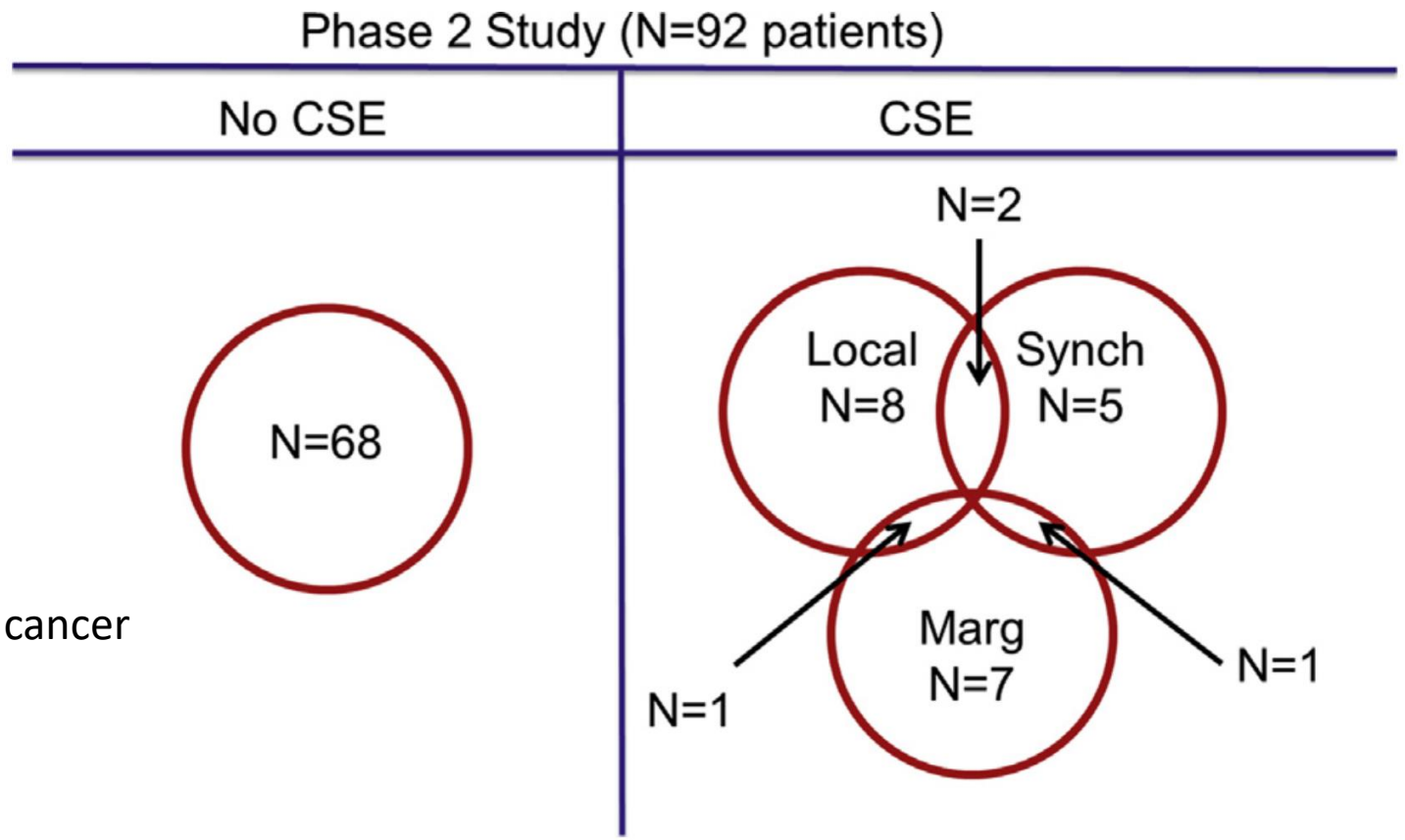

- 9 of 24 additional nodules found by IMI were cancer

- Is PPV of 38% adequate?
- In retrospect were these occult to CT imaging?
- What would the NPV be?

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- Margins
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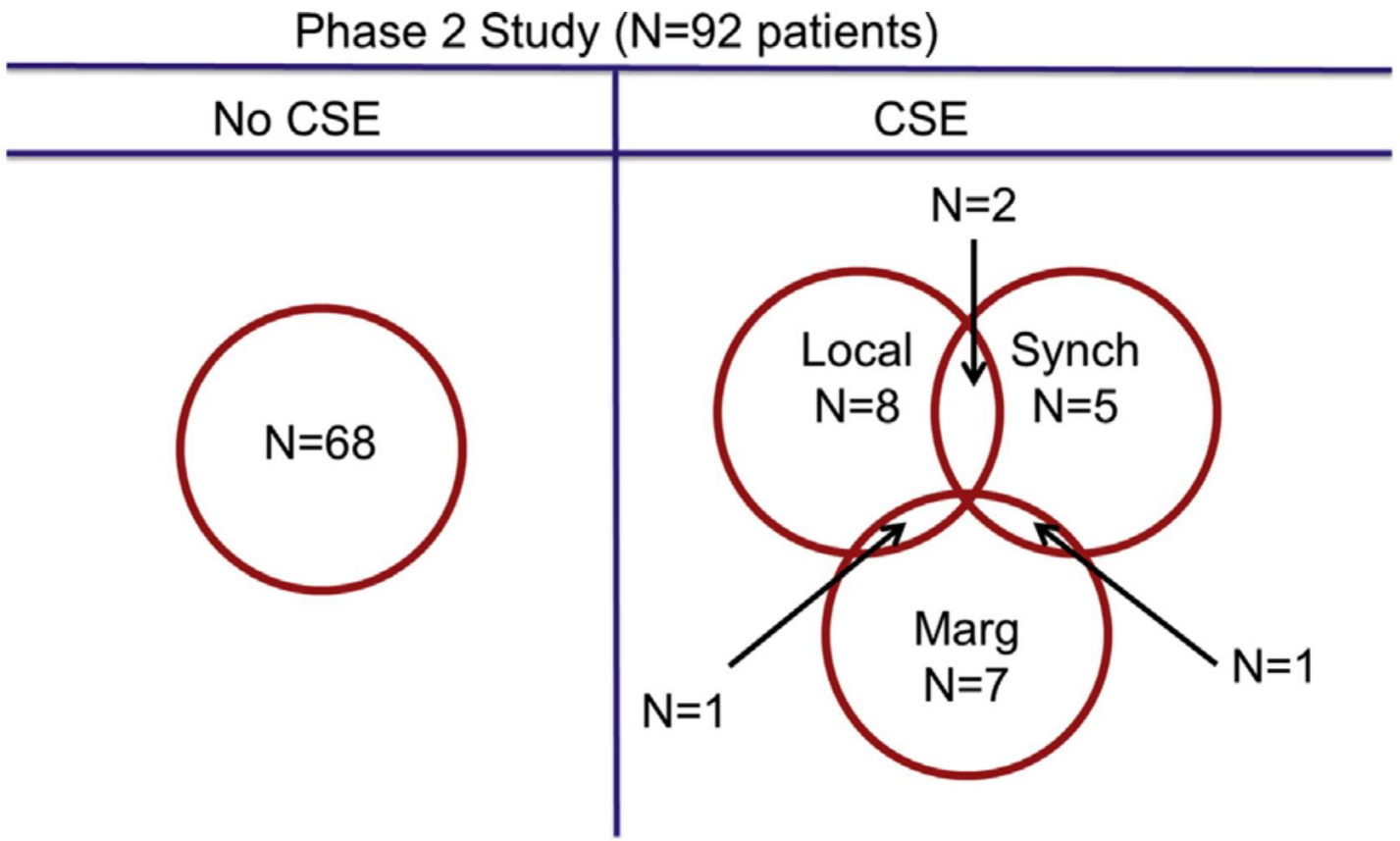

- What is the cost of administration in preop holding (day of) or infusion unit (day before)?
- Will patients make a separate trip or come in early?

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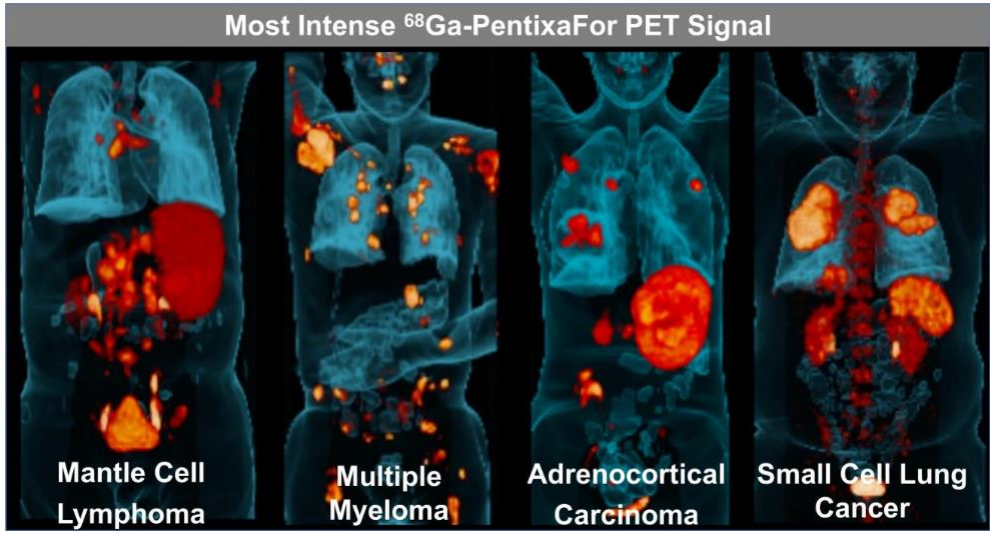
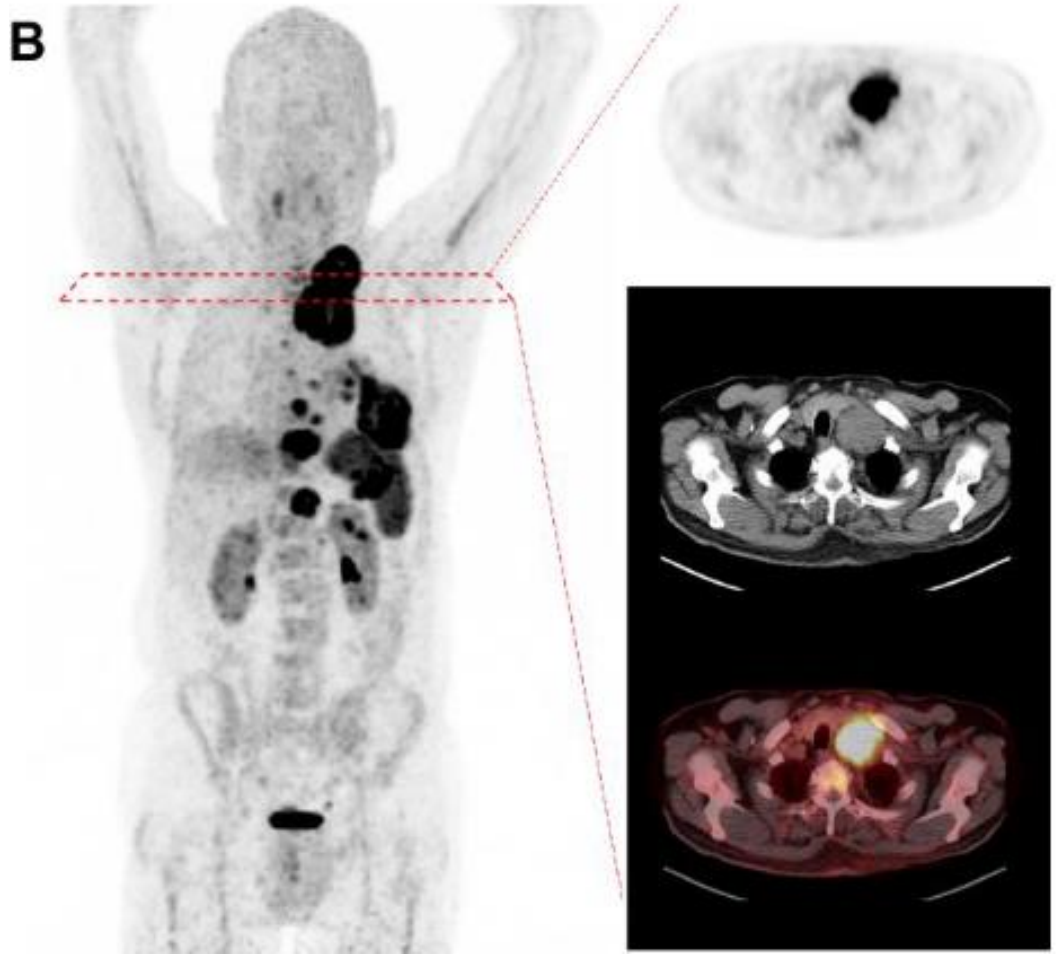
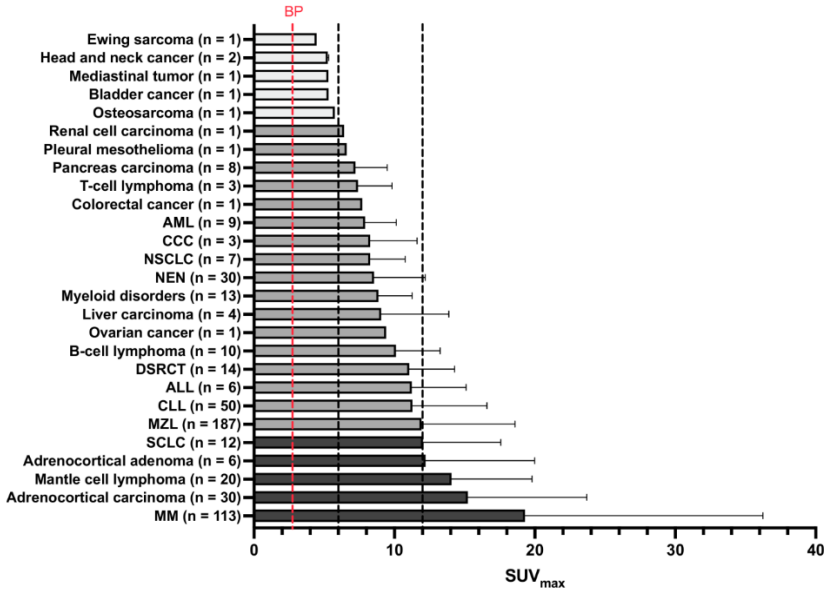


Notice lack of background noise in brain, liver, heart





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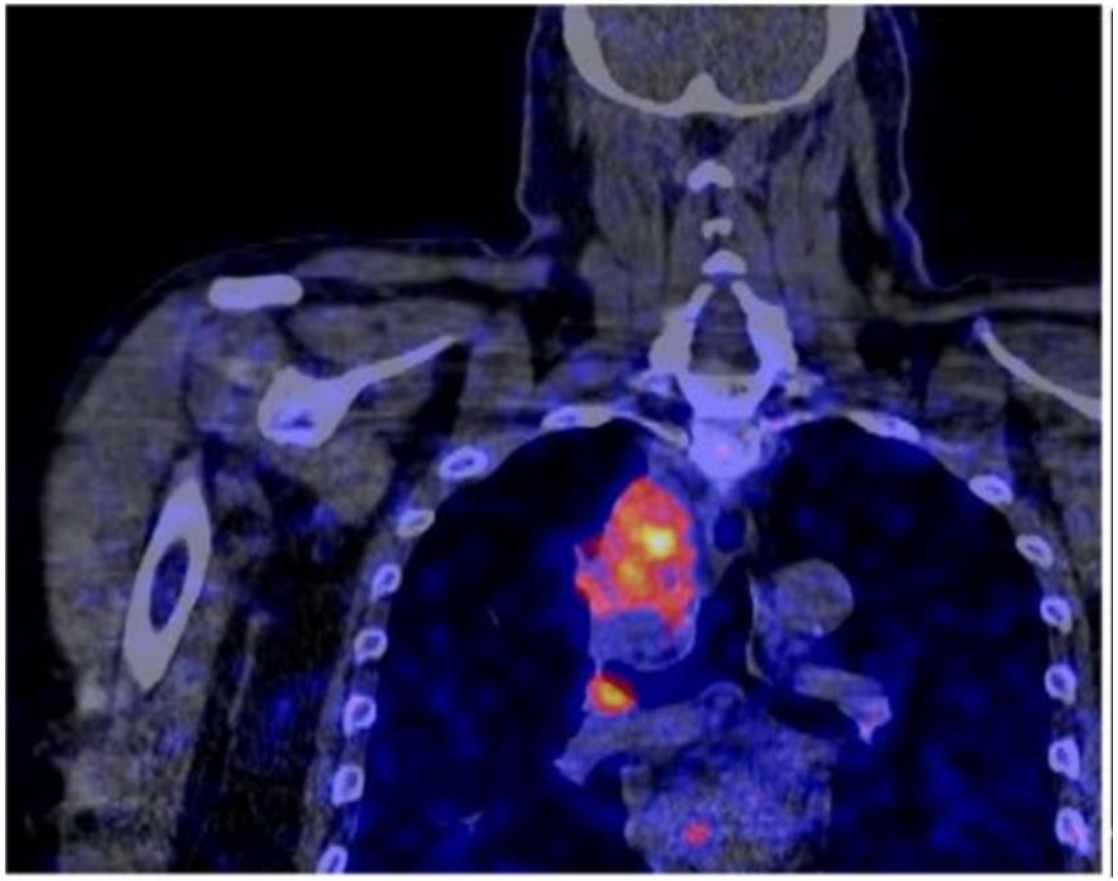
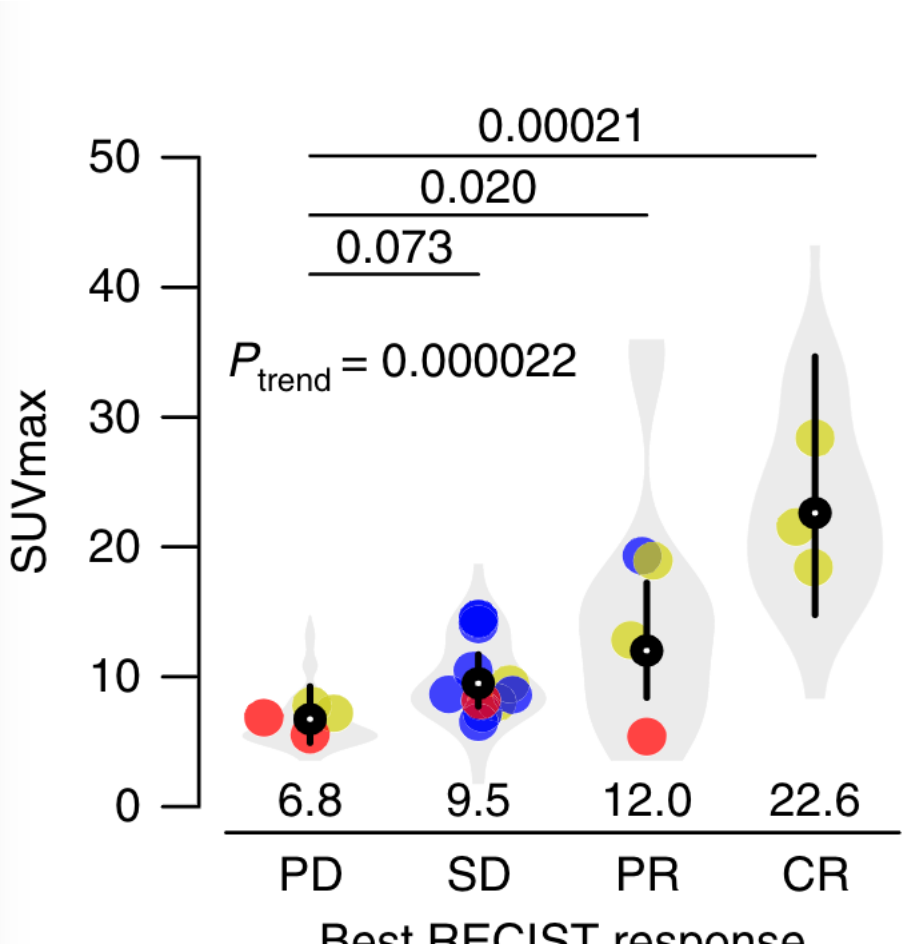
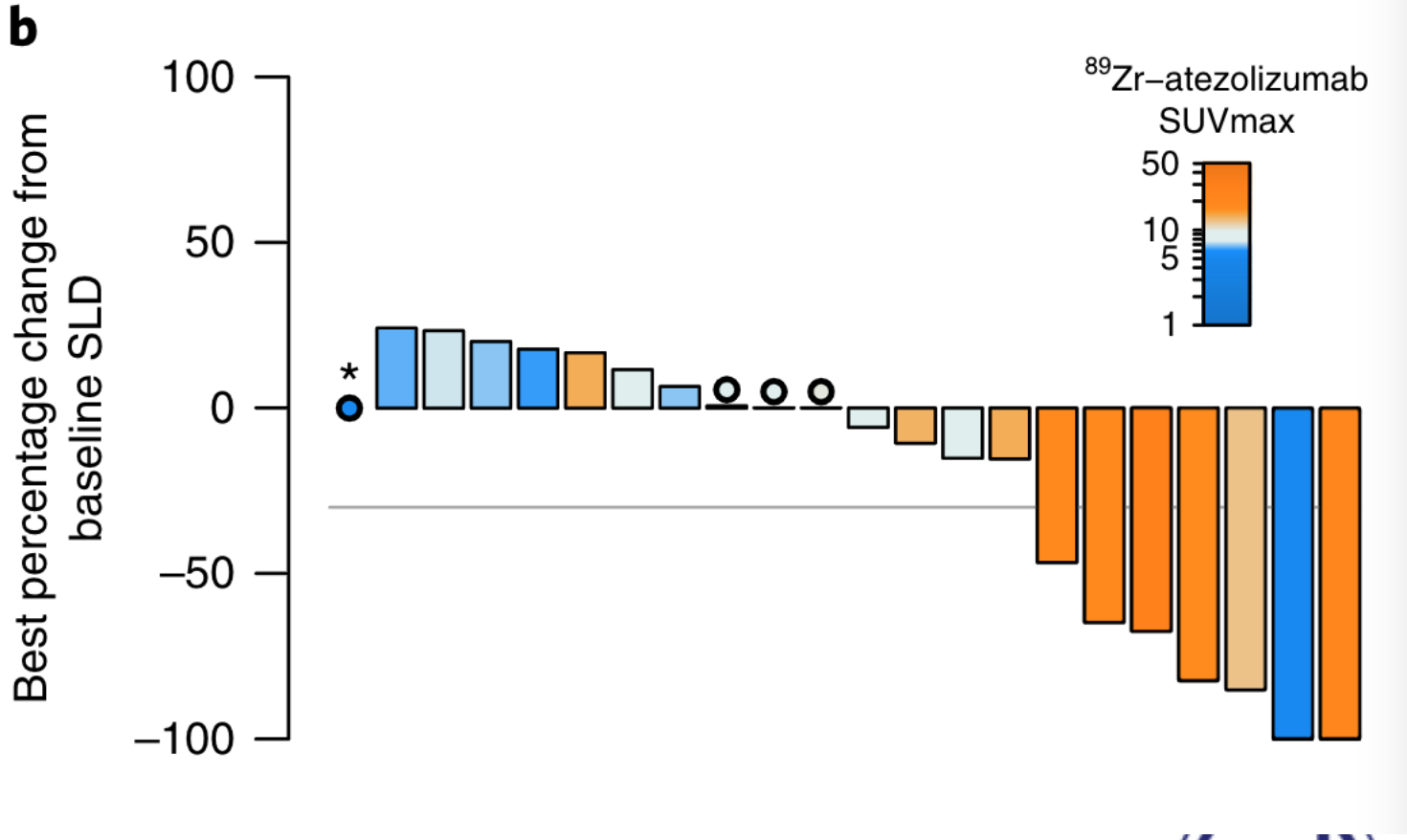


Bensch F. Nat. Med. 2018, 24 (12), 1852−1858.





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RGB

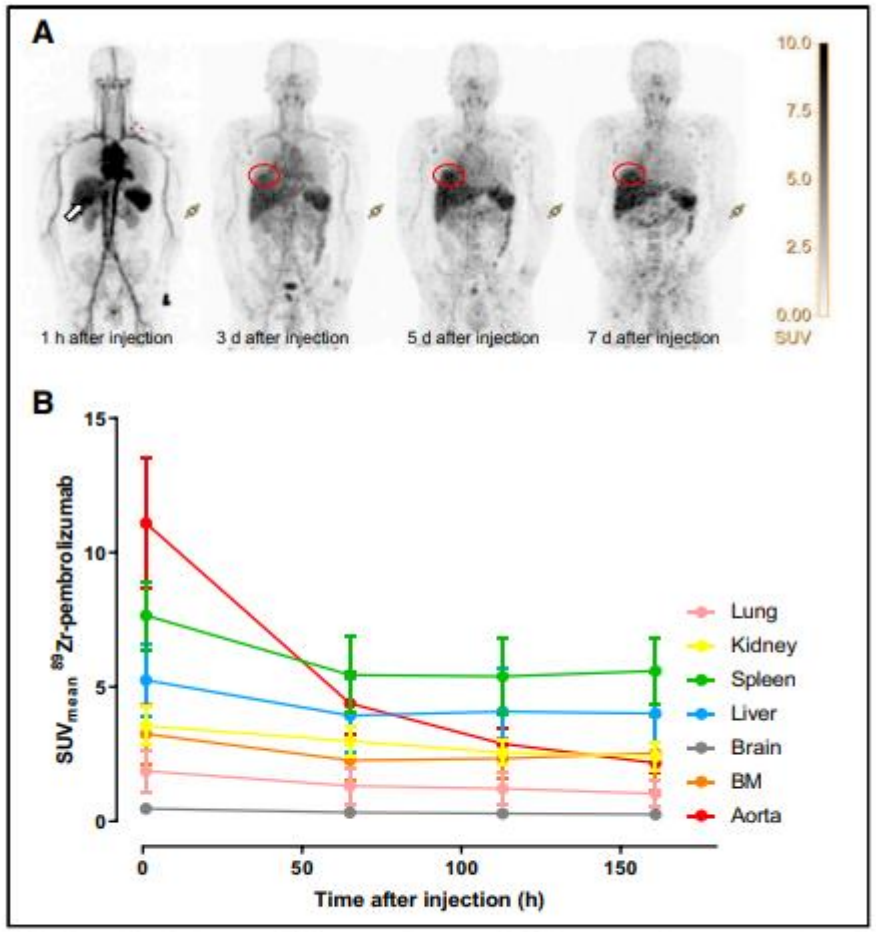


FIGURE 1. Biodistribution of ^{89}Zr-pembrolizumab. (A) Maximum-intensity-projection image of patient 1. White arrow indicates gallbladder. Red circle indicates primary tumor. (B) Tracer uptake per time point, measured as mean SUV_{mean} for first 3 patients at 1.1 ± 0.3, 65.8 ± 0.3, 113.2 ± 0.7, and 161.4 ± 0.81 h after injection. BM = bone marrow.

RGB

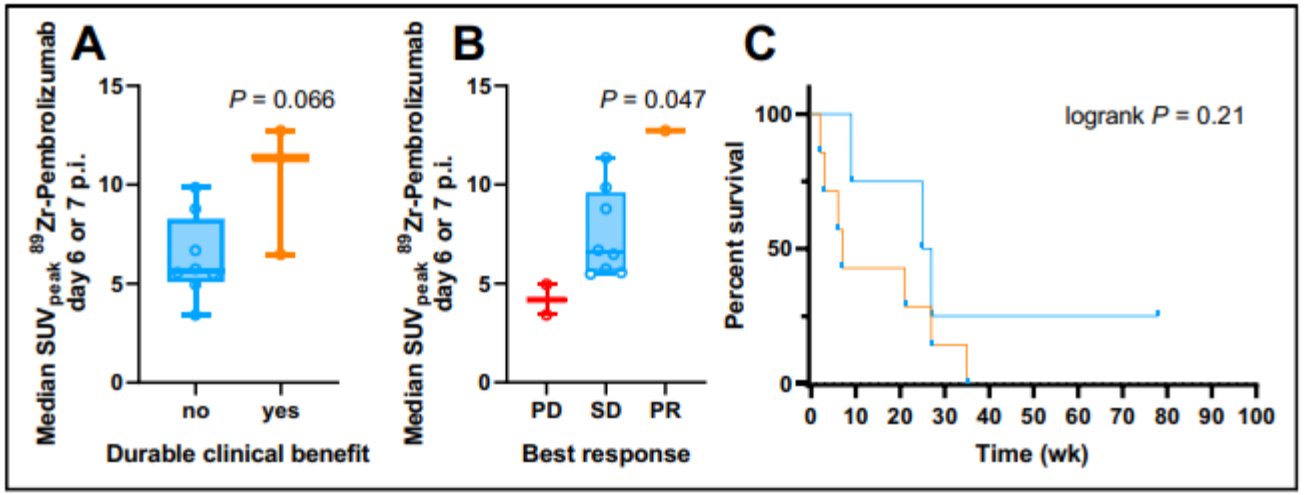


FIGURE 5. Relationship between tracer uptake and response. (A) Median tracer uptake of all lesions > 20 mm for responders and nonresponders. (B) Median tracer uptake per best RECIST response category. (C) Progression-free survival curve according to median SUV_{peak} (blue, above median SUV_{peak} of 6.7; orange, below median SUV_{peak}). p.i. = postinjection.

Niemeijer AN. J. Nucl. Med. (2021) 121

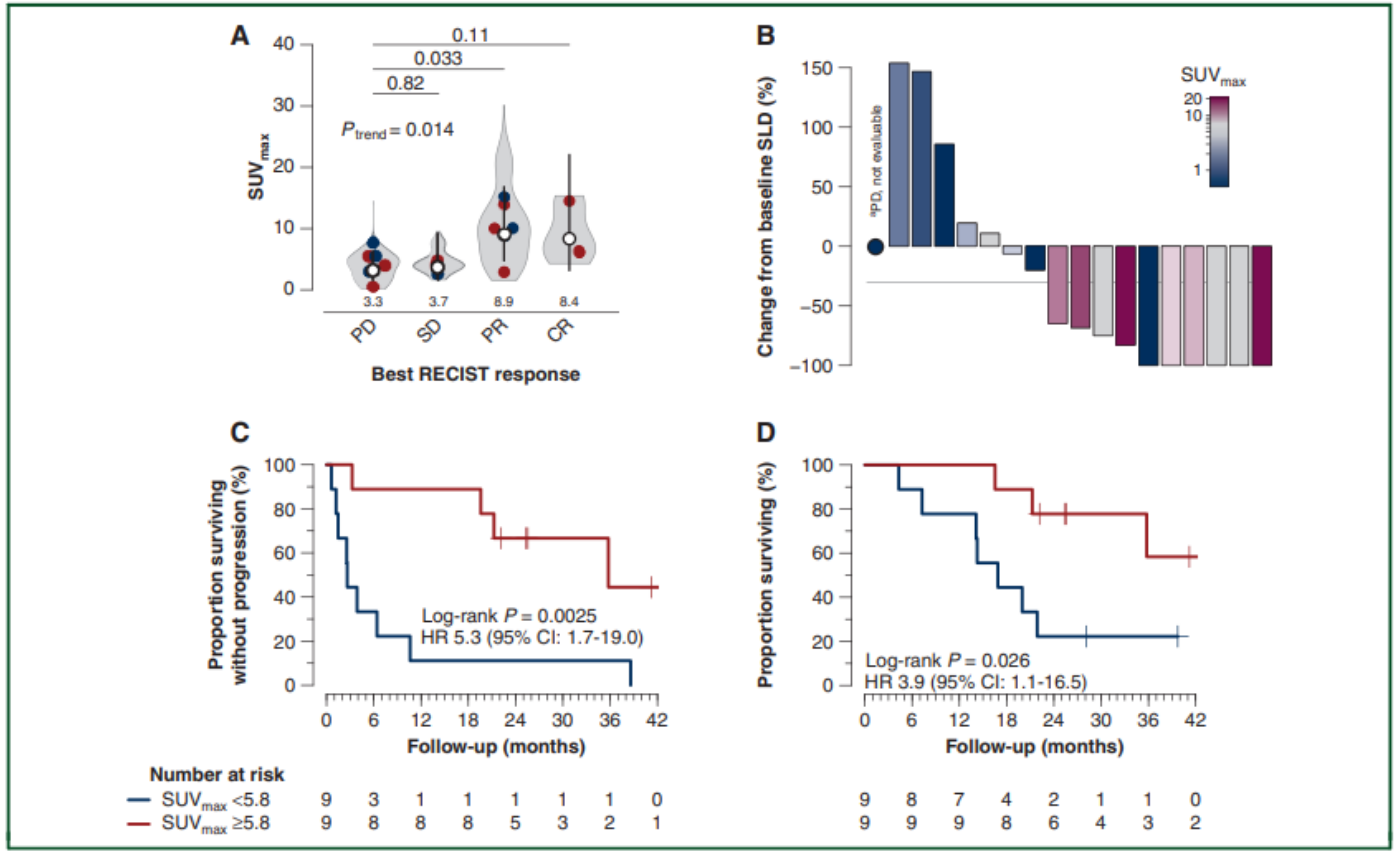
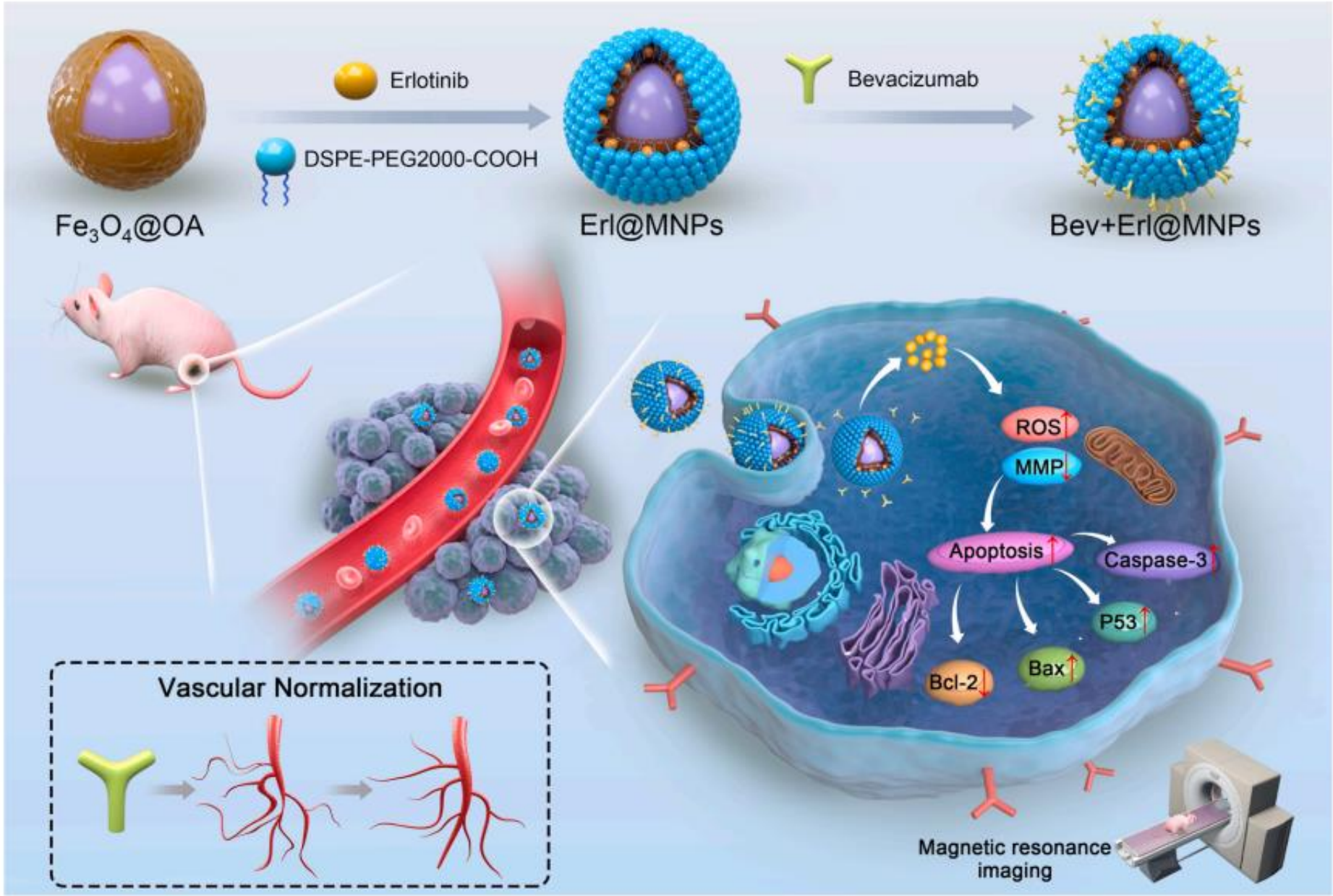


Figure 4. **^{89}Zr-pembrolizumab tumor uptake and clinical outcome measures.**
(A) ^{89}Zr-pembrolizumab tumor uptake as geometric mean maximum standardized uptake value (SUV_{max}) on day 7 and best tumor response ($n = 18$ patients). Gray violin plot areas show the distribution of SUV_{max} at the tumor level per best response category, with bottom and top 1% values truncated [1st, 50th, and 99th SUV_{max} percentile: 0.1, 4.4, 14.5 for progressive disease (PD); 1.6, 4.2, 9.5 for stable disease (SD); 1.6, 9.9, 30.2 for partial response (PR); 4.2, 7.9, 15.4 for complete response (CR)]; points show geometric mean uptake per patient, with colors indicating tumor type [red, melanoma; dark blue, non-small-cell lung cancer (NSCLC)]; black vertical lines are 95% confidence intervals (CIs) of geometric mean SUV_{max}, and white dots within black lines and values below the violin plot are the actual geometric means; with two-sided Wald *P* values, supplemented with a two-sided likelihood ratio *P* for trend; PD = 27 lesions in six patients, SD = 29 in three patients, PR = 41 in six patients, CR = 6 in three patients. (B) Waterfall plots depicting percentage change in sum of longest diameters of the target lesions (SLD) from baseline [measured on computed tomography (CT)], with color scale indicating geometric mean SUV_{max} of the tumor lesions per patient; [a]indicates patient with PD, however no SLD change data are available. (C) Progression-free survival according to geometric mean tumor SUV_{max} per patient (red depicts the group above and dark blue the group below the median geometric mean uptake of an SUV_{max} of 5.8). (D) Overall survival of the patients binned and represented as in panel C (red depicts the group above and dark blue the group below the median geometric mean uptake of an SUV_{max} of 5.8).

Kok IC. Ann Oncol. 2022 Jan;33(1):80-88



Wang D. Bioact Mater. 2021 Nov 4;13:312-323

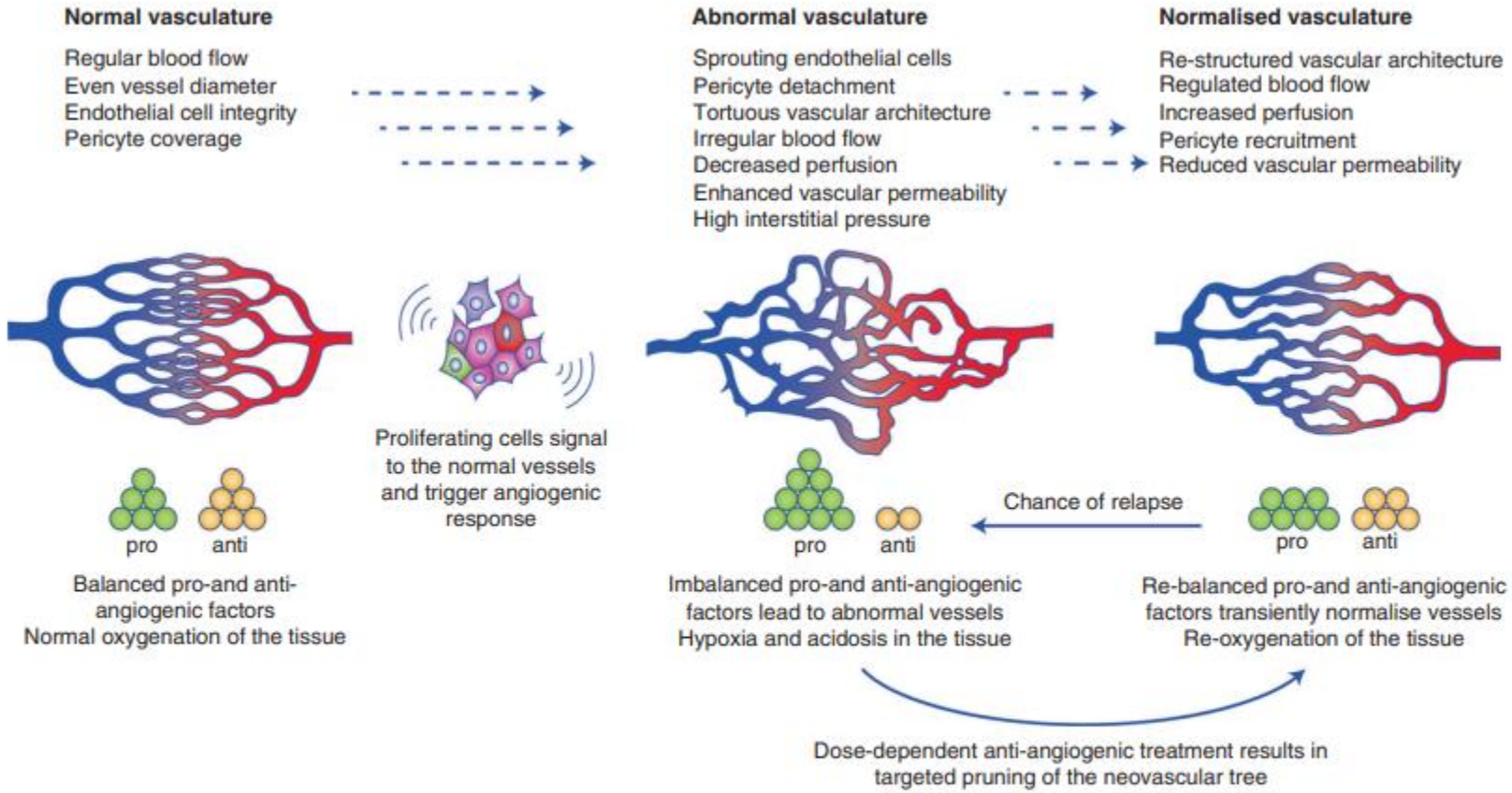
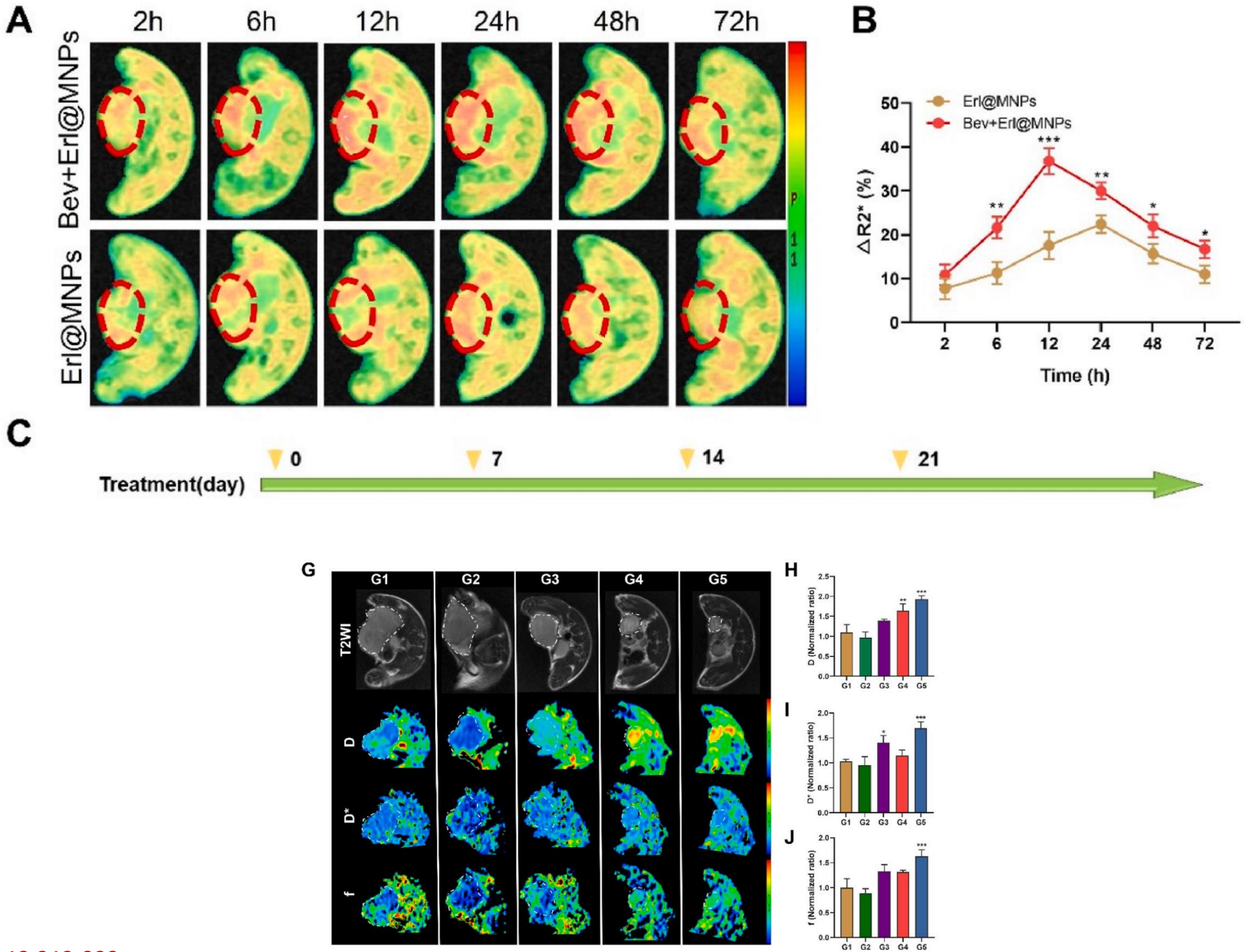


Fig. 2 Schematic illustration of the vascular network in its normal, abnormal and normalised state. Angiogenic and anti-angiogenic factors are finely tuned in healthy tissues to create an organised vessel structure and to maintain vascular function. In tumours, the angiogenic switch has taken place and the balance has tipped in favour of angiogenic factors. As a result, the structure of neovessels is abnormal on all levels, with highly impaired vascular function. In the normalised state, angiogenic and anti-angiogenic factors are nearly balanced and vascular function is transiently re-established.

Magnussen AL. Br J Cancer 125, 324–336 (2021).



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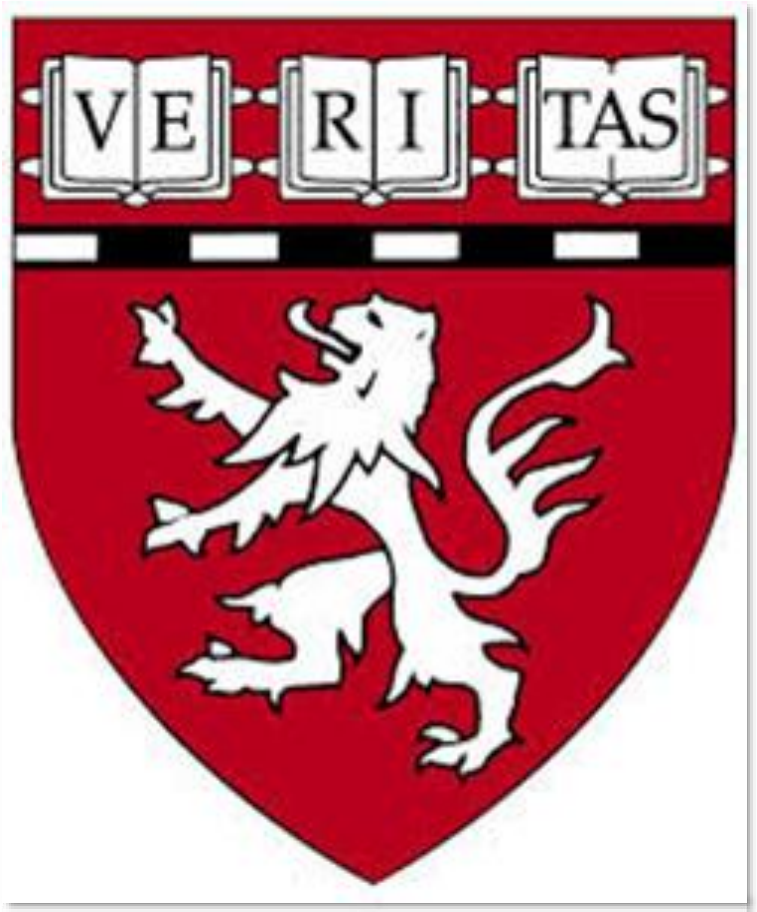
Summary

- Molecular imaging for lung cancer surgery still has technical challenges, but these should be solvable
- The theranostic implications of molecular imaging for lung cancer are still evolving
  - Link to precision medical therapy
  - Appropriate therapeutic window for surgery



THANK YOU

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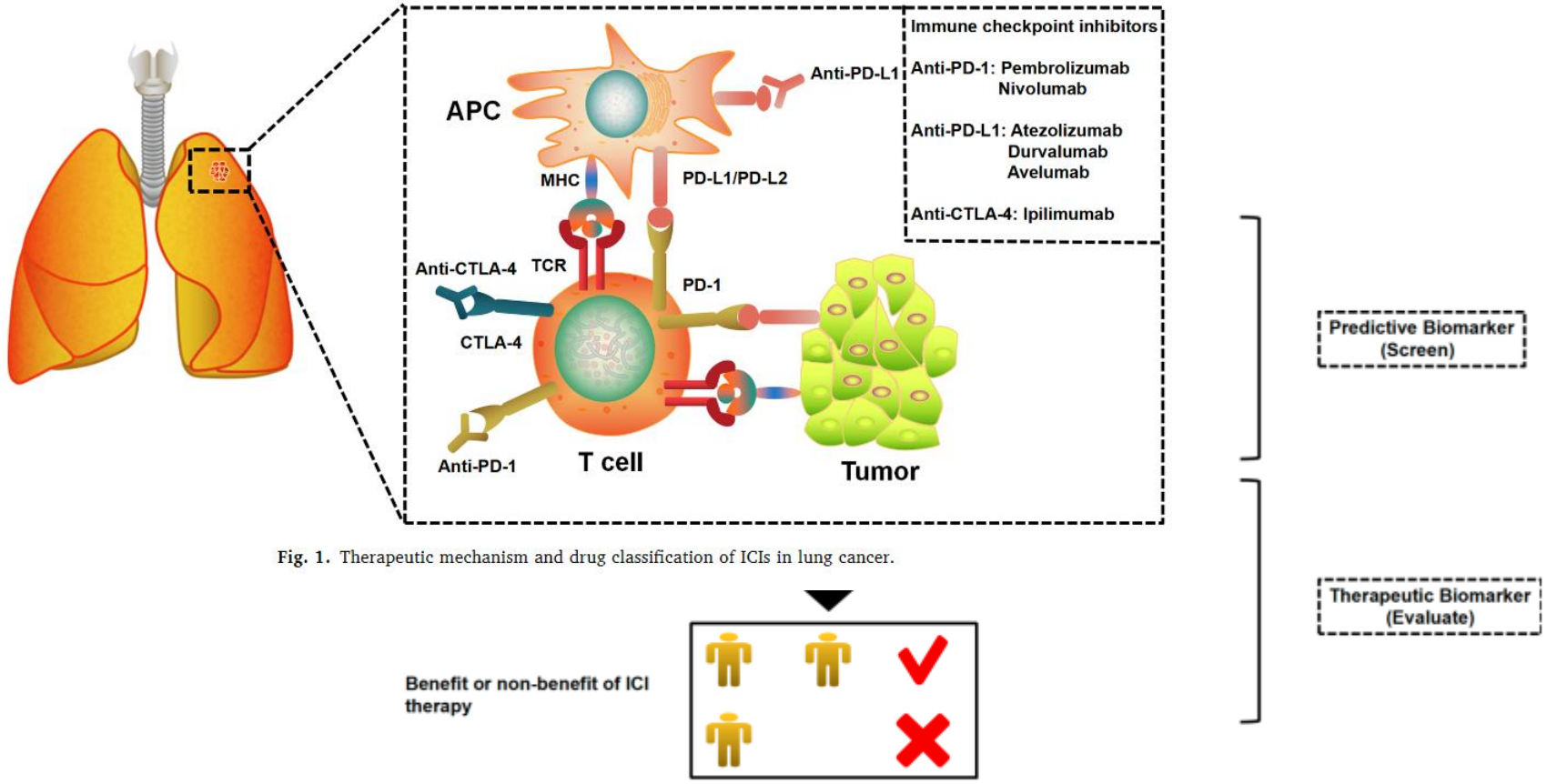

Fig. 1. Therapeutic mechanism and drug classification of ICIs in lung cancer.

Fig. 5. The role of PET molecular imaging in lung cancer patients receiving ICI therapy.

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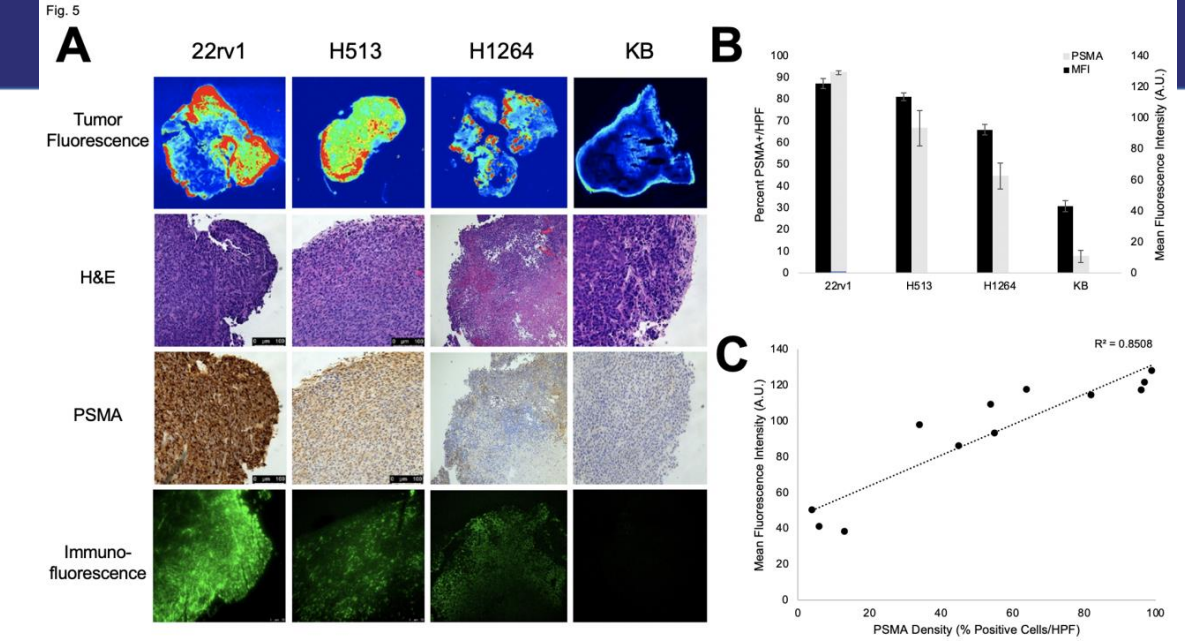
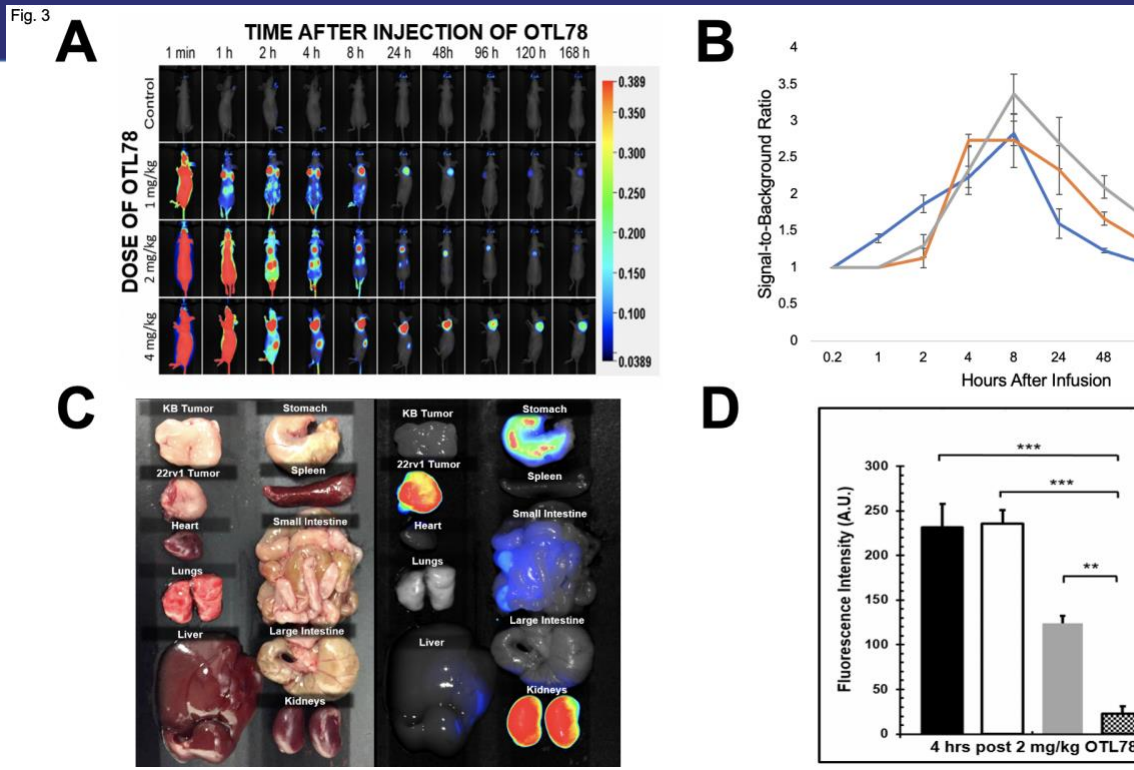
The role of PET molecular imaging in immune checkpoint inhibitor therapy in lung cancer: Precision medicine and visual monitoring
Yuan Yao 1, Xin Zhou 1, Annan Zhang 1, Xiaopan Ma 1, Hua Zhu 1, Zhi Yang 1, Nan Li 2





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A Prostate Specific Membrane An
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During Resection
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Bilal Nadeem 1, Ashley E Chang 1,
Isvita Marfatia 1, Azra Din 1, Char
Kucharczuk 3, Philip S Low 4, Suni