

# Locoregional Therapies for Liver Metastases from GIST

Steven Y Huang, MD

Associate Professor

Department of Interventional Radiology

September 21, 2019

[syhuang@mdanderson.org](mailto:syhuang@mdanderson.org)

THE UNIVERSITY OF TEXAS

MD Anderson ~~Cancer~~ Center®



# Objectives

---

- Epidemiology of GIST liver metastases
- Role of liver-directed therapy
- Options for liver-directed locoregional therapy
  - Thermal ablation
  - Embolization
    - Bland/chemoembolization
    - Radioembolization with Yttrium-90

THE UNIVERSITY OF TEXAS

MD Anderson ~~Cancer~~ Center®

# Epidemiology

---

- Gastrointestinal stromal tumors (GIST) are low-incident tumors with approximately 3,000-5,000 cases per year in the United States
- Liver is the most common site of solid organ metastases from GIST
- GIST metastases to the liver present at initial diagnosis up to 20% of the time
- 50-65% of patients with metastatic disease have isolated liver metastases
- Only approximately 30% of patients with GIST liver metastases will have potentially resectable disease

THE UNIVERSITY OF TEXAS

MD Anderson ~~Cancer~~ Center®

# Epidemiology

Selected series reporting outcomes after multi-modality therapy for GIST liver metastases

Author	Patients	Pre-op TKI	Post-op TKI	Survival	Factors
DeMatteo RP, 2000	200	None	None	Disease specific survival, median 19 months	<ul style="list-style-type: none"> <li>N=53 of 94 patients (56.4%) with liver-only disease</li> <li>Significant risk factors include male, tumor &gt; 5 cm, prior incomplete/unresectable tumors</li> </ul>
Xia L et al, 2010	19	19	19	3-year OS 89.5% in surgical versus 60% in non-surgical patients	Surgery also improved OS in patients who responded poorly to 6 months of preoperative imatinib compared to non-operative patients
Turley RS, 2012	39	19	27	OS: 1-year 97% and 3-year 67%	Surgery and post-operative TKI therapy improve survival

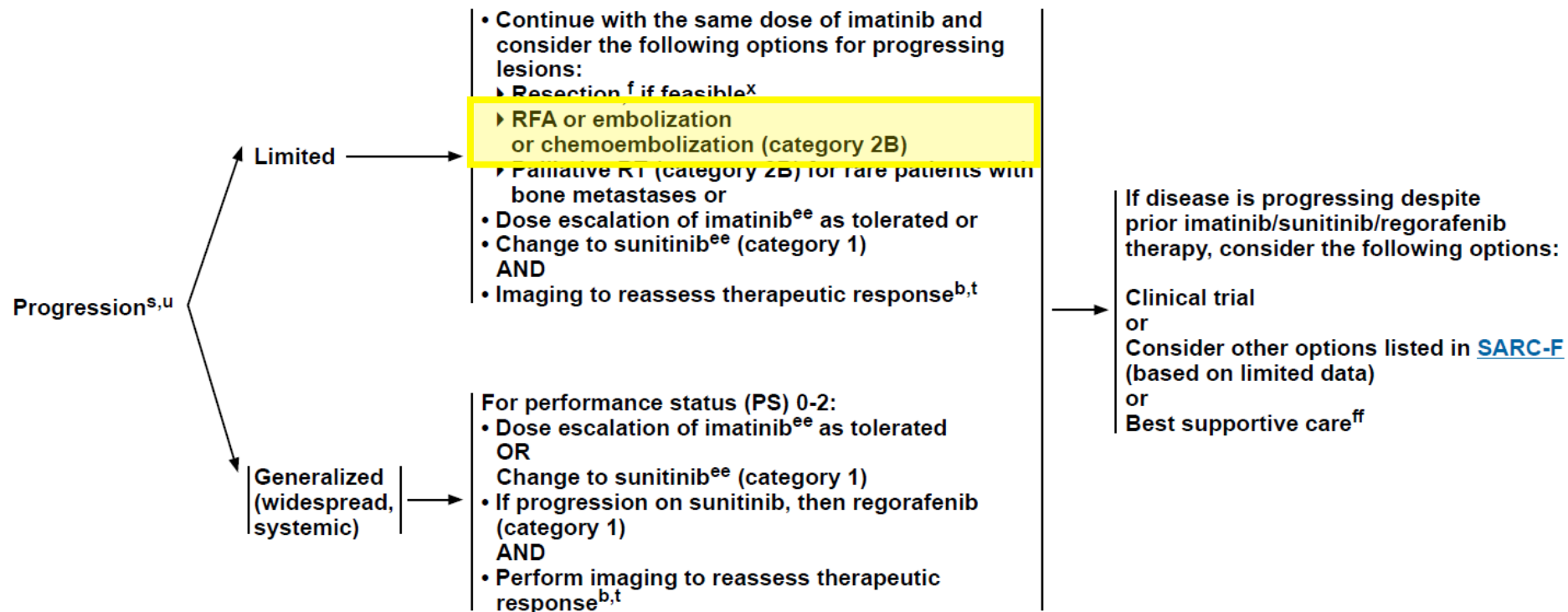
Pre-imatinib

Post-imatinib

THE UNIVERSITY OF TEXAS

MD Anderson Cancer Center®

TREATMENT FOR PROGRESSIVE DISEASE



<sup>b</sup>See Principles of Imaging (SARC-A).

<sup>f</sup>See Principles of Surgery for GIST (GIST-C).

<sup>s</sup>Rarely, increase in tumor size may not indicate lack of drug efficacy; all clinical and radiographic data should be taken into account, including lesion density on CT.

<sup>t</sup>Progression may be determined by abdominal/pelvic CT or MRI with contrast with clinical interpretation; PET scan may be used to clarify if CT or MRI are ambiguous.

<sup>u</sup>Suggest referral to a sarcoma specialty center.

<sup>x</sup>Imatinib can be stopped right before surgery and restarted as soon as the patient is able to tolerate oral medications. If other TKIs, such as sunitinib or regorafenib, are being used, therapy should be stopped at least one week prior to surgery and can be restarted based on clinical judgment or recovery from surgery.

<sup>ee</sup>Clinical experience suggests that discontinuing TKI therapy, even in the setting of progressive disease, may accelerate the pace of disease progression and worsen symptoms.

<sup>ff</sup>In patients with GIST progressing despite prior imatinib, sunitinib, and regorafenib consider other options listed in [SARC-F](#) (based on limited data) or reintroduction of a previously tolerated and effective TKI for palliation of symptoms. Consider continuation of TKI therapy life-long for palliation of symptoms as part of best supportive care.

**Note:** All recommendations are category 2A unless otherwise indicated.  
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

# Progression following TKI Therapy

---

- Resistance to TKI treatment
  - *Primary resistance*: disease progression following initiation of imatinib therapy and observed in approximately 10% of patients
  - *Secondary resistance*: disease progression following initial radiographic response to imatinib driven by a secondary KIT or PDGF-R mutation
- Increasing the dose of imatinib can be the first step following primary or secondary resistance
- Second-line therapy with sunitinib (multikinase inhibitor that preferentially targets PDGF-R and VEGF-R)
  - Response rates attained with sunitinib salvage therapy (improved progression-free survival (PFS) compared to placebo, 27.3 weeks vs. 6.4 weeks PFS,  $P \leq 0.0001$ )
- Third-line therapy with regorafenib demonstrates an increase in PFS of <5 months

# Prognostic Factors Affecting OS After Imatinib Secondary Resistance

- Retrospective review of 48 patients who developed imatinib secondary resistance between 2001-2012
- Median follow-up 58 months
- OS at 1, 3, 5 years were 64.6%, 32.8%, and 20.4%, respectively
- Median OS was 22 months (95% confidence interval, CI, 15-29 months)
- *Factors associated with improved OS:*
  - *ECOG, size, surgical resection, ?focal progression*

**Table 2** Survival analyses in 48 patients with imatinib secondary resistance (ISR) using the log-rank test

Variable	N	MST (months)	P value
Age at diagnosis of ISR			0.73
≤65 years	23	23	
>65 years	25	18	
Sex			0.25
Male	34	19	
Female	14	30	
PFS in first-line IM (months)			0.07
≤20	24	13	
>20	24	30	
Effect of IM			0.27
PR	32	23	
SD/NE	16	13	
ECOG PS			0.01
0	29	25	
1/2	19	12	
Primary site			0.94
Stomach	22	18	
Small intestine	26	25	
Type of mutation <sup>a</sup>			0.78
<i>KIT</i> exon 9	6	33	
<i>KIT</i> exon 11	27	25	
Serum albumin (g/dL)			0.63
<4.0	17	8	
≥4.0	31	25	
Hemoglobin concentration (g/dL)			0.07
<11.0	23	18	
≥11.0	25	30	
White blood cell count (cells/mm <sup>3</sup> )			0.07
<4500	24	33	
≥4500	24	12	
Granulocyte count (cells/mm <sup>3</sup> )			0.25
<2500	21	30	
≥2500	26	18	
History of gastric or duodenal resection <sup>b</sup>			0.49
Present	13	12	
Absent	35	25	
Distribution of PD			0.43
Limited	28	25	
Generalized	20	13	
Focal progression			0.09
Yes	8	56	
No	40	19	
New lesion			0.33
Present	17	23	
Absent	31	22	
Diameter of PD <sup>c</sup> (cm)			0.001
≤5.0	29	33	

**Table 2** continued

Variable	N	MST (months)	P value
>5.0	19	12	
PD in the liver			0.12
Present	23	19	
Absent	25	30	
PD in the peritoneum			0.78
Present	29	25	
Absent	19	22	
Involved organ by PD			0.39
Single	34	25	
Multiple	14	19	
Surgical resection of PD			<0.001
Performed	24	51	
Not performed	24	12	
TACE			0.74
Performed	15	25	
Not performed	33	17	
Sunitinib therapy			0.26
Performed	22	19	
Not performed	26	25	
Multimodality treatment <sup>d</sup>			0.60
Performed	14	33	
Not performed	34	18	

# Locoregional Liver-Directed Therapy

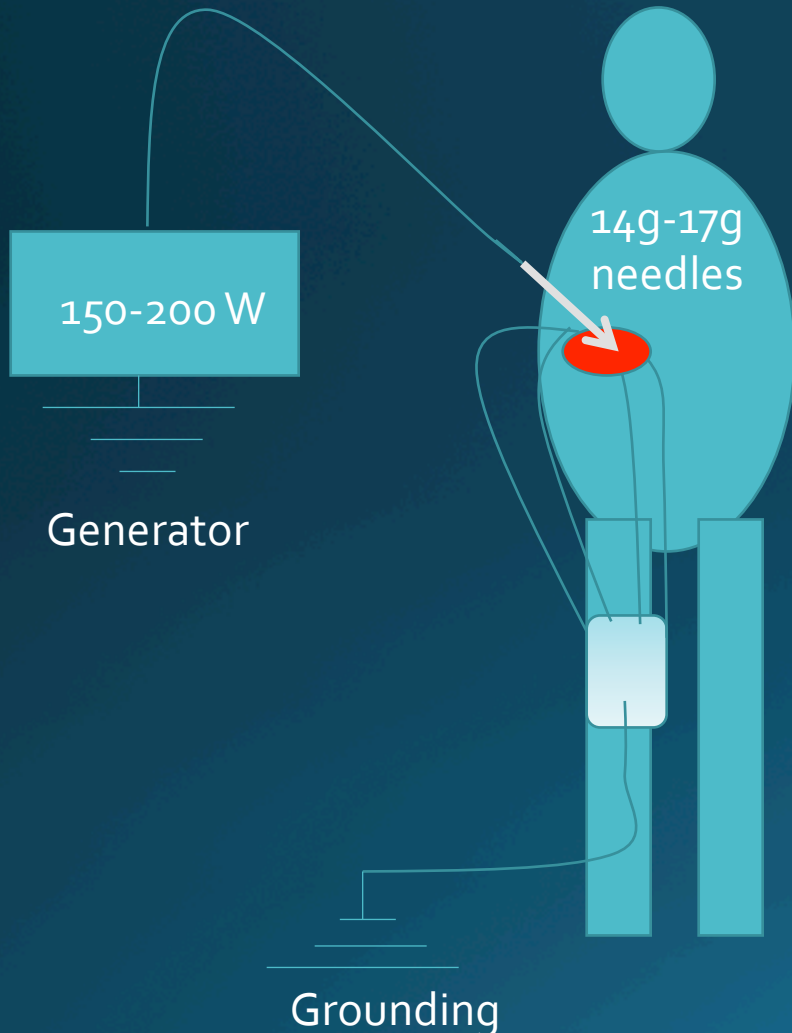
---

- Thermal ablation
- Transarterial embolization
  - Bland and Chemoembolization
  - Radioembolization



# Locoregional Liver-Directed Therapy

## *Radiofrequency Ablation*

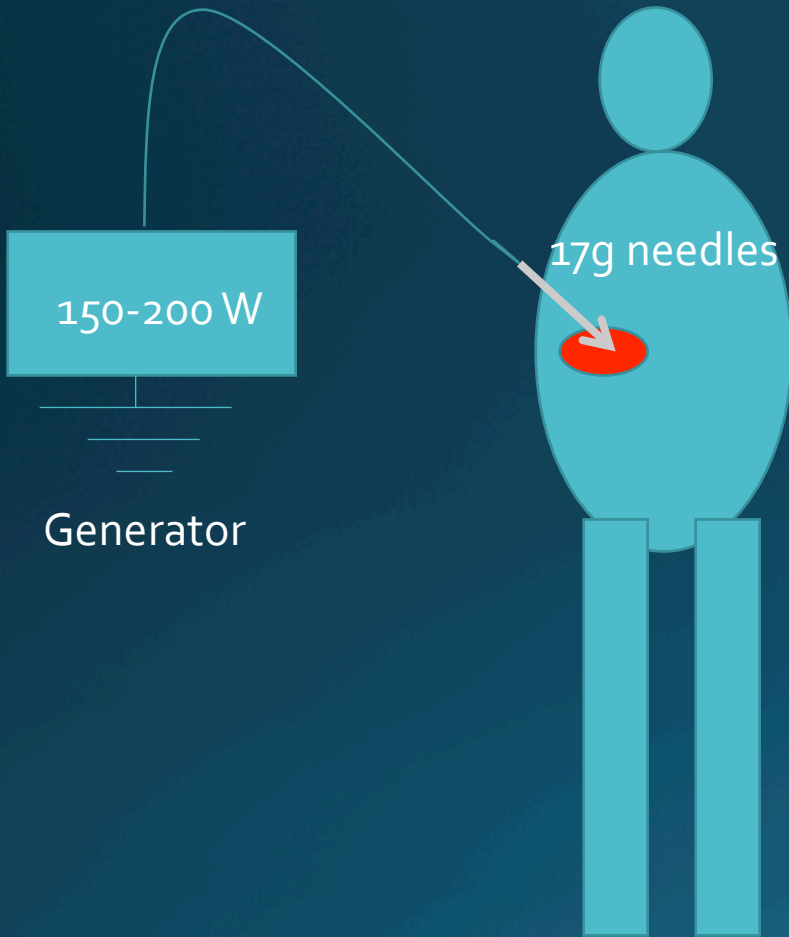


- Physics and Principles

- RF refers to EM spectrum between 3 kHz and 300 GHz
- RFA probe acts as cathode of electric circuit closed by dispersing pads
- Small cross-sectional area of probe leads to high energy flux
- Large cross-sectional area of grounding pads leads to energy dispersion
- Dipole molecules adjacent to probe (mostly water) align in direction of current and vibrate with AC
- Frictional energy losses between molecules results in local energy deposition and temperature increase
- Energy deposition and temperature decrease as a function of distance from source
- Time and energy input is critical to achieving desired ablation volumes
  - At 55°C, tissue death occurs in 2 seconds
  - Objective is to heat tissue for 4-6 minutes at 50-100°C

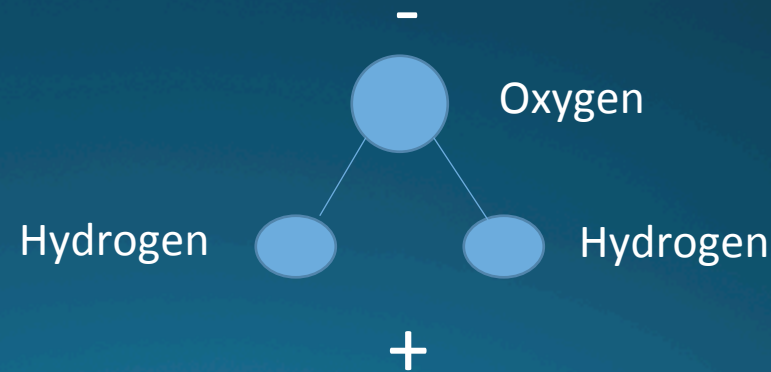
# Locoregional Liver-Directed Therapy

## *Microwave Ablation*



- Physics and Principles

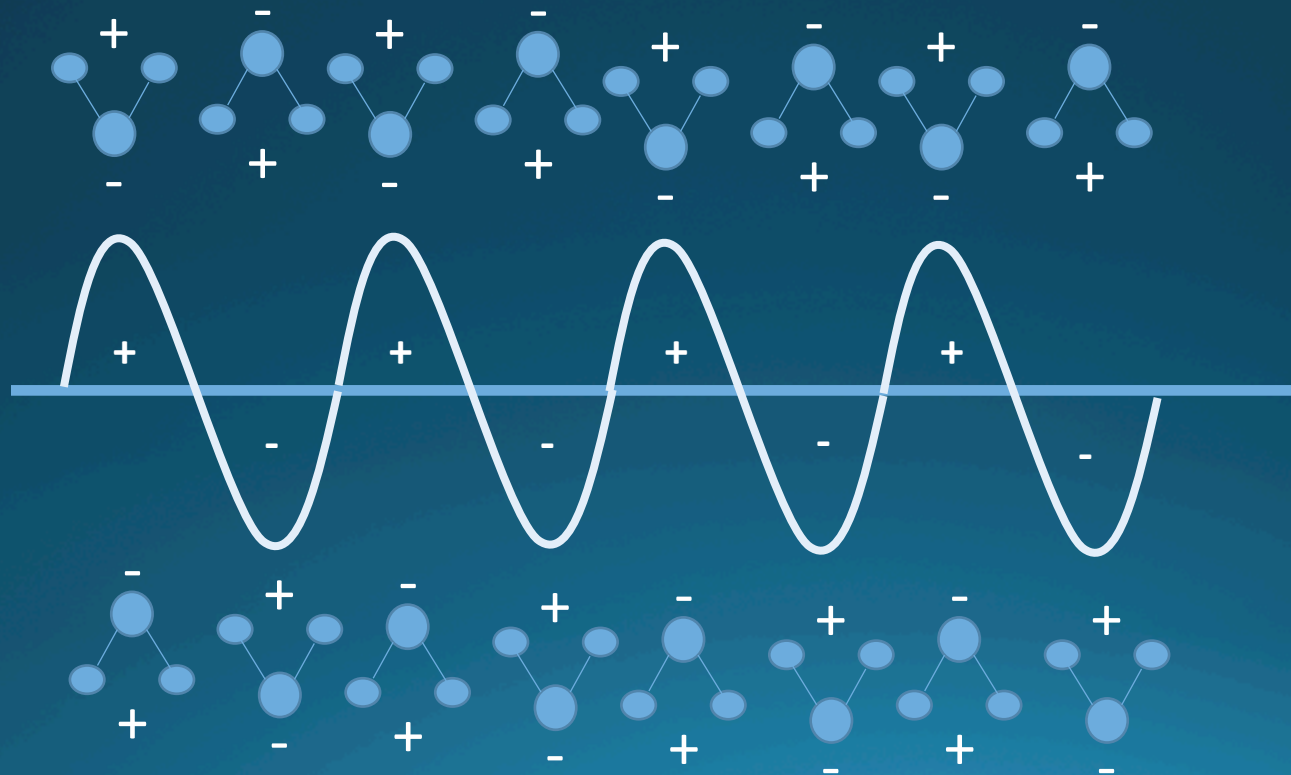
- Form of EM radiation with frequencies ranging from 900 to 2450 MHz
- Energy carries an electric charge that oscillates between positive and negative values
- Water also carries an electric charge (polarity)



# Locoregional Liver-Directed Therapy Microwave Ablation

- Physics and Principles

- MW is able to cause water molecules to change spatial orientation 2 to 5 billion times per second



- MW is able to cause water molecules to change spatial orientation 2 to 5 billion times per second
- Rapid flipping and molecular agitation against frictional forces results in a rise in water temperature and heating of target tissues
- Optimal temperature end point is 50-100°C
- Cellular death proceeds by coagulative necrosis

# RFA and Microwave Ablation Devices

Covidien  
RFA  
generator  
and probes



Cool-tip™ RF Ablation Single Electrode Kits

Cool-tip™ RF Ablation Cluster Electrode Kits

Cool-tip™ RF Ablation Switching Electrode Kits

Cool-tip™ RF Ablation System Grounding Pad and Extension Cable

Neuwave  
microwave  
generator  
and probes



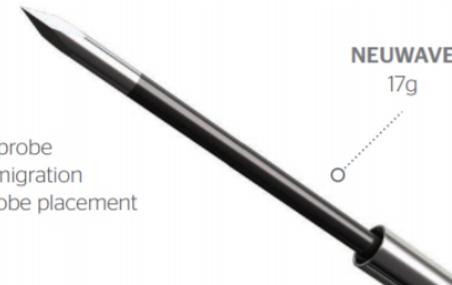
17

17 gauge probe =  
Less invasive procedures†



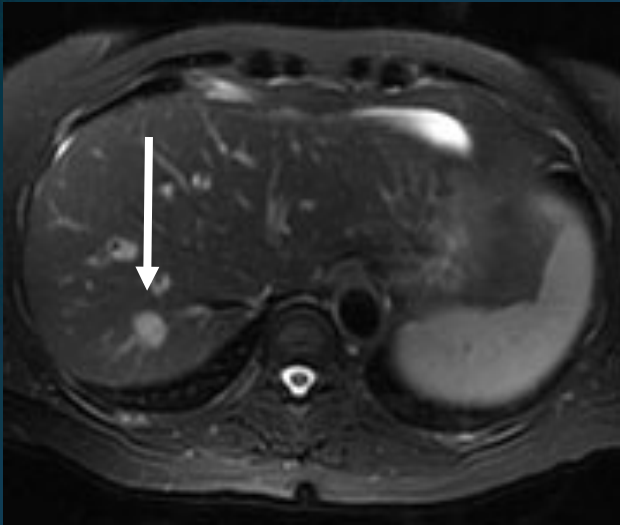
**Helps reduce probe migration**

Tissu-Loc technology "sticks" the probe in place, to help minimize probe migration during imaging and additional probe placement

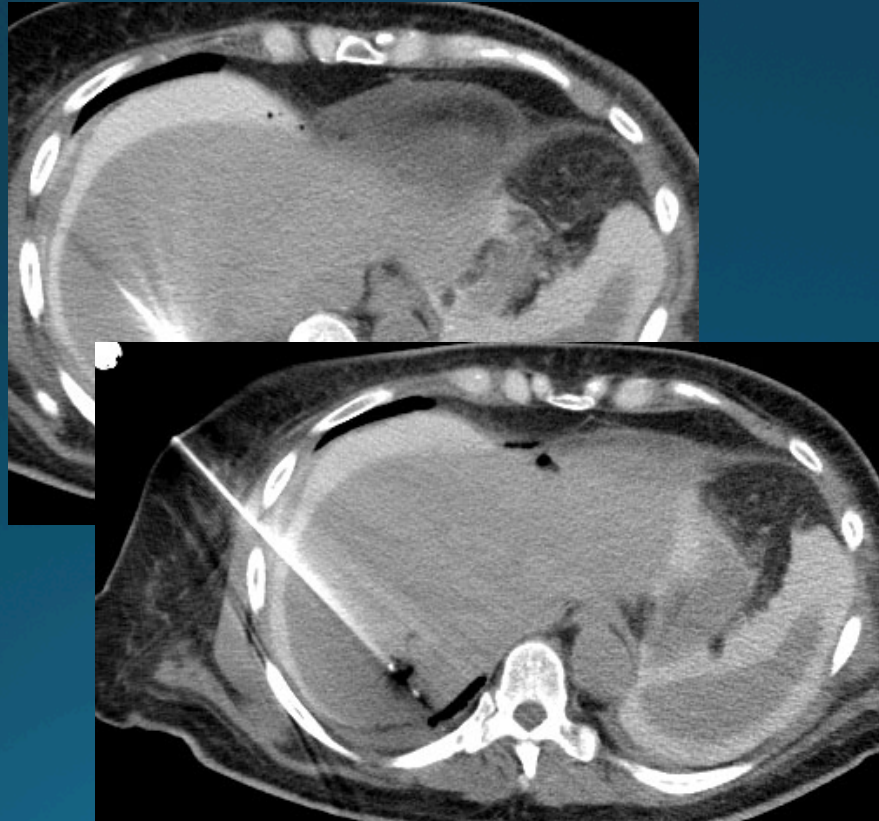


# 67 Year-Old Female with Gastric GIST Metastatic to the Liver on Regorafenib

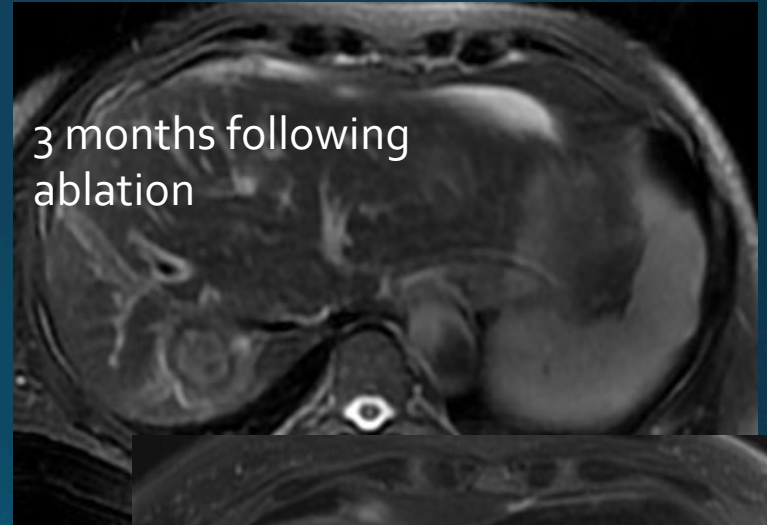
New liver metastasis  
identified 6 years after initial  
diagnosis



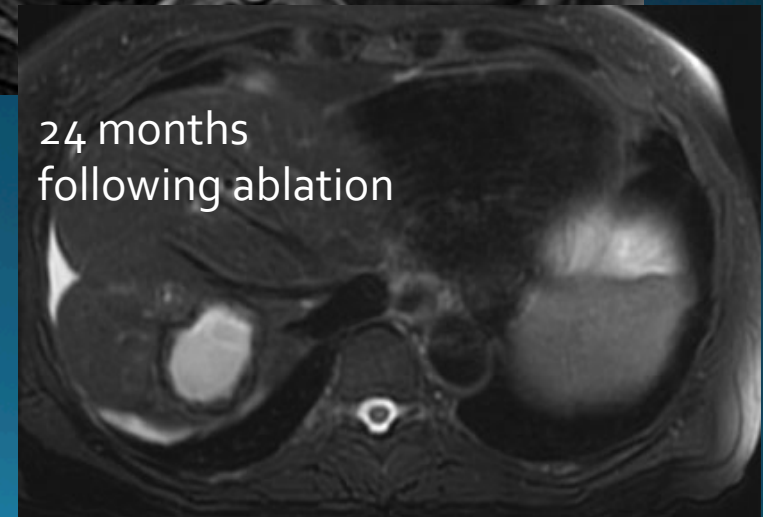
Microwave ablation  
performed of liver  
metastasis



Follow-up MRI scans



24 months  
following ablation



# Locoregional Liver-Directed Therapy

## *Cryoablation*

---

- Physics and Principles
  - Cryoprobe is rapidly cooled, removing heat from the tissue by conduction via physical contact with the cryoprobe
  - Rapid cooling of the cryoprobe takes place by means of the Joule-Thompson effect (rapid expansion of a gas results in a temperature change)
  - Most gases, including oxygen, nitrogen, and argon, exhibit Joule-Thompson cooling when rapidly expanded at room temperature
  - Hydrogen and helium, however, warm when rapidly expanded at room temperature

— · · · 0° C isotherm

- - - Lethal (-20° C) isotherm

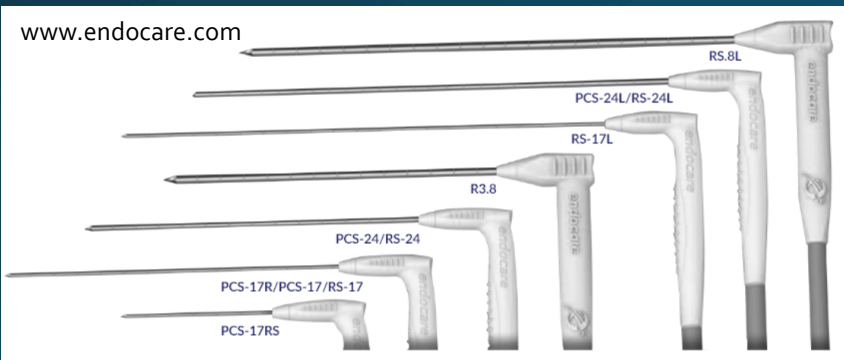
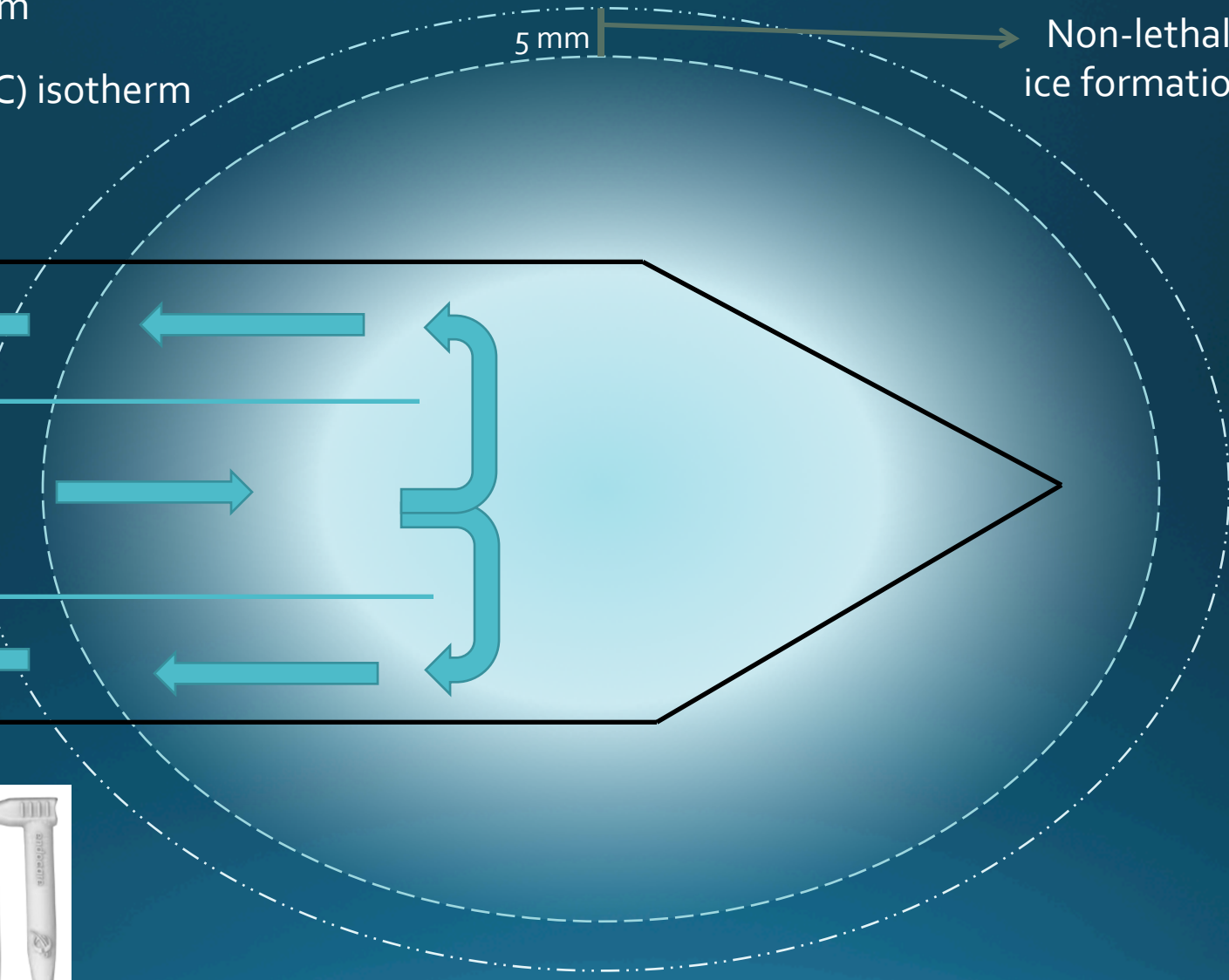
5 mm

Non-lethal  
ice formation

1 atm  
low T

Argon  
high P  
Low T

1 atm  
low T



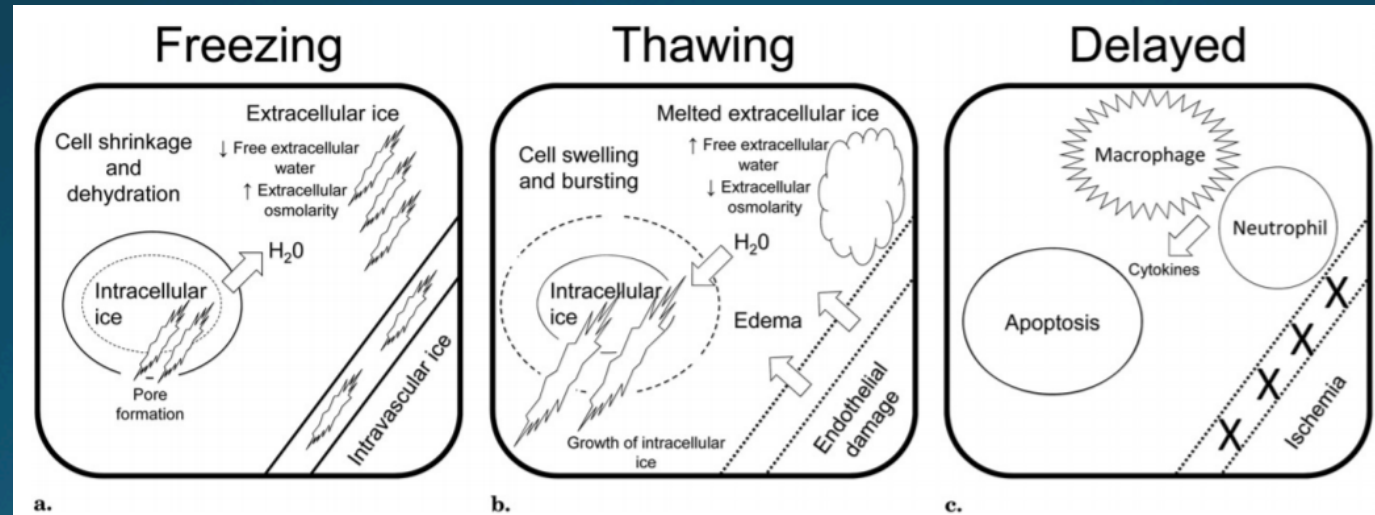
# Cryoablation – Mechanism of Injury

## Direct Mechanisms of Cellular Injury

- Ice crystals in the extracellular space sequester free water resulting in HYPERTonicity relative to the intracellular space, drawing free water from cells
- Resulting intracellular solute concentration causes damage to cytoplasmic enzymes and destabilization of cell membrane
- During thawing, melting ice results in HYPOTonicity of the extracellular space leading to an osmotic fluid shift and cell swelling

## Indirect Mechanisms of Cellular Injury

- Ice crystal formation in blood vessels causes thrombus formation and tissue ischemia
- Release of inflammatory cytokines begins a cascade of molecular events
  - Increases vascular permeability/tissue edema
  - Ischemia results in the production of vasoactive substances, causing regional hyperemia
  - Influx of inflammatory cells ensues, which aids in the cleanup of cellular debris



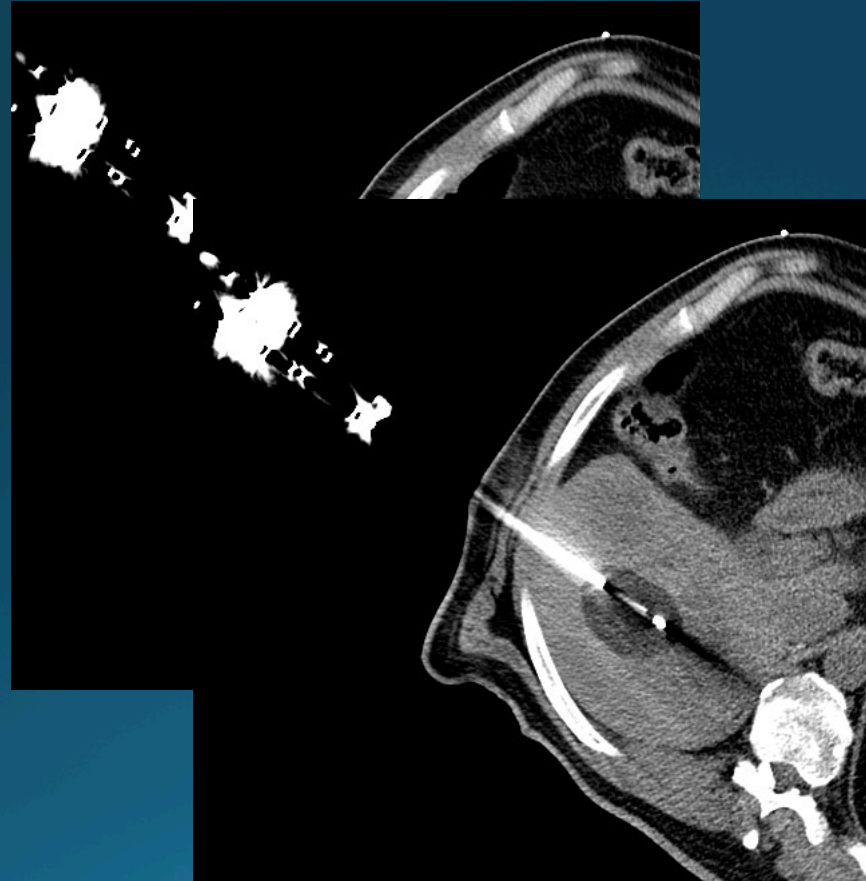


# 38 Year-Old Male with Metastatic Renal Cell Carcinoma

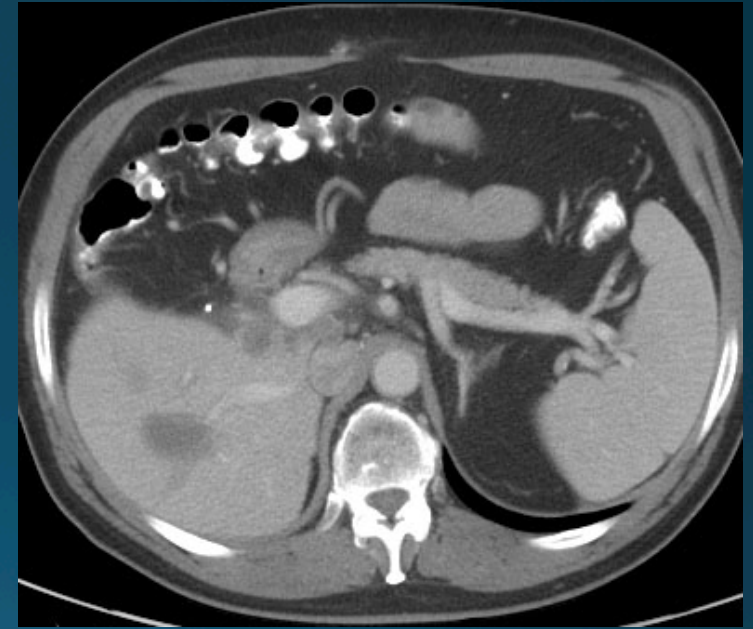
Liver metastasis



Cryoablation

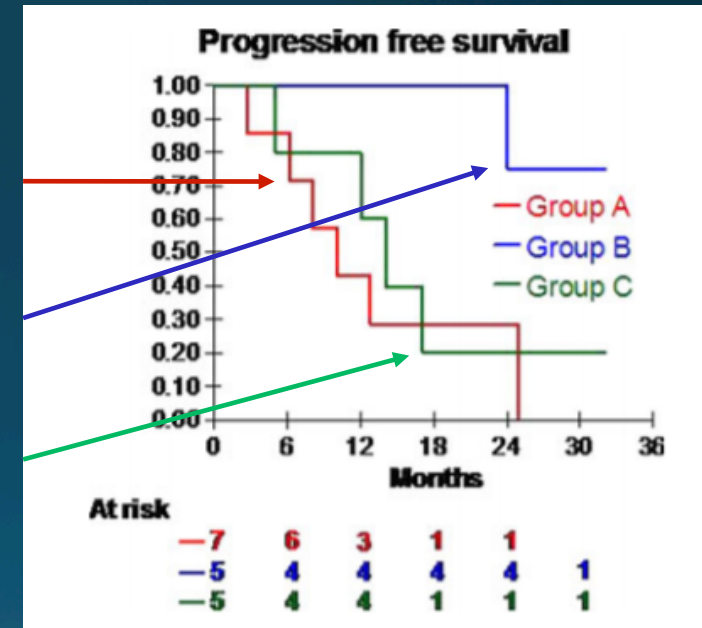


CT 3 months following cryoablation



# Thermal Ablation Benefits from Adjunctive TKI

- Retrospective review of patients with metastatic GIST (n=17) from 2004-2012
- Patients grouped into 3 categories:
  - A. RFA of all residual liver tumors on achievement of at least SD during imatinib treatment **WITHOUT** adjuvant imatinib (median neoadjuvant treatment duration 8 months, range 4-33 months), n=11 tumors in 7 patients
  - B. RFA of all residual liver tumors on achievement of at least SD during imatinib treatment **WITH** adjuvant imatinib (median neoadjuvant treatment duration 10 months, range 4-21 months), n=11 tumors in 5 patients
  - C. RFA of individual progressive lesions (median “neoadjuvant” treatment duration 37 months, range 14-70 months), n=5 tumors in 5 patients
- Complications (n=2, 11.8%):
  - A. Subsegmental liver infarction (self-limited)
  - B. Subcapsular hematoma



# Thermal Ablation Provides Durable Local Control

---

- Review of 13 patients with metastatic GIST from 2003-2009
- Inclusion: single site of progression with otherwise stability of other metastatic sites while receiving systemic therapy (median 2 agents, range 1-6)
- Tumor size ranged from less than 10 mm to 42 mm
- CR observed at treated lesions in 12 of 13 patients
- Median TTP of disease was 26 months following radiofrequency ablation
- At 21 months follow-up, 7 patients were on imatinib
- 2-year OS following RFA was 77% (95% CI, 35-94%)
- Complications (n=2): atrial fibrillation and infection

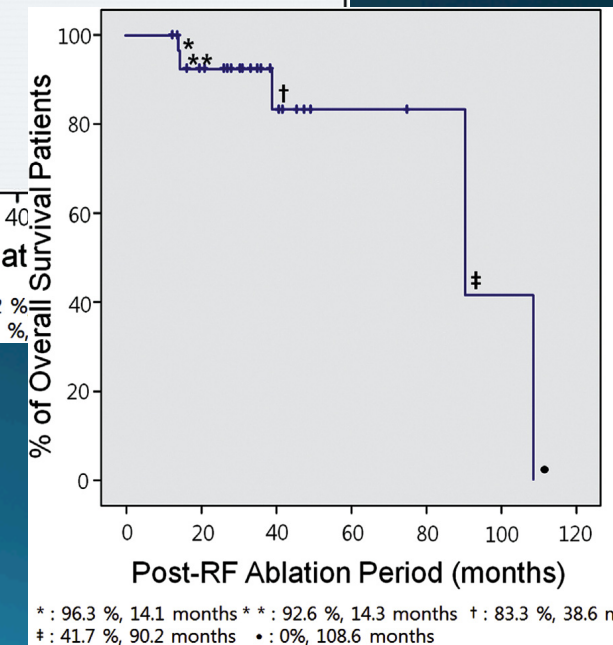
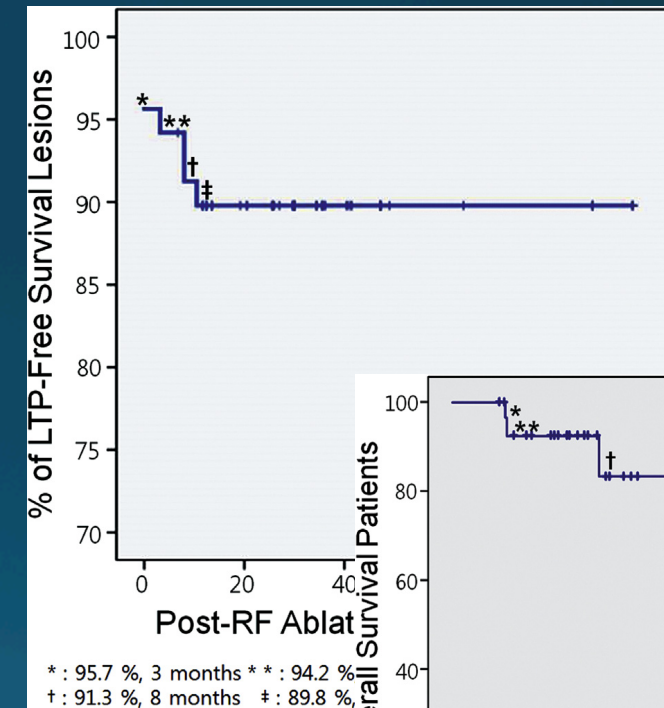
# Thermal Ablation Provides Durable Local Control *and Overall Survival*

---

- Retrospective review of 29 patients with metastatic GIST were included from 2002-2010
- Inclusion: progressive liver metastases which demonstrated primary or secondary resistance to TKI
- Mean number of treated lesions was 2.3 per procedure (range 1-8)
- Mean lesion diameter 1.3 cm (range, 0.4-3.6 cm)
- Complications
  - Post-ablation syndrome (n=4, 14%)
  - Bleeding requiring transfusion (n=1, 3%)
  - Peritoneal seeding (n=1, 3%)

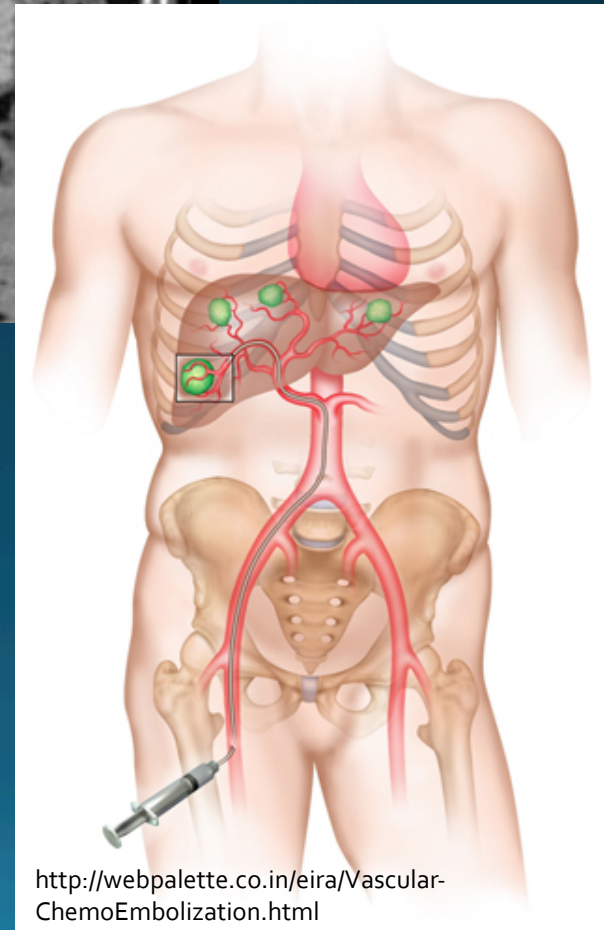
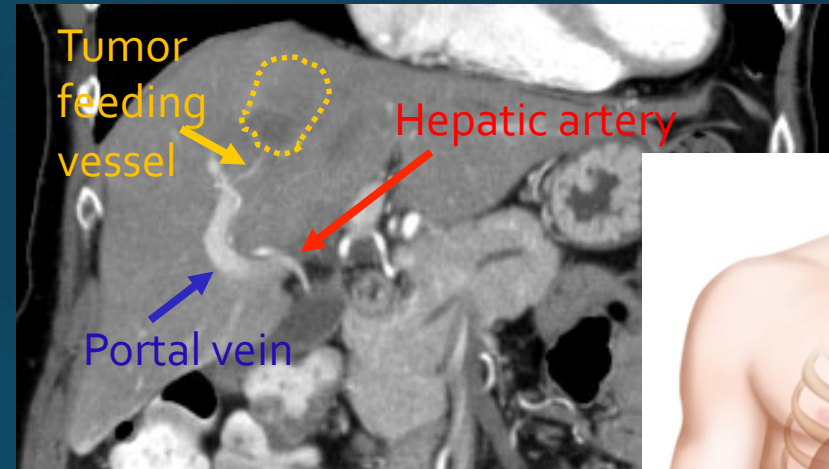
# Thermal Ablation Provides Durable Local Control *and Overall Survival, #2*

- Median follow-up period was 33.1 months (range, 12.3-108.6 months)
- Locoregional recurrence rate was 6% (n=4 of 66 treated lesions)
- *1-year progression free survival was 89.8%*
- Mean time to progression was 26 months
- *Overall survival was 90.2 months after RFA (range, 12.3-108.6 months)*



# Transarterial Embolization (TAE)

- Liver has a dual-blood supply arising from the portal vein and hepatic artery
- Liver metastases from GIST derive up to 90% of their blood supply from the hepatic artery
- TAE involves injection of an embolic agent into the vessel supplying the tumor resulting in tumor ischemia
- Transarterial chemoembolization (TACE) is a type of TAE in which there is intra-arterial delivery of chemotherapy in combination with arterial embolization
  - In theory, injection of an embolic agent produces tumor ischemia and prolongs the dwell time of the chemotherapy



# Transarterial Embolization - Technique

---

- Preliminary arteriography is performed to evaluate the arterial supply to the tumor
- Selected tumor supplying artery is catheterized
- TAE performed via one of two methods:
  - TACE: chemotherapeutic agents emulsified with ethiodized oil is injected followed by embolization with particulate agents
  - Bland TAE: Particulate agents (e.g. polyvinyl alcohol or tris-acryl particulates) are injected
- No consensus on whether TAE should be performed with versus without chemotherapy



# TAE: Bland versus Chemoembolization

- Retrospective study involving 45 patients with GIST liver metastases (>2 metastases) who were resistant and/or intolerant to imatinib and/or sunitinib between 2009-2013
- Patients underwent TAE
  - Bland embolization, n=19
  - TACE, n=26
- *Complications: post-embolization syndrome (self-limited)*
- *PFS was improved in bland embolization (median, 56.6 weeks) compared to TACE (median, 42.1 weeks), P=0.003)*
- *OS was longer in bland embolization (median, 74.0 weeks) compared to TACE (median, 61.7 weeks), P=0.045)*

**Table 2 Adverse events**

Adverse events	All grades (%)	
	cTACE (n=26)	Embo-TAE (n=19)
Fever	23 (88.5)	13 (68.4)
Fatigue	16 (61.5)	10 (52.6)
ALT abnormality	22 (84.6)	9 (47.4)
Nausea	14 (53.8)	14 (73.7)
Ascites	5 (19.2)	4 (21.1)
Diarrhea	5 (19.2)	3 (15.8)
Hematochezia	3 (11.5)	4 (21.1)
Neutropenia	12 (46.2)	5 (26.3)
Anemia	22 (84.6)	12 (63.2)
Thrombopenia	10 (38.5)	7 (36.8)
Hepatic abscess	NA	NA

NA, not applicable; cTACE, conventional transcatheter embolization.

**Table 1 Patients' clinical characteristics**

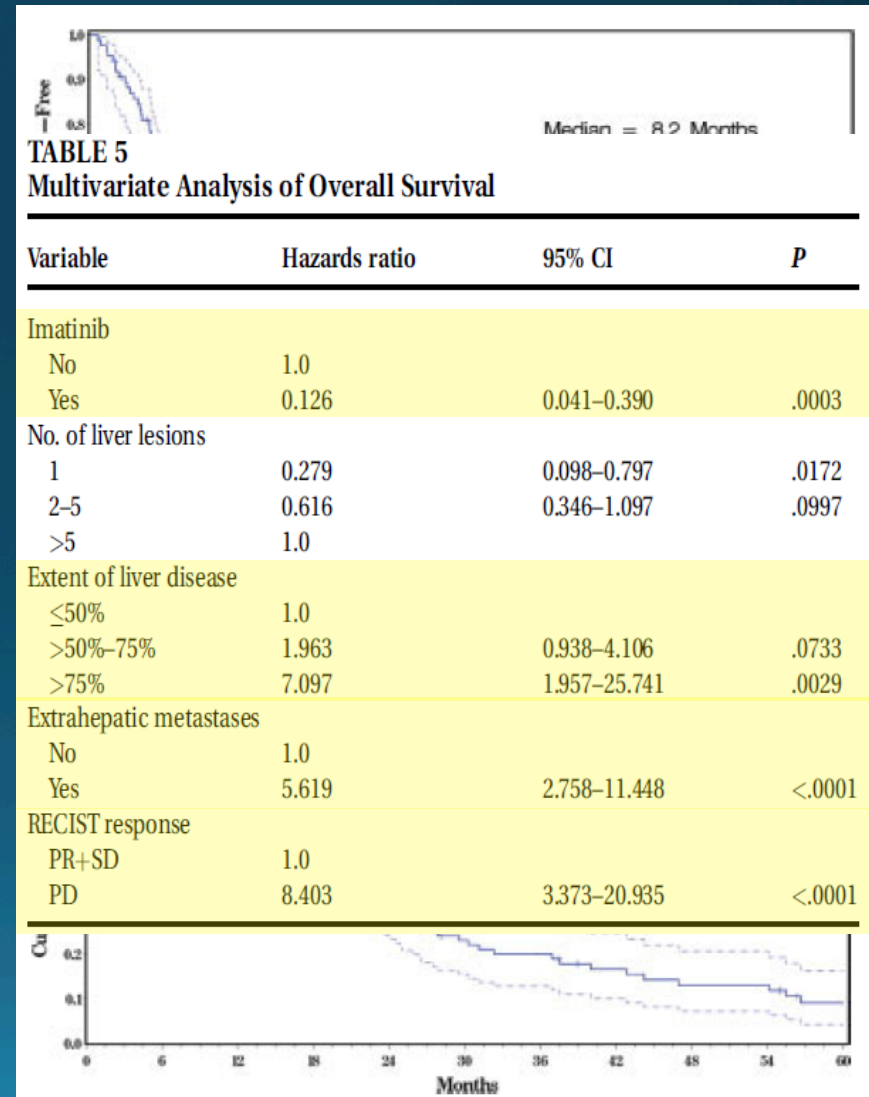
Characteristics	Total	cTACE	Embo-TAE	P
Sex				0.619
Male	33	19	14	
Female	12	7	5	
Age (year)	53.1	53	55	0.158
ECOG PS				0.668
0-1	35	20	15	
2	10	5	5	
Primary location				0.166
Stomach	21	12	9	
Small intestine	17	12	5	
Other	7	2	5	
Number of liver lesions				0.987
1	17	10	7	
2-3	19	11	8	
>5	9	5	4	
Extent of liver involvement				0.165
<50%	34	17	17	
50-70%	10	8	2	
>70%	1	1	0	
Extrahepatic metastasis				0.076
Yes	26	12	14	
No	29	14	15	
TKI reintroduction				0.125
Yes	40	24	16	
No	5	4	1	

cTACE, conventional transcatheter arterial chemoembolization; Embo-TAE, Embosphere®-transcatheter arterial embolization; ECOG, Eastern Cooperative Oncology Group; TKI, tyrosine kinase inhibitor.



# TACE prior to Imatinib

- Retrospective study at MD Anderson using TACE with cisplatin administered in 110 patients from 1993-2005
- Imatinib used in n=11 patients (10%)
- Tumor size > 5 cm, n=69 (63%)
- No. of liver metastases > 2, n= 87 (77.3%)
- *Median progression free survival was 8.2 months*
- *Median overall survival (OS) was 17.2 months*
- *Factors associated with OS*



# TAE following Imatinib +/- Sunitinib

- Retrospective review of patients with GIST metastatic to the liver in 11 patients who underwent bland embolization from 2002-2013
- Patients stratified according to prior treatment
  - A. TAE used as second-line treatment after failing imatinib, n=3 (median PFS 3.9 months; median OS 14.9 months)
  - B. TAE used as third-line treatment after failing sunitinib, n=8 (median PFS 3.4 months; median OS 23.6 months)
  - C. *Most patients had tumors with a maximum diameter > 5 cm and numbering > 5*
- Complications: post-embolization syndrome (self-limited)

**Table 1** Patient background and tumor characteristics

Parameter	Overall	Group A	Group B	p value
Patient no.	11	3	8	
Age (years)	58.0±11.6	61.7±12.7	59.9±13.0	0.54
≤60	7 (63.6)	1 (33.3)	6 (75.0)	0.49
>60	4 (36.4)	2 (66.7)	2 (25.0)	
Gender				>0.99
Male	6 (54.5)	2 (66.7)	4 (50.0)	
Female	5 (45.5)	1 (33.3)	4 (50.0)	
Primary site				p.49
Stomach	8 (72.7)	3 (100)	5 (62.5)	
Other	3 (27.3)	0	3 (37.5)	
Ileum	1 (9.1)	0	1 (12.5)	
Duodenum	1 (9.1)	0	1 (12.5)	
Retroperitoneum	1 (9.1)	0	1 (12.5)	
Maximum diameter of liver metastasis (cm)				>0.99
≤5	5 (45.5)	1 (33.3)	4 (50.0)	
>5	6 (54.5)	2 (66.7)	4 (50.0)	
Tumor number				>0.99
≤5	4 (36.4)	1 (33.3)	4 (50.0)	
>5	7 (63.6)	2 (66.7)	4 (50.0)	
Extrahepatic lesion				>0.99
Absent	6 (54.5)	2 (66.7)	4 (50.0)	
Present	5 (45.5)	1 (33.3)	4 (50.0)	
Peritoneum, lung, rectum	1 (9.1)	1 (9.1)	0	
Peritoneum	1 (9.1)	0	1 (9.1)	
Lung	1 (9.1)	0	1 (9.1)	
Stomach	1 (9.1)	0	1 (9.1)	
Leg	1 (9.1)	0	1 (9.1)	

Numbers in parentheses are percentages

# 56 Year-Old Female with Metastatic GIST on Imatinib (800 mg)

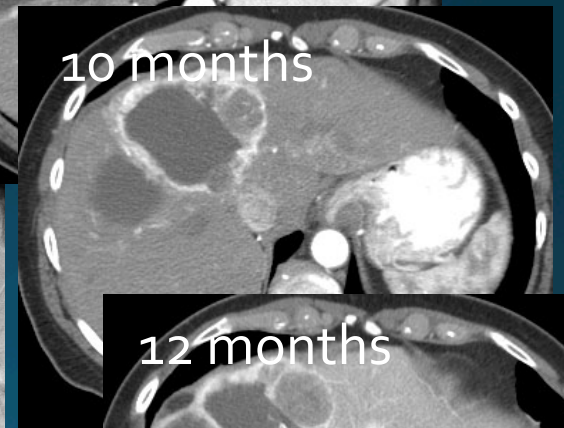
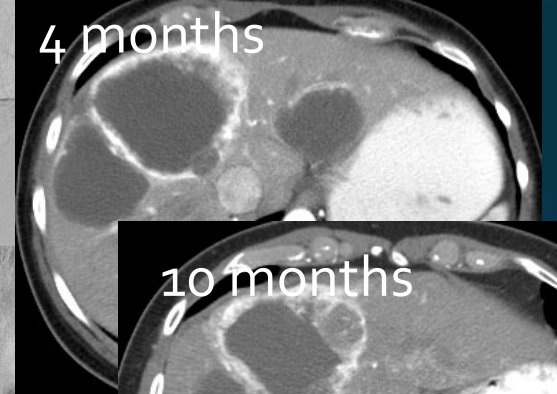
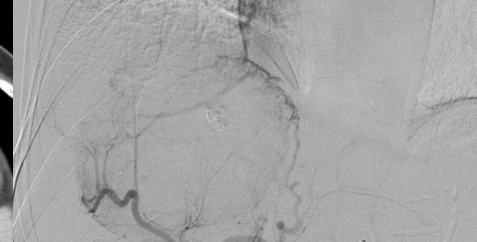
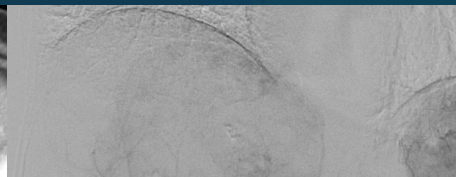
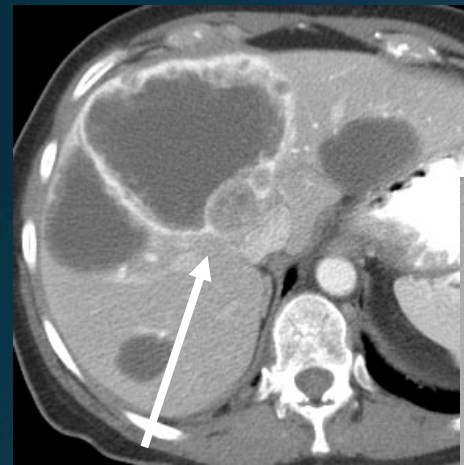
Liver metastasis

TAE

CT follow-up

TAE #2

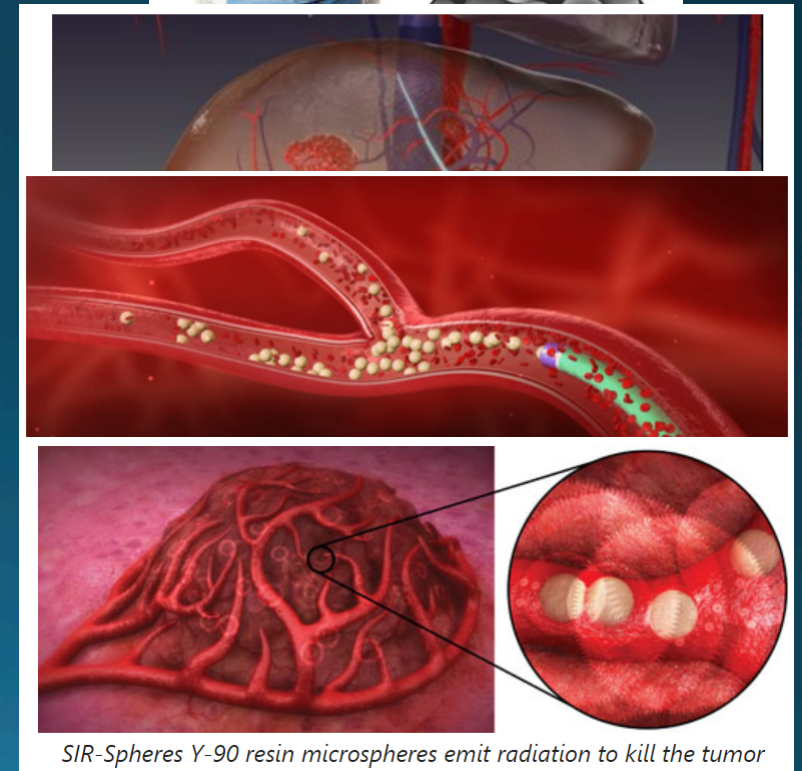
CT follow-up



# TAE with Yttrium-90 (TARE)

## Yttrium-90

- Y-90 is a pure  $\beta$ -emitter with limited tissue penetration (mean 2.5 mm, maximum 11 mm) and short-half life (64.1 hours)
- Microspheres are not degraded and remain permanently implanted allowing local tumor doses ranging from 50 to > 1000 Gy
- Y90 requires 2 procedures
  - Planning procedure to localize particle distribution and avoid lung shunting
  - Y90 administration procedure
- Surrogate for Y90 localization is performed with administration intra-arterial of  $^{99m}\text{Tc}$ -MAA (planning procedure), which distributes according to blood flow and trapped in the liver on the first pass
- Delivery of radiation complete in ~2 weeks



# TARE for Patients with Progressive GIST Liver Metastases

- Retrospective review of 11 patients with GIST metastases to the liver failing TKI therapy between 2008-2013
- $\geq 2$  lines of therapy administered in entire cohort
- Patients received maintenance therapy following TARE

**Table 1 . Patient Age at RE, Diagnosis Date, and Chemotherapies Administered**

Pt. No./Sex/Age (y)	Initial Diagnosis Date	Time to RE (mo)	Chemotherapy	
			Before RE	After RE
1/F/34	06/1999	104	Imatinib 400 mg, imatinib 600 mg + everolimus, sunitinib	Sunitinib, nilotinib, regorafenib
2/F/52	09/2006	22	Imatinib 400 mg, imatinib 600 mg + everolimus, sunitinib	Imatinib 800 mg, nilotinib, sorafenib
3/M/73	05/2005	50	Imatinib 400 mg, imatinib 800 mg, sunitinib, nilotinib	Sorafenib, everolimus
4/M/55	09/2003	70	Imatinib 400 mg, imatinib 600 mg, imatinib 800 mg	Sunitinib, imatinib 600 mg + everolimus
5/M/55	07/2007	26	Imatinib 400 mg, imatinib 800 mg, imatinib 1,000 mg, sunitinib	Sunitinib, nilotinib, sorafenib
6/M/61	03/2007	34	Imatinib 400 mg, sunitinib, sorafenib	Imatinib 800
7/M/58	06/2008	43	Imatinib 400 mg, sunitinib	Sorafenib
8/M/48	12/2004	85	Imatinib 400 mg, imatinib 800 mg, sorafenib	Nilotinib
9/M/74	08/2011	20	Imatinib, sunitinib	Pazopanib

RE = radioembolization.

Median, 43 months; range, 20-104 months

# TARE for Patients with Progressive GIST Liver Metastases

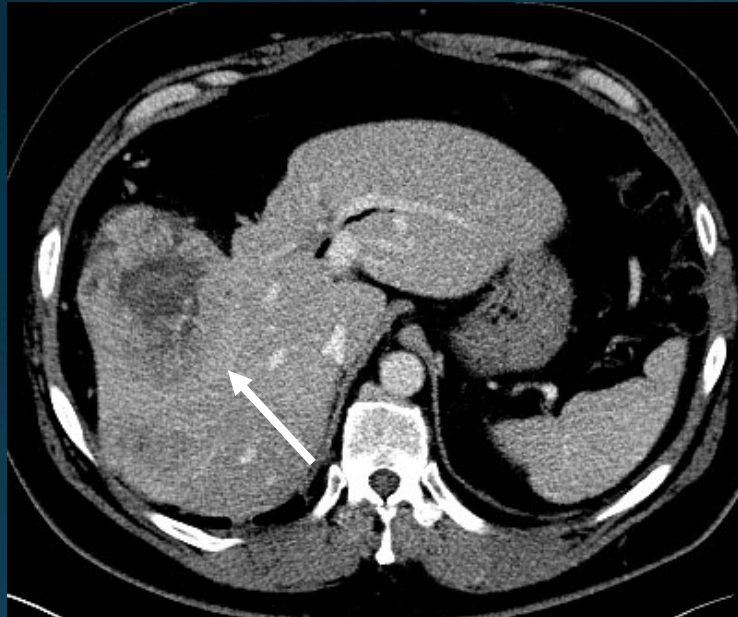
---

- Sixteen liver lobes were treated with mean activity 1.06 GBq (range, 0.55-1.88) per lobe
- All patients demonstrated radiographic response (3 CR, 5 PR, 1 SD)
- Median progression free interval 15.9 months (range, 4-29 months)
- Median overall survival 29.8 months (range, 10-72 months)
- Complications: Gastric ulcer (n=1)

# 58 Year-Old Male with Metastatic Retroperitoneal Leiomyosarcoma

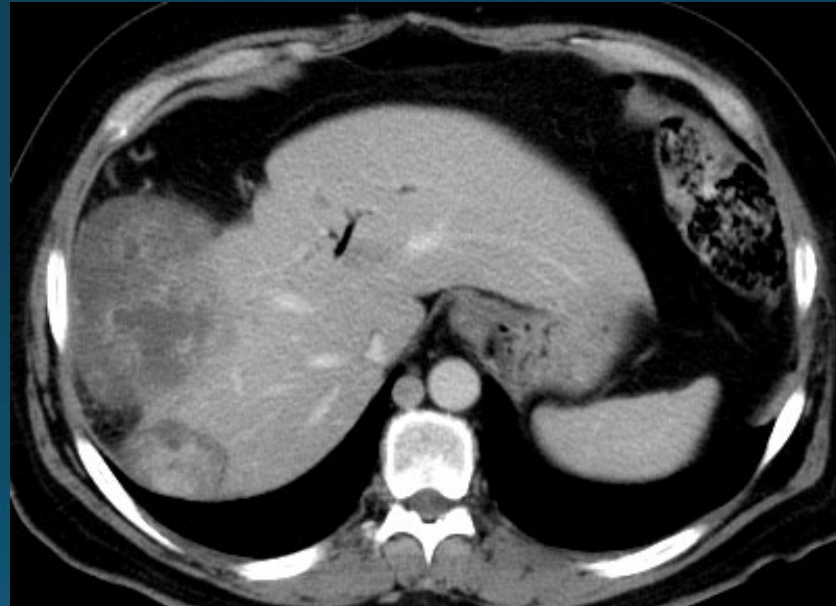
---

Liver metastasis

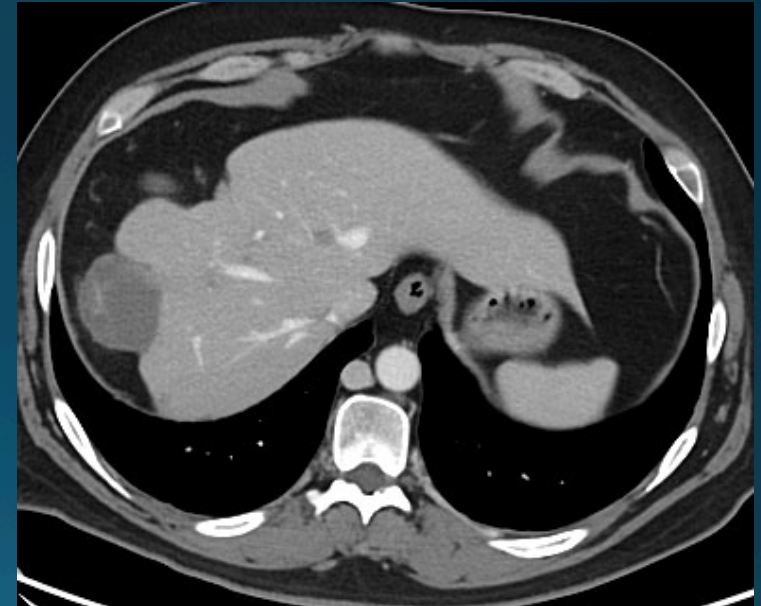


Patient treated with Y90

CT scan 3 months following Y90



CT scan 6 months following Y90



# 44 Year-Old Female with Metastatic Gastric GIST Failing Imatinib Therapy

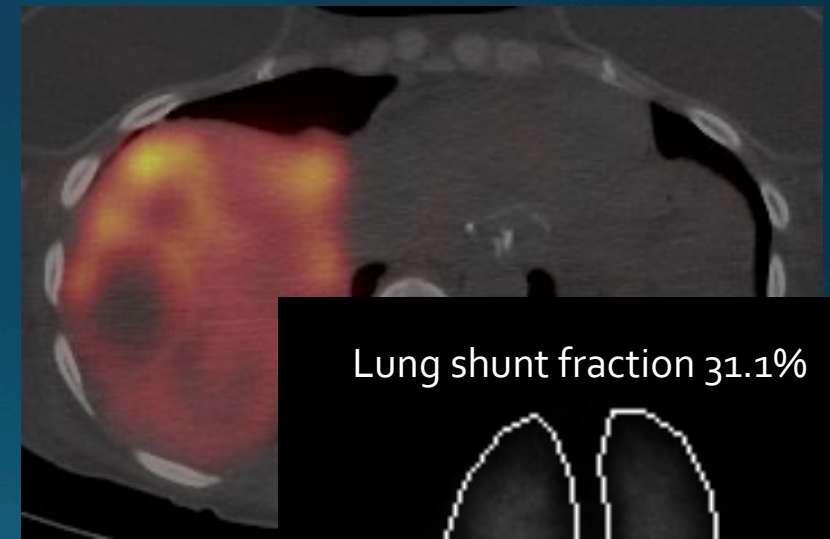
Multiple liver metastases



MRI 2 years after 2 years of imatinib



Y90 planning procedure performed



Lung shunt fraction 31.1%





# Dose Calculation for TARE

- Body Surface Area Method
  - Simple
  - Likely suitable for "small" tumors

$$BSA(m^2) = 0.20247 \times height(m)^{0.725} \times weight(kg)^{0.425}$$

$$Activity(GBq) = (BSA - 0.2) + Volumetumor \times 100 / Volumeliver$$

- Partition Method (PM)
  - Personalized dosimetry
  - Control over radiation doses to lung, liver, and tumor

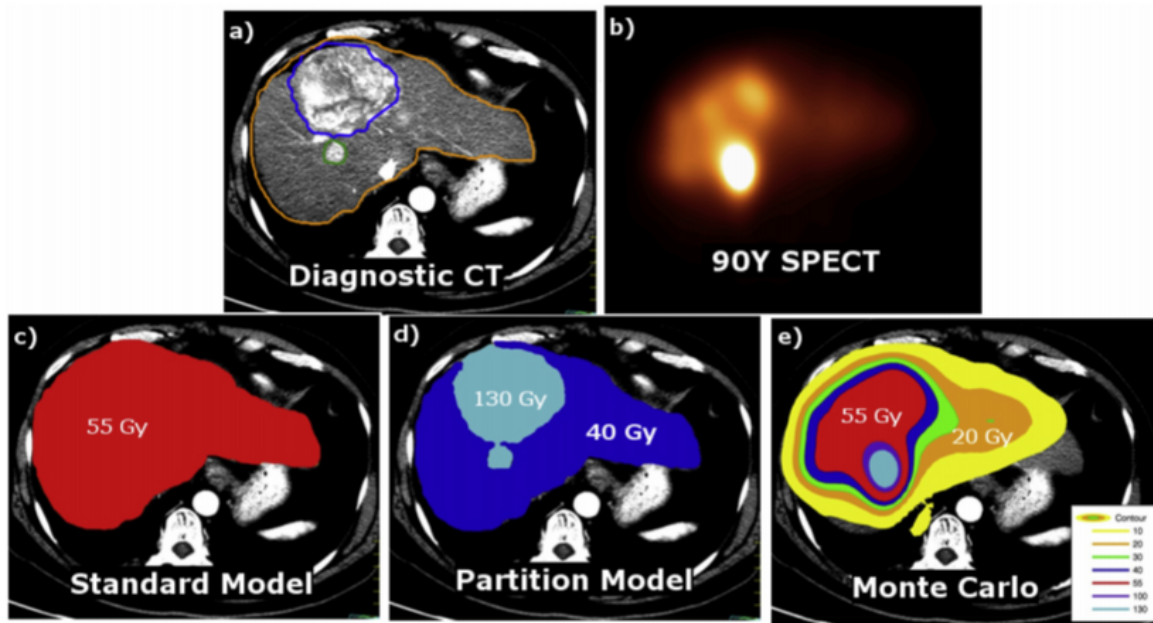
$$Activity(GBq) = D(Gy) \times [(T/N \times masstumor(kg)) + massliver(kg)] / 49,670 \times (1 - \text{shunt fraction})$$

$$T/N = (Activitytumor(GBq) / Masstumor(kg) / Activityliver(GBq) / Massliver(kg) )$$

# Importance of Dose Calculation

*Absorbed dose is NOT uniform and affected by*

- Heterogeneous normal liver uptake*
- Heterogeneous tumor uptake*
- Size and multiplicity of tumors*



**Fig. 1.** Spatial representation of the dosimetry models. (a) Diagnostic computed tomography (CT), (b) <sup>90</sup>Y single photon emission computed tomography (SPECT), (c) standard model, (d) partition model, (e) Monte Carlo. Gold, blue, red, and cyan color washes represent 20, 40, 55, and 130 Gy, respectively. (A color version of this figure is available at [www.redjournal.org](http://www.redjournal.org).)

# Activity of Radiation Delivered Affects Response and OS

- Retrospective study involving 64 patients with biliary tract cancers
- Patients not treated with concomitant chemotherapy (n=31), dose delivered to the tumor affected **objective response and OS**
- Median OS 28.2 months when dose<sub>tumor</sub> > 260 Gy vs 11.4 months when dose<sub>tumor</sub> < 260 Gy, P=0.019

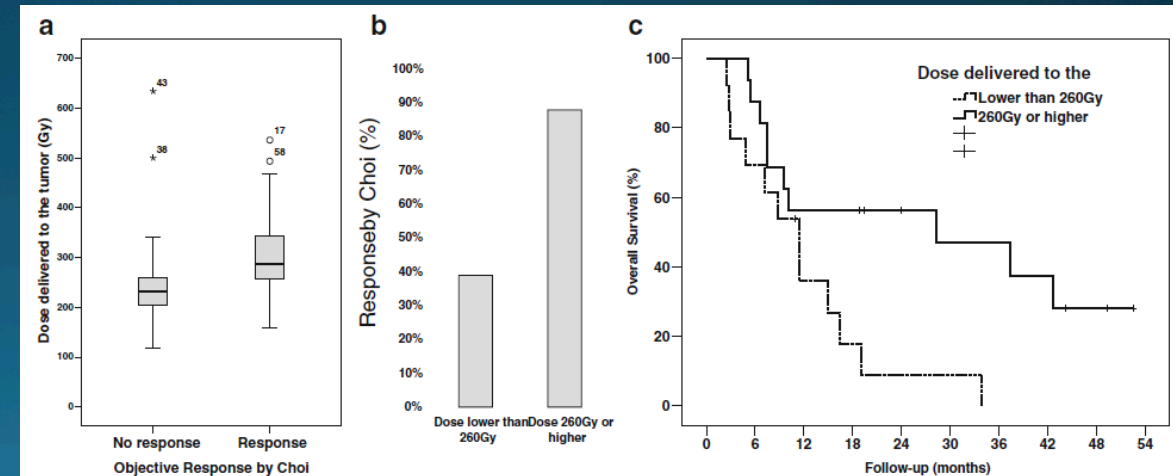


Fig. 3 Dosimetric analysis of patients treated without concomitant chemotherapy. A: Dose delivered to the tumor in patients with or without Choi response. B: Response rate assessed by Choi criteria

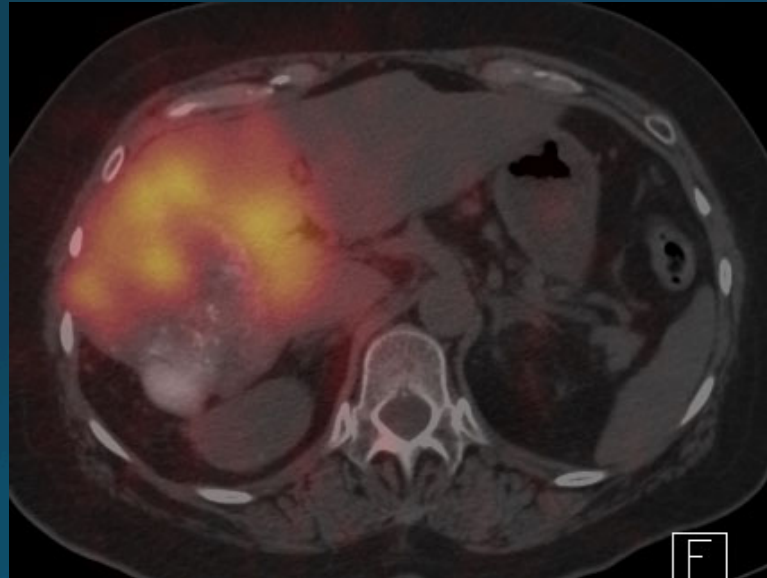
according to the dose delivered to the tumor. C: Overall survival according to the dose delivered to the tumor

# 61 Year-Old Female with Metastatic Uterine Leiomyosarcoma

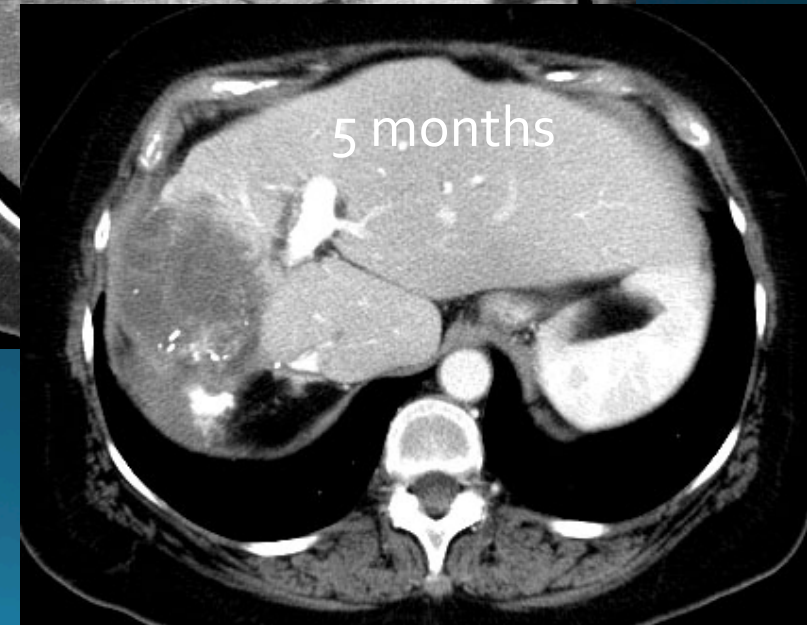
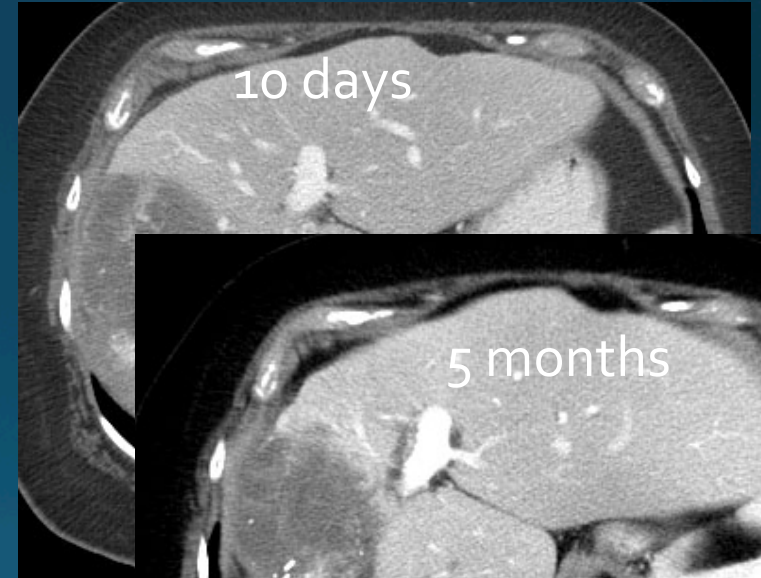
Liver metastasis



MAA mapping



Follow-up



## *Achievements*

- 1. Disease control*
- 2. Contralateral liver hypertrophy*
- 3. ?More targeted approach for resistant disease*
- 4. ?Liver resection*

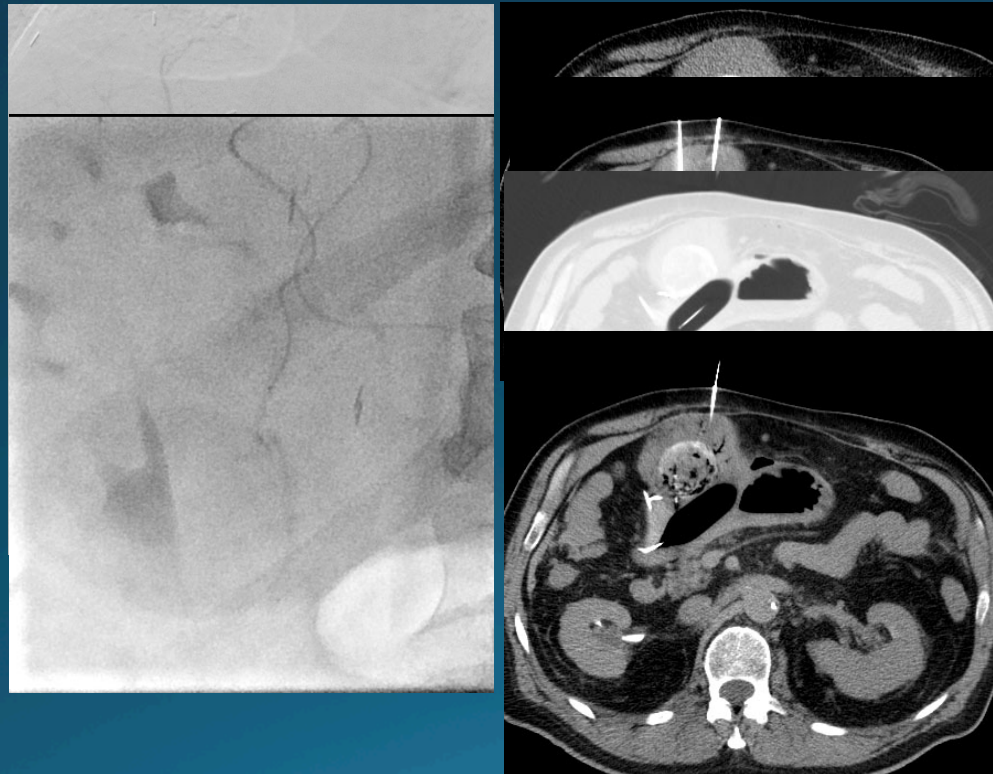
# Combination Locoregional Therapies

65 year-old male with metastatic carcinoid tumor

Liver metastasis



Combination TAE and thermal ablation



Follow-up



# Conclusions

---

- Locoregional therapies for GIST liver metastases are safe and well-tolerated
  - Thermal ablation
  - TAE (including bland embolization, chemoembolization, and radioembolization)
- Thermal ablation is best for lesions  $<3$  cm (potentially  $<5$  cm) and “few” in number
- TAE may be used to target TKI-resistant tumors larger in size and number than those treated with thermal ablation



Thank You!

THE UNIVERSITY OF TEXAS  
MD Anderson ~~Cancer~~ Center®