MANAGEMENT OF OLIGOMETASTATIC DISEASE IN THE LIVER BY IR: NOVEL ADVANCES

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Oligometastatic Disease

- Traditionally defined as less than 3 lesions or 5 lesions in the liver.
- More recent data suggests that surgical or percutaneous treatment of up to 10 lesions shows survival benefit.
- Distribution of lesions is not a limiting factor (i.e. bilobar disease)
- Underlying functioning liver volume and patient functional status important
- ESMO Clinical Practice Guideline for mCRC defines "oligometastatic" as patients for whom complete eradication through resection and/or ablation is feasible.

Ann Oncol. 2023; **34**:10-32

Why Surgical/Ablative Therapy?

- In patients with metastatic colorectal cancer cure rates of up 20% and 10-year survival rates of 24% or more can obtained with definitive resection and/or ablation.
  - *Surgery*. 2018; **163**:1238-1244
- Predictors of poor response to surgery/ablation
  - Extrahepatic disease
  - Carcinoembryonic antigen >200 ng/mL
  - Positive margin
  - **>10 tumors**
- **Aggressive removal/treatment of all sites of disease provides a real chance of cure with significant improvement in long term survival in select patients.**

Interventional Radiology

- Image guided procedures
  - CT and/or US typically
- Less morbid than open surgery
  - Supported in numerous trials.
- Can be performed outpatient or office-based.
- Significant learning curve. Registry data from a single site showed 2 – year Long Term Progression Free Survival in Ablation Patients with Curative Intent increased from 37.7% to 86.3% over a ten-year period with the same operators.
  - *Cardiovasc Intervent Radiol.* 2022; **45**:1074-1089

IR Treatment Modalities

- Percutaneous Ablation
  - Thermal vs Electrical
- Radiation Segmentectomy (Y90)
- Histotripsy

Percutaneous Ablation

- Thermal
  - Cryoablation – less painful but susceptible to “heat sink”
  - Radiofrequency Ablation – Susceptible to ”heat sink”. Most widely studied
  - Microwave Ablation – Largely replaced RFA due to better energy generation, less “heat sink” and ease of use

- Electrical
  - Irreversible Electroporation (IRE)
    - Requires General Anesthesia
    - More difficult to perform due to requirement for probe precision
    - Less widely studied.
    - Safe for adjacent neurovascular structures
    - Likely to see expanded utilization now that a CPT code will become widely available.

PERCUTANEOUS ABLATION

Safety and Efficacy

Morbidity META analysis comparing complications between RFA and resection

Variables (no. evaluated studies[refs])	Total no. events/patients RFA (%)	Total no. events/patients resection (%)	Odds Ratio RFA vs resection (95% CI)	P-value	I^2
Total complications (n = 14[24,25,27,28,30–32,34,36–39,41,42])	119/956 (12)	317/1249 (25)	0.44 (0.26–0.75)	0.002	65%
30-day mortality (n = 7[24,26,28,31,34,36,38])	2/524 (0.4)	8/636 (1)	0.56 (0.18–1.75)	0.32	0%
Pulmonary complications (n = 7[24,25,27,32,37–39])	12/669 (2)	26/684 (4)	0.59 (0.17–2.05)	0.41	52%
Hemorrhages (n = 6[24,25,27,32,37,39])	7/644 (1)	18/664 (3)	0.61 (0.22–1.69)	0.34	7%
Wound complications (n = 7[24,25,27,32,34,37,39])	3/672 (0.4)	51/689 (7)	0.31 (0.11–0.83)	0.02	0%
Abscess (n = 4[24,30,32,39])	10/525 (2)	29/496 (6)	0.64 (0.29–1.38)	0.25	0%
Cardiovascular complications (n = 3[24,25,27])	1/407 (0.2)	7/244 (3)	0.24 (0.05–1.19)	0.08	0%
Intestinal complications (n = 7[24,25,27,30,32,37,39])	3/669 (0.4)	28/706 (4)	0.31 (0.10–0.95)	0.04	14%
Renal complications (n = 3[24,25,27])	5/407 (1)	3/244 (1)	1.16 (0.26–5.17)	0.84	0%
Biliary complications (n = 2[24,27])	0/363 (0)	6/107 (6)	0.10 (0.01–0.79)	0.03	0%
Other (n = 2[34,39])	0/56 (0)	14/107 (13)	0.15 (0.02–1.28)	0.08	0%

RFA: radiofrequency ablation; CI: confidence interval.

Martinus J. van Amerongen, Sjoerd F.M. Jenniskens, Peter B. van den Boezem, Jurgen J. Fütterer & Johannes H.W. de Wilt Radiofrequency ablation compared to surgical resection for curative treatment of patients with colorectal liver metastases– a meta-analysis. HPB 2017, 19, 749–756

Trials - COLLISION

- Randomized controlled trial of Thermal Ablation versus Surgery (COLLISION trial)
  - 296 patients randomly 1:1 assigned to surgical or ablative treatment for mCRC

- Overall survival was 92.7% (ablation) vs 92.9% (surgery) at 1 year, 78.5% vs 79.6% at 2 years, and 51.2% vs 58.0% at 5 years.

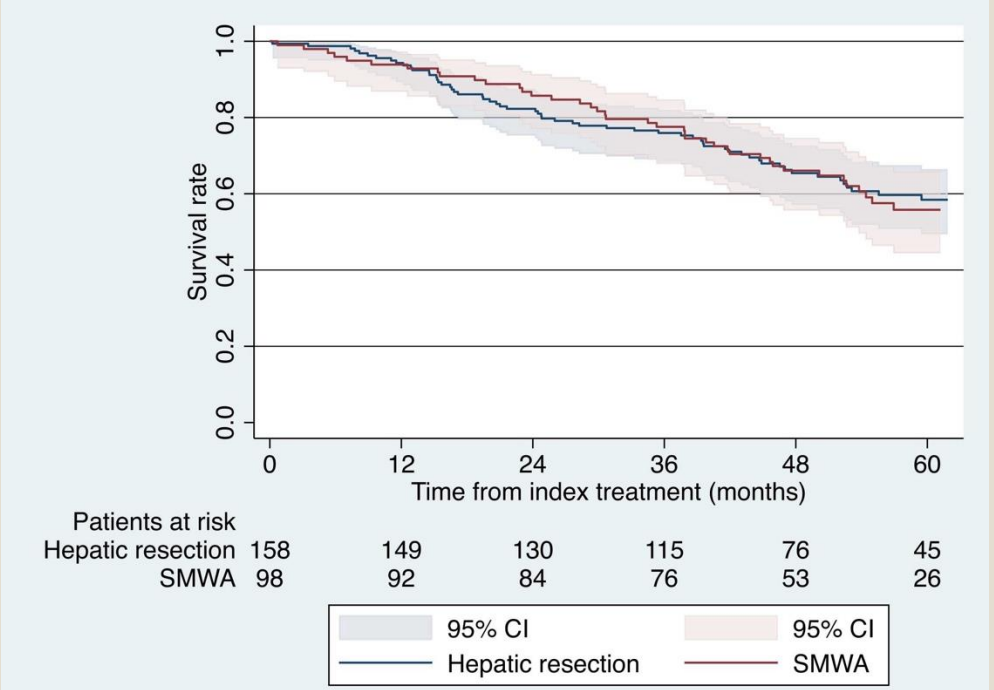
- No difference in Local Control of Tumor

- The thermal ablation group had a superior safety profile. Adverse events of any grade occurred in 19% vs 46% of patients ($P < .0001$). Grade 3 or 4 adverse events occurred in 7% vs 18% of patients.

van der Lei, Susan et al. Thermal ablation versus surgical resection of small-size colorectal liver metastases (COLLISION): an international, randomised, controlled, phase 3 non-inferiority trial. The Lancet Oncology, Volume 26, Issue 2, 187 – 199

Trials - MAVERRIC

- Cohort studies and subsequent randomized controlled trials of Microwave Ablation (MWA) versus surgery further confirms that for lesions ≤ 3 cm, ablation and surgery have similar local control and long-term survival.
- 67 % reduction in complications with MWA vs Resection
- Overall 2yr medical costs showed an average 26% reduction in medical costs with MWA versus Surgery.



Eur J Surg Oncol. 2020; **46**:476-485
Eur J Surg Oncol. 2023 Feb;49(2):416-425.
Tinguely, P · Ruiter, SJS · Engstrand, J · et al. A prospective multicentre trial on survival after microwave ablation versus resection for resectable colorectal liver metastases (MAVERRIC). *Eur J Cancer.* 2023; **187**:65-76

Trials

- In patients with Bilobar metastatic disease, 5 -year survival rates were similar between bilobar resection and combination resection/ablation or ablation alone
- These findings despite the ablation group being demonstrably poorer prognosis
- Decreased complications in ablation group
  - *JAMA Surg*. 2013; **148**:597-601

- Conclusions:
  - Consider Ablation First for small lesions.
  - Expand definition of "OLIGOMETASTATIC DISEASE" and patients with "curative intent"

Y90 Radiation Segmentectomy (RS)

- Transarterial therapy, typically outpatient.
- Targeted delivery of high dose of Y90 particles (glass) to vascular territories containing oligometastatic disease
- Data from Liver Explant after RS for HCC shows complete necrosis of treated segment if >400Gy delivered
  - Eur J Nucl Med Mol Imaging 2021; 48 (02) 580-583
- No tumor size limit for RS. Limitation is only based on being able to isolate and cover vascular territory and preserve underlying liver function
  - Thermal Ablation with curative intent limited to metastases up to 3-4cm.

Y90 Radiation Segmentectomy (RS)

- In a long term observational study of oligometastatic disease patients who were NOT a candidate for ablation or surgery, Radiation Segmentectomy was performed on up to three lesions.
  - One, two- and three-year LTPFS were 83%, 83% and 69%
  - Very low toxicity profile with 1/10 patients experiencing a liver abscess 6 months post procedure.
  - Abdom Radiol (NY) . 2021 July ; 46(7): 3428–3436.

- A similar small study nonsurgical candidates with oligometastatic disease showed a mean time to progression of 7.1 months with minimal complications.
  - Gastrointest Oncol 2018;9(2):311-315

Y90 Radiation Segmentectomy (RS)

- Retrospective analysis of 18 patients treated for oligometastatic neuroendocrine tumors NOT candidate for surgery or ablation.
  - Tumor objective response was achieved in 83% of patients by RECIST size criteria and 100% by mRECIST enhancement criteria.
  - Median OS was 69.4 months, and median PFS was 12.2 months. Median overall TTP was 13.0 months
  - J Vasc Interv Radiol. 2025 Feb;36(2):293-300.

- Another multicenter study of 36 patients showed a high response rate across multiple tumor types with low complication rates.
  - Tumor type does not seem to matter with RS due to high radiation dose.
  - J Surg Oncol. 2021 Jan;123(1):172-178.

Histotripsy

- Ultrasound mediated cavitation causing tissue destruction
- Non-invasive
- International multicenter trial shows effective in creating ablation zone
  - HOPE4LIVER trial of 44 patients
- Effective on HCC and metastatic disease
- Early evidence of immune stimulation similar or increased compared with other ablation modalities.

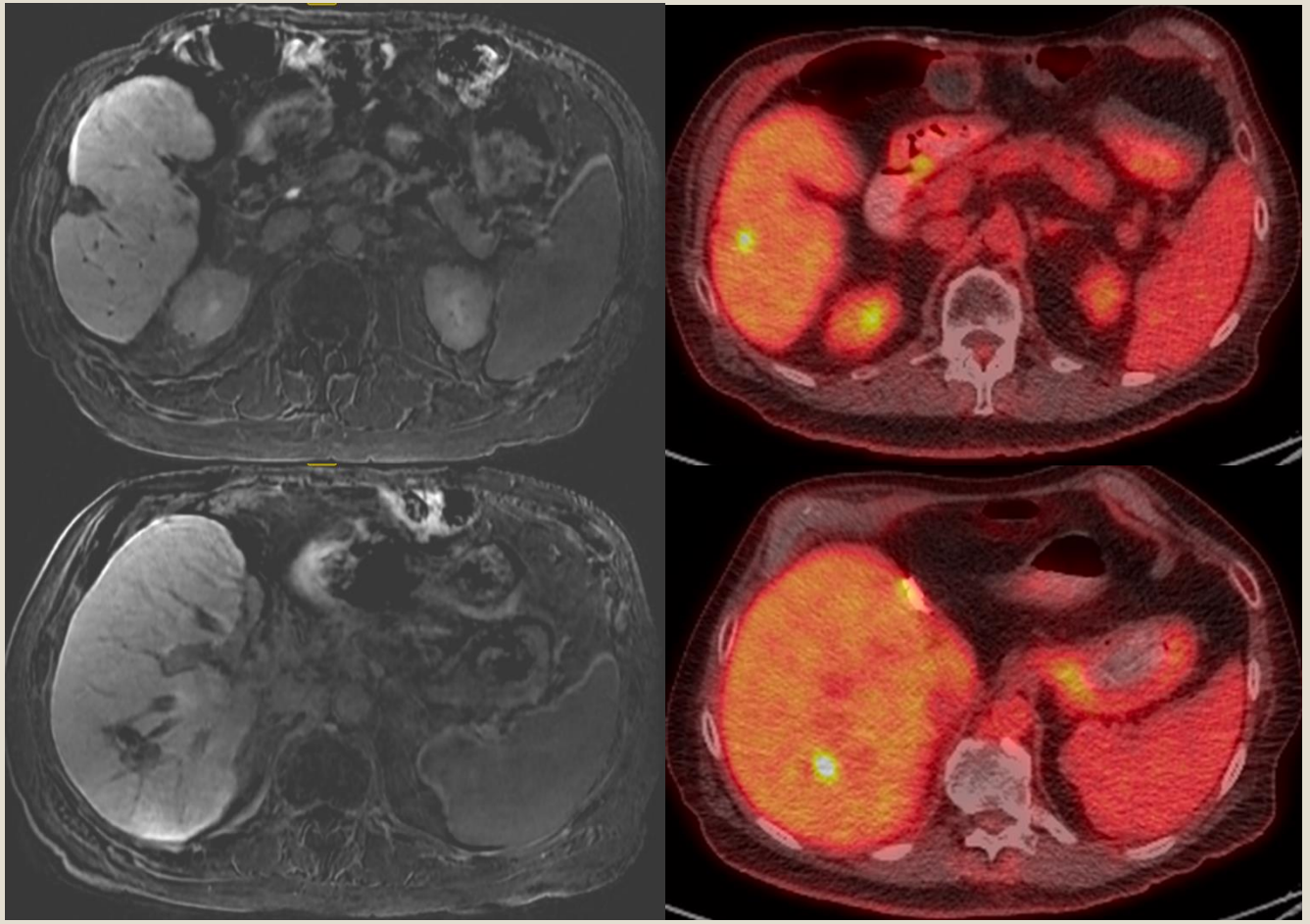
Challenges:

- High rate of anatomic exclusion 21/83 screened patients
- No long-term data or controlled trials
- 13.6% major complication rate through 30 days, higher than percutaneous ablation
  - Radiology: 312 (3). September 2024

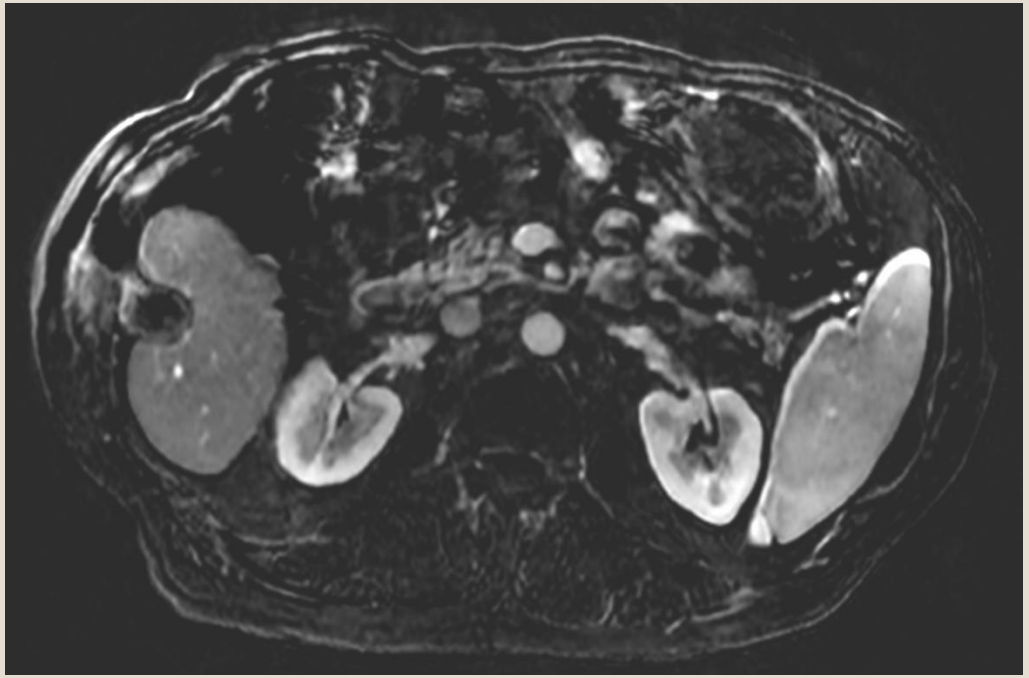
CASE EXAMPLES

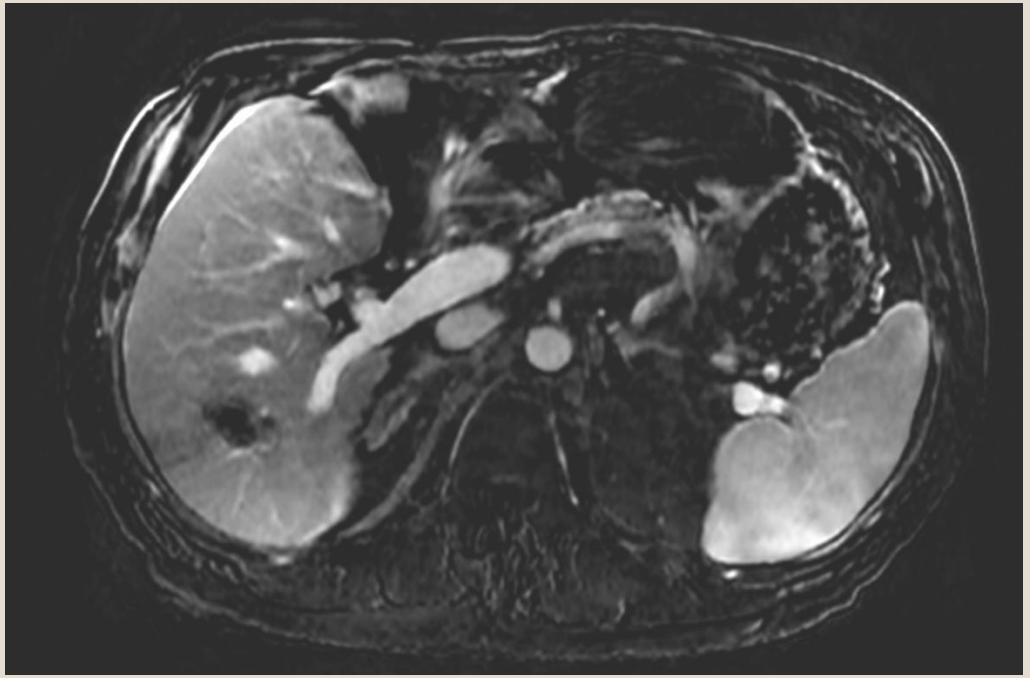
Case Examples

- 72 yo M with a history of cholangiocarcinoma
- S/p OTLTx now with oligometastatic disease in transplant liver
- Liver function WNL but not a good open surgical candidate
- Cryoablation of both lesions performed as an outpatient



Case Examples

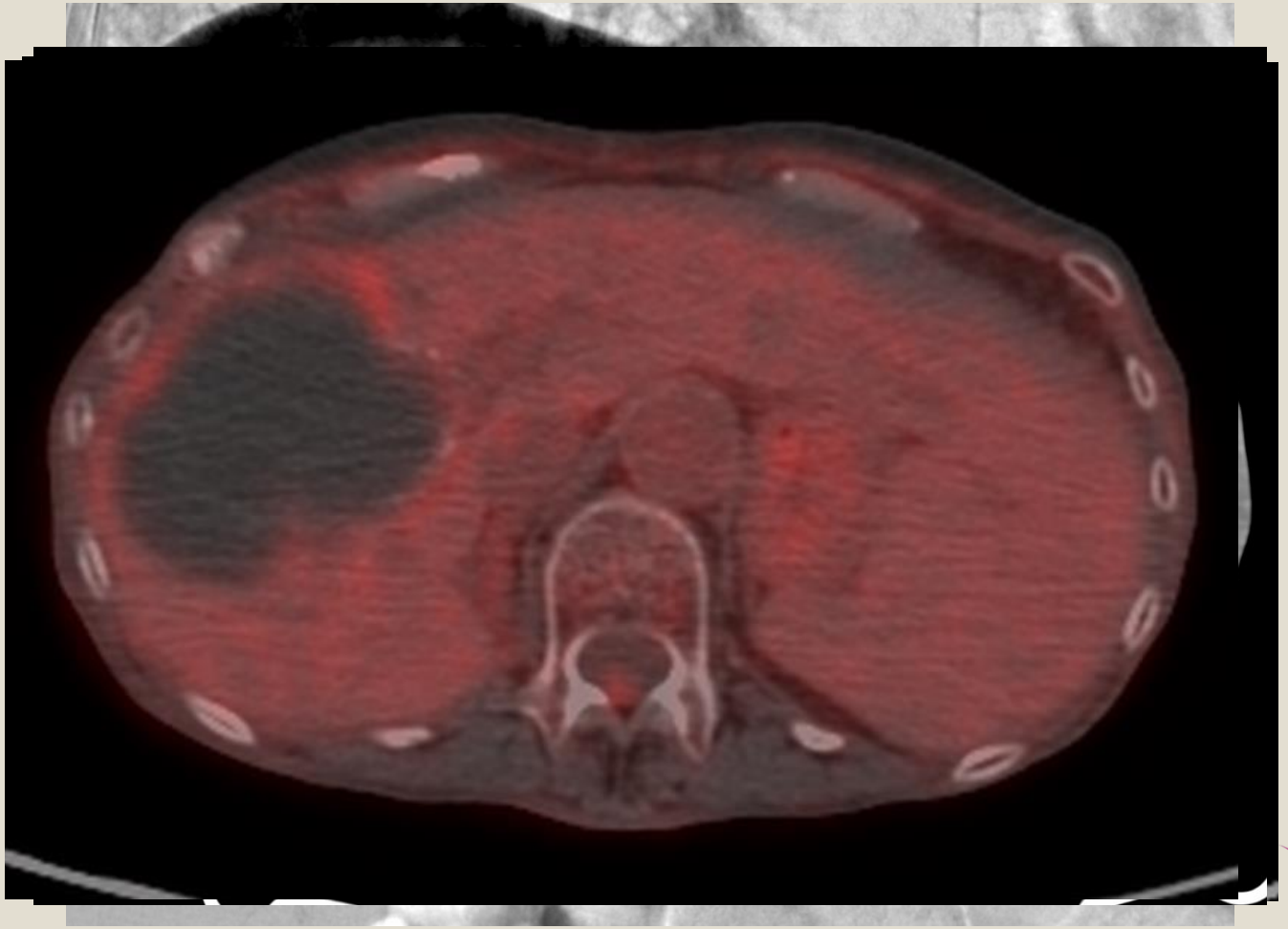




No local recurrence at ablation sites. Patient has had two additional lesions appear 1 yr later which were also ablated.

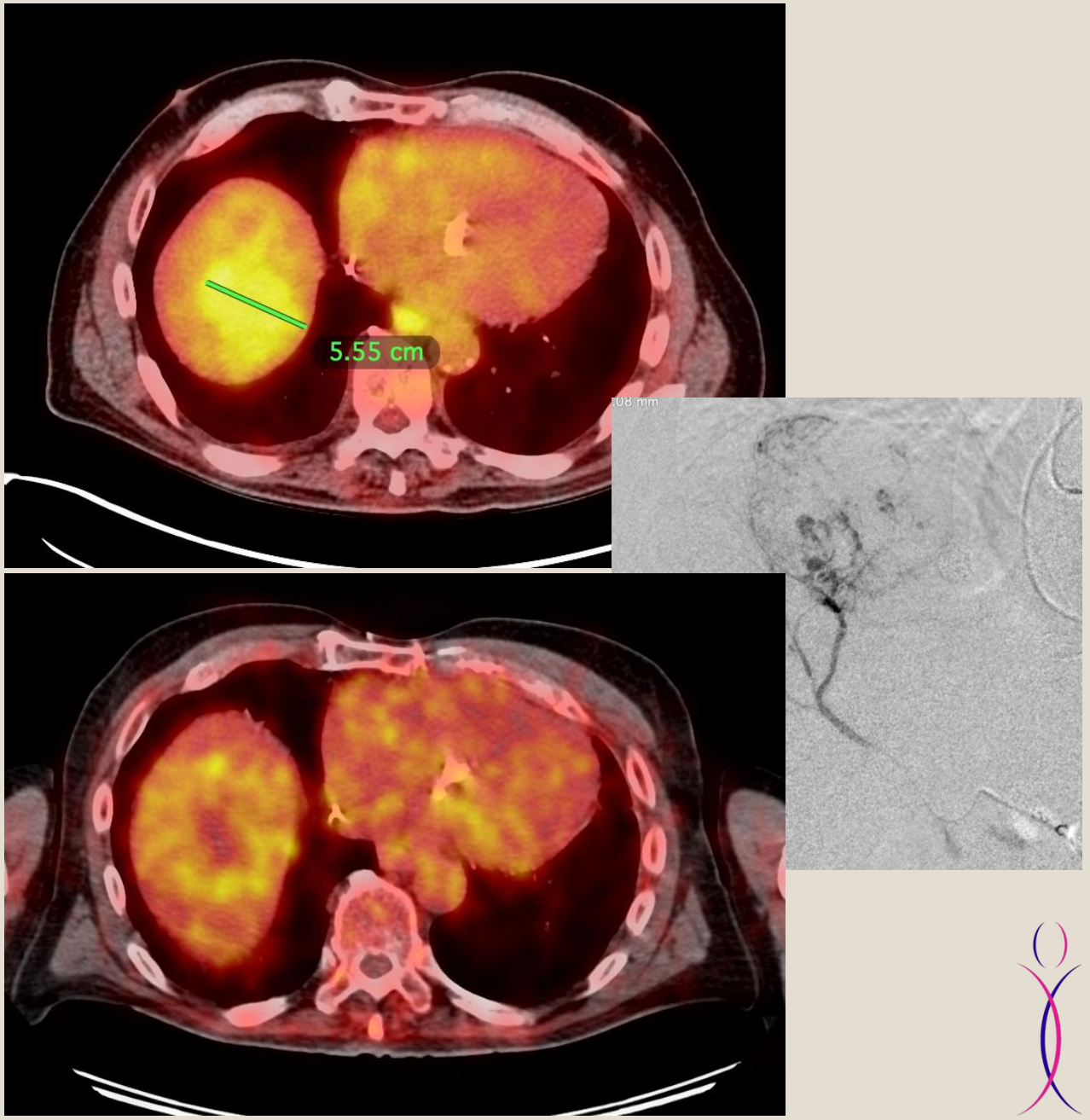
Case Examples

- 66yo F with bilateral RCC requiring nephrectomies resulting in ESRD.
- Presented with large single liver metastasis. Not a surgical or ablation candidate.
- Underwent RS with >600Gy to the treated volume.
- On followup had complete response with a new satellite lesion
- Underwent CT guided cryoablation as outpatient
- Complete response in liver.



Case Examples

- 74 yo M with anaplastic sarcoma after whole body radiation as a young man for Hodgkins disease.
- Solitary liver metastasis, nearly 6 cm in diameter. Not a good surgical candidate due to cardiac history.
- Selective Y90 delivering >300Gy to tumor volume
- Lesion complete response
- Have treated several additional lesions with Y90 and cryoablation with >5 yrs of survival to date.



Conclusion

- Percutaneous and Transarterial procedures show increasing promise in treating oligometastatic disease to the liver with curative intent.
- Randomized controlled trials support percutaneous ablation as safer and as effective as surgical resection in the appropriate scenario
- Ablation and Radiation segmentectomy preserve liver function and can be used additively and sequentially as needed to control disease long term

- As always, Multidisciplinary Collaboration and experienced operators result in the best outcomes for our patients.