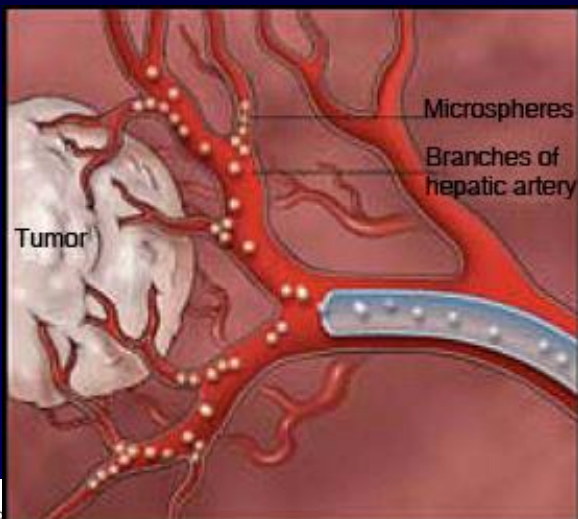
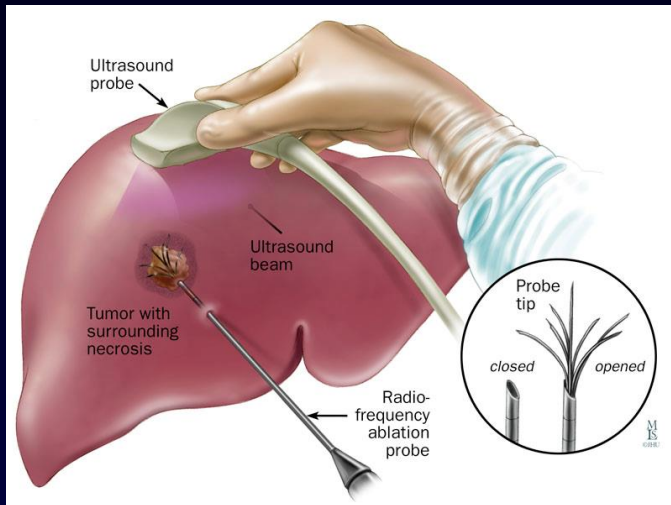




Interventional Radiology Approaches to Treat Recurrent GIST

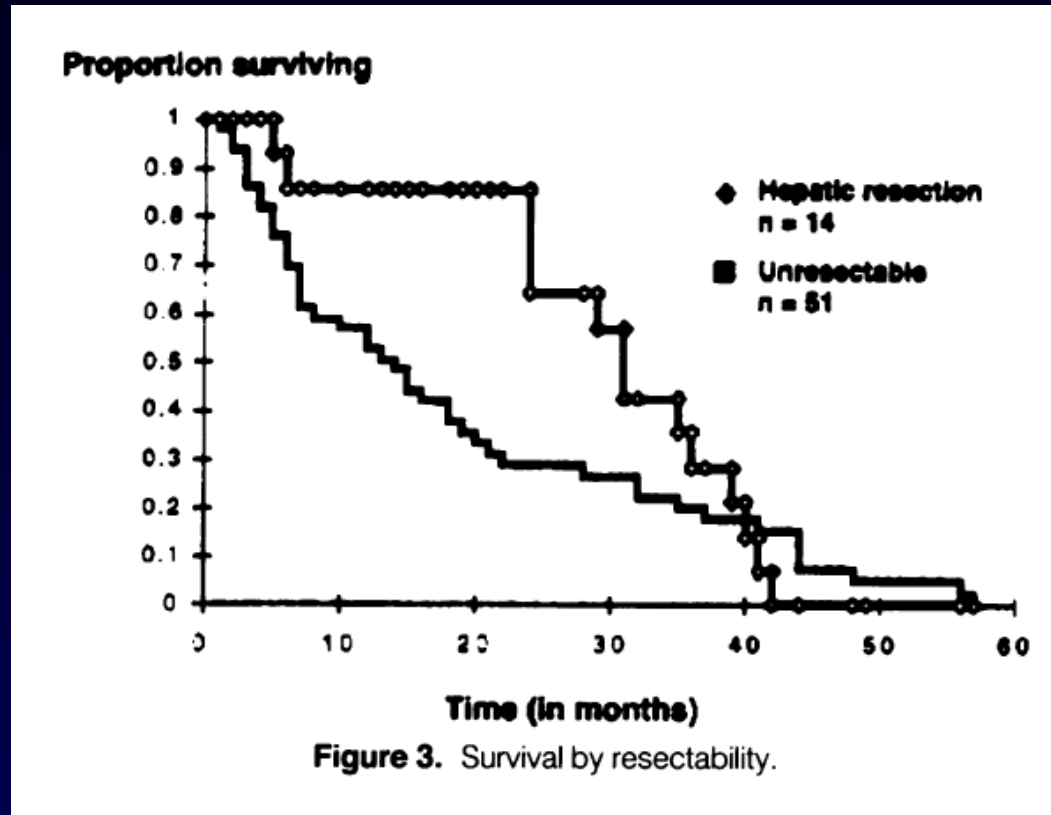
Joseph P. Erinjeri, MD, PhD
Interventional Radiology Service
Memorial Sloan-Kettering Cancer Center

Percutaneous Treatment of GIST Metastasis

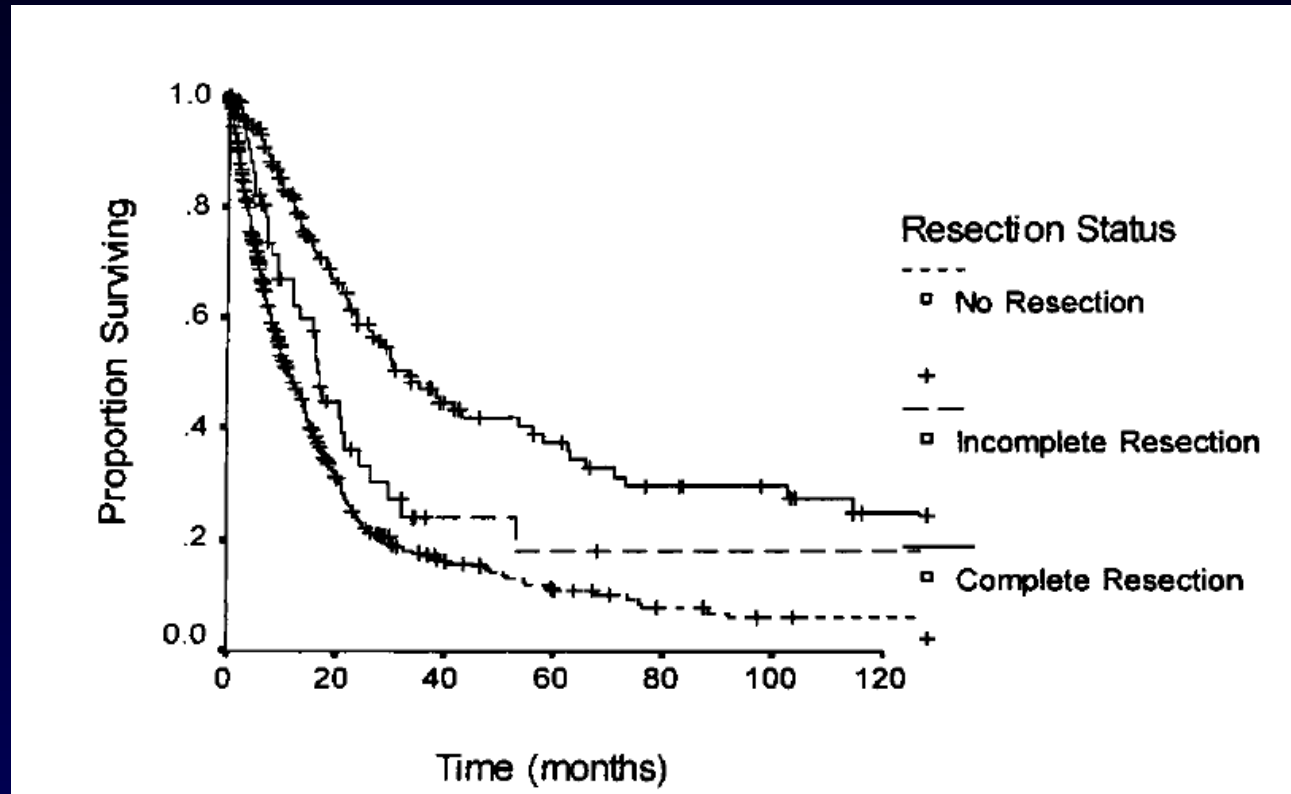


- Why IR for locoregional therapy?
- Transarterial therapies for GIST metastases
 - Hepatic artery embolization
 - Chemo-embolization
 - Drug-eluting bead chemo-embolization
- Percutaneous ablation for GIST metastases

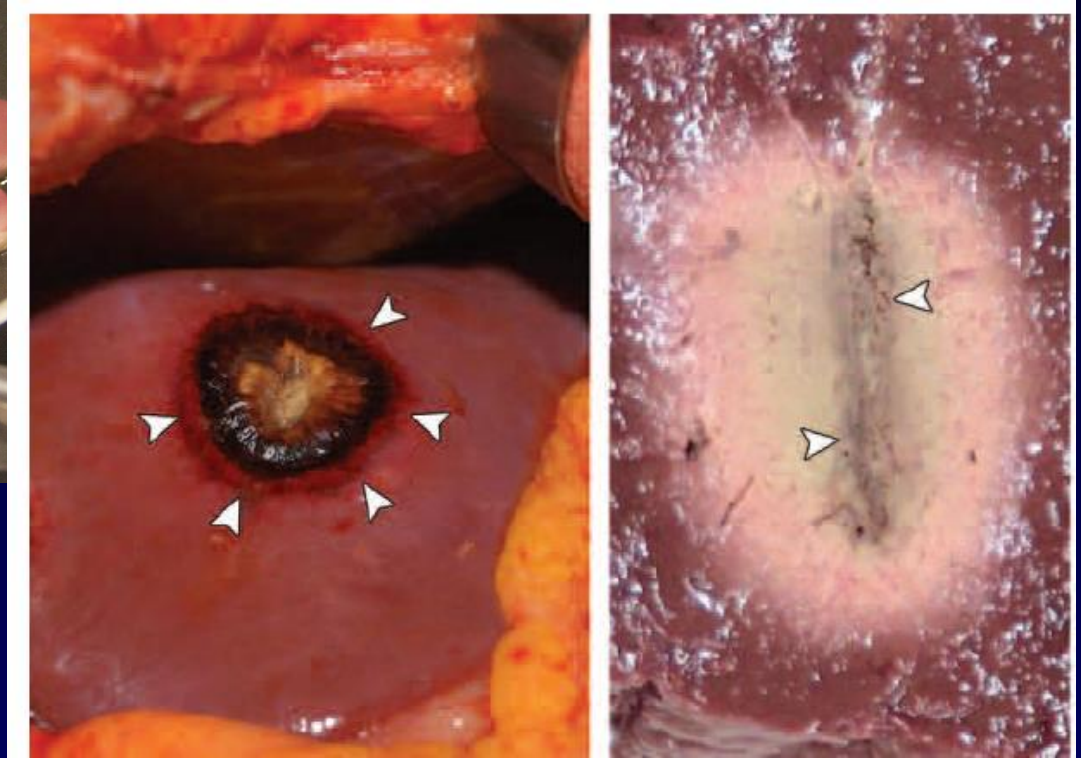
Resection of hepatic metastases results in improved patient survival compared to patients who are not resected



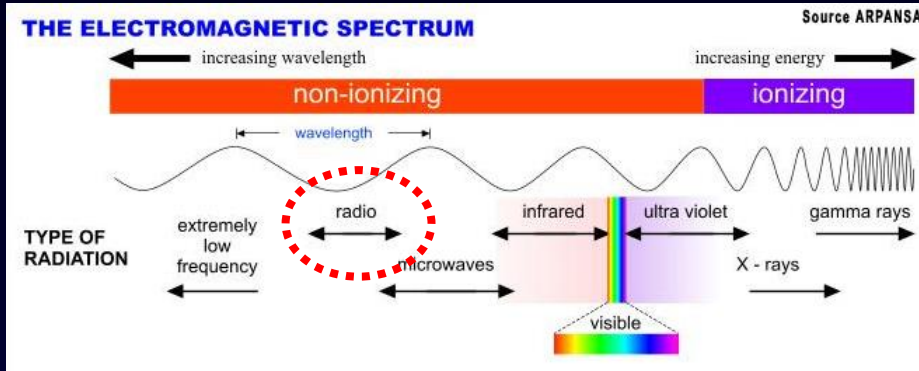
Complete resection of metastasis results in longest survival for sarcoma patients



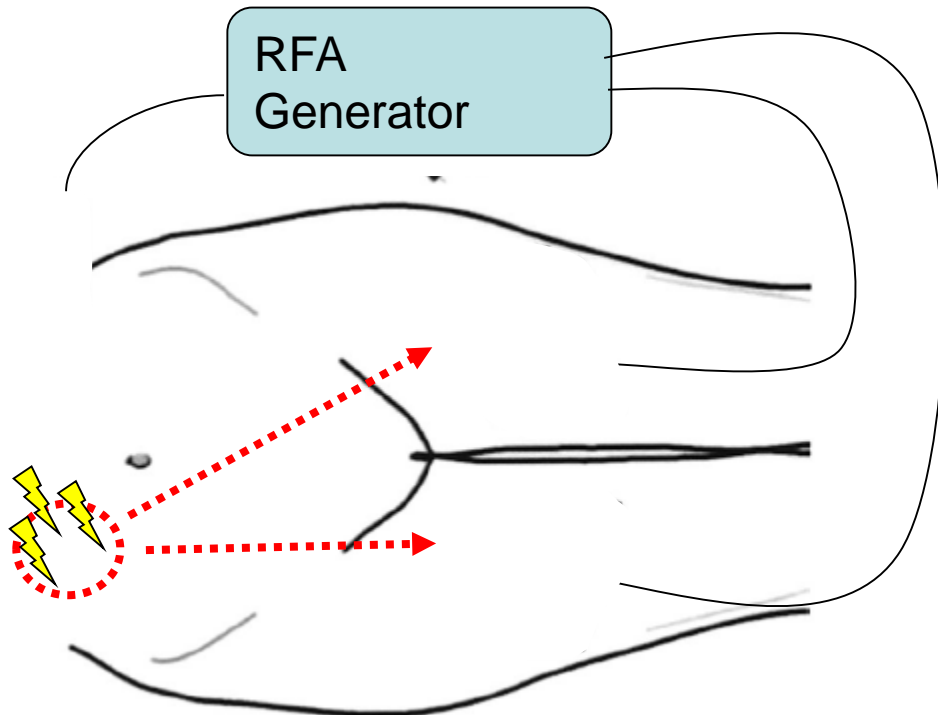
Any heat based technique (RFA or microwave) denature proteins and desiccates tumors, rendering them non-functional.



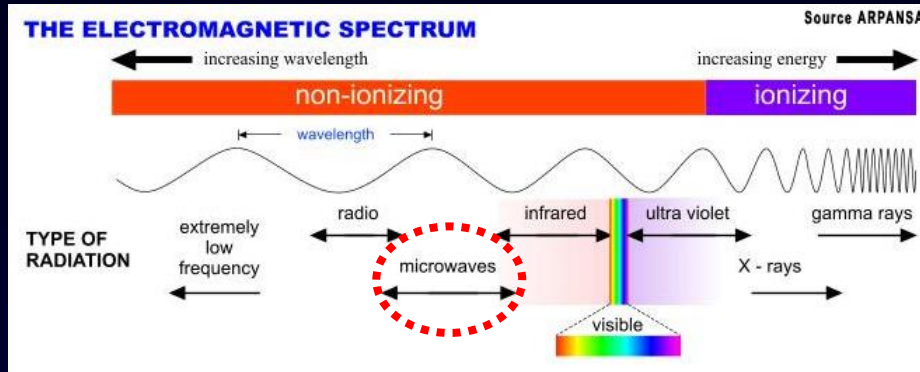
Radiofrequency ablation uses an alternating electrical current which is converted to ionic frictional heat



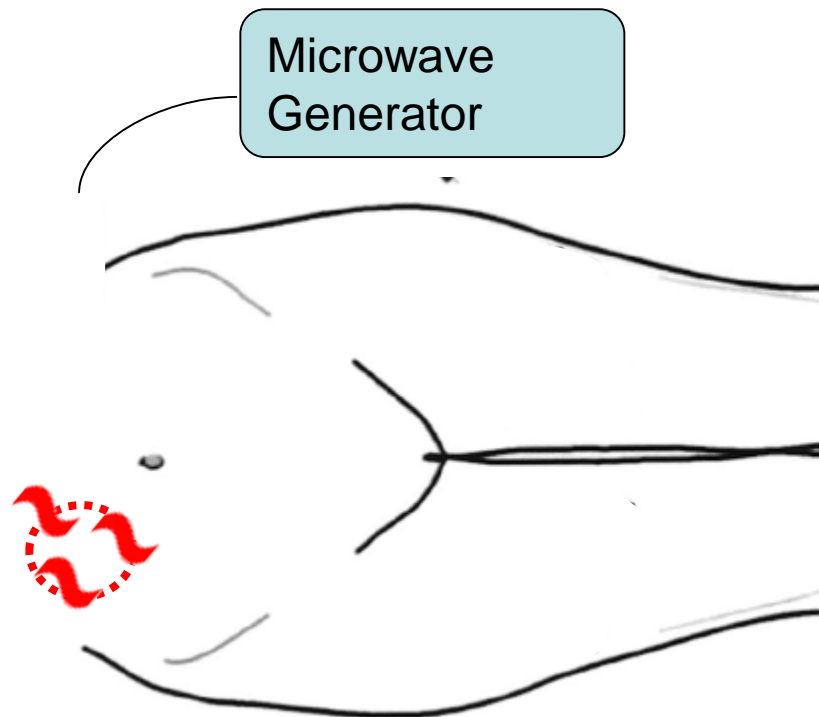
- Radiofrequency probe targeted to lesion
- Alternating electric current causes ionic friction
- Heat denatures proteins
 - Temp 60-100 deg C
 - Range 1-3 cm
- Electric circuit must be completed
 - Grounding pads



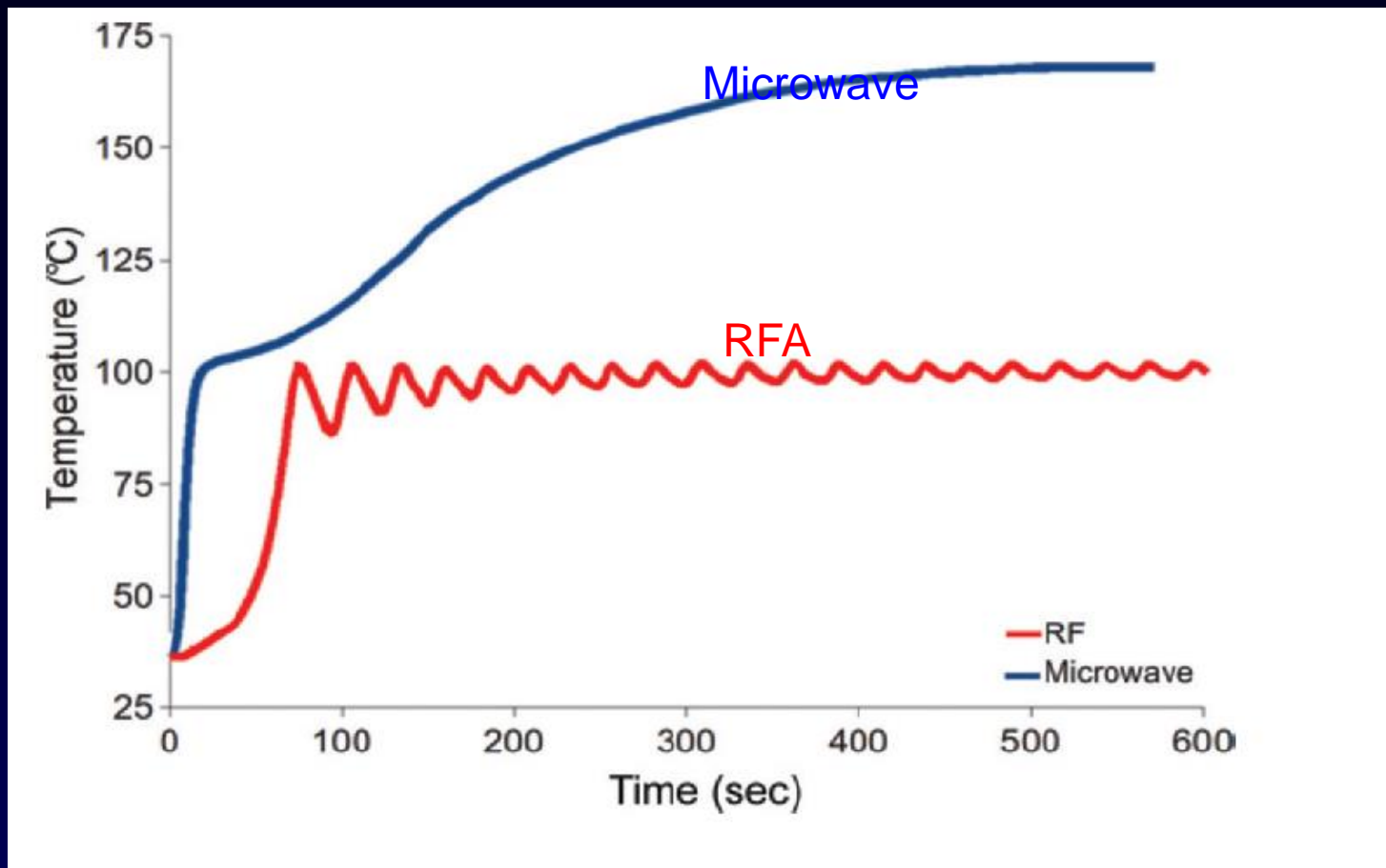
Microwave ablation uses a needle antennae that emits microwaves to heat tissues



- Microwave probe targeted to lesion
- Microwave energy causes water to boil
- Heat denatures proteins
 - Range 1-5 cm
 - 80-150 degree range
- Dont need grounding pads
- Energy is radiated, not conducted = less heat sink effect



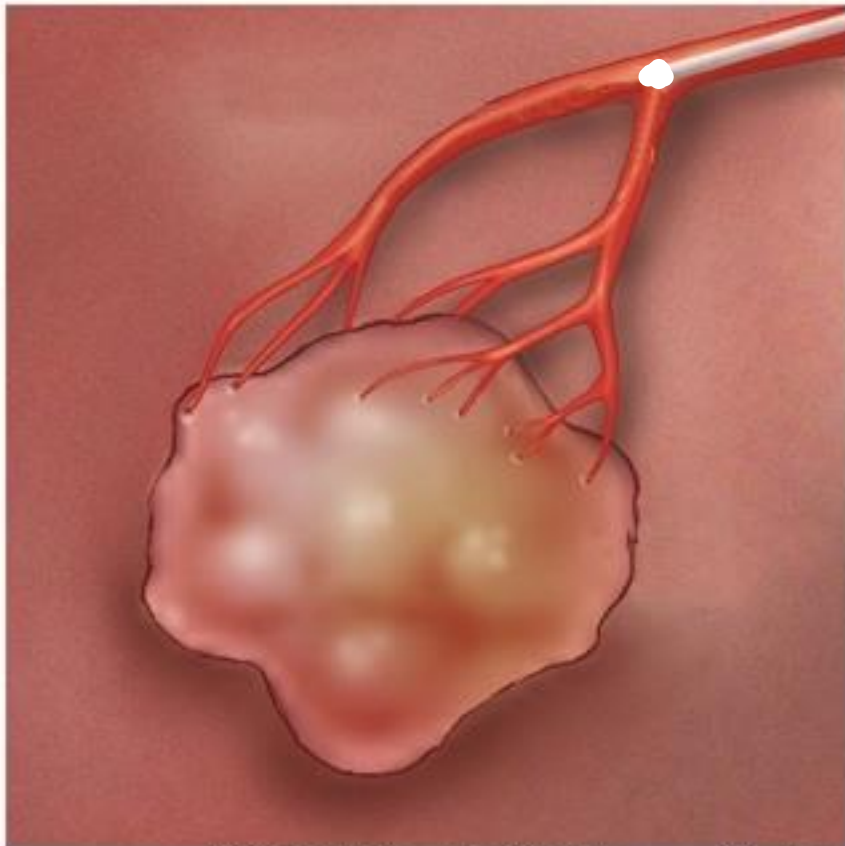
Microwave ablation can generate greater thermal damage to tumors than radiofrequency ablation.



RadioGraphics 2011; 31:377–390

Hepatic Artery Embolization

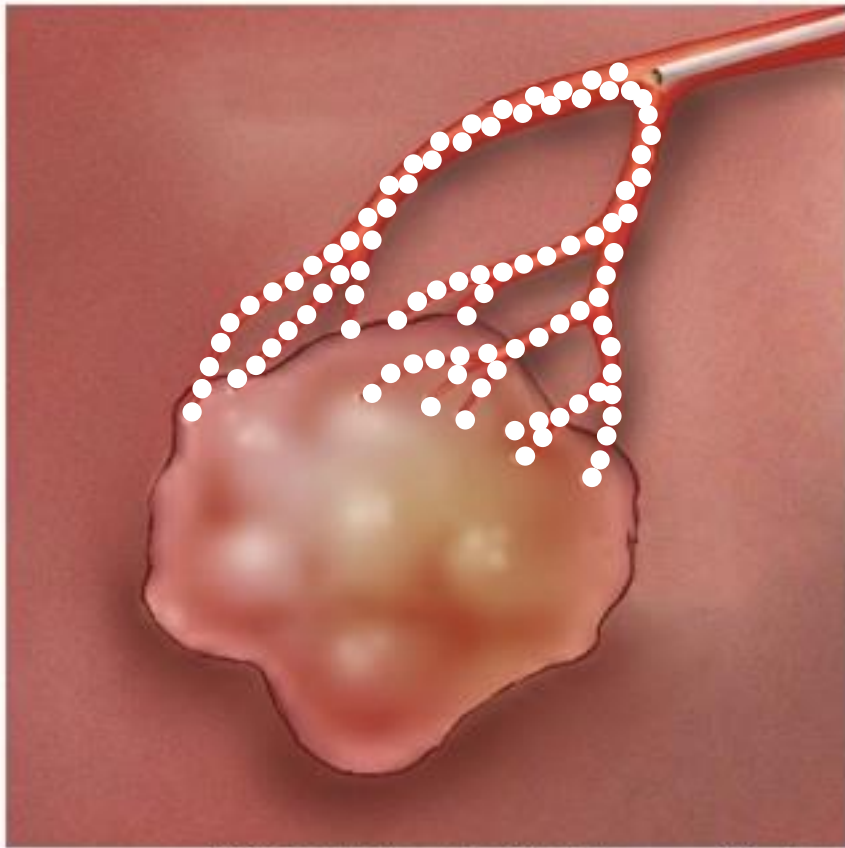
- Goal
 - Devitalize tumor via ischemic damage
 - Small particles for terminal vessel blockade
 - Endpoint of procedure
 - Stasis of flow in feeding blood vessels



© Society of Interventional Radiology, www.SIRweb.org

Hepatic Artery Embolization

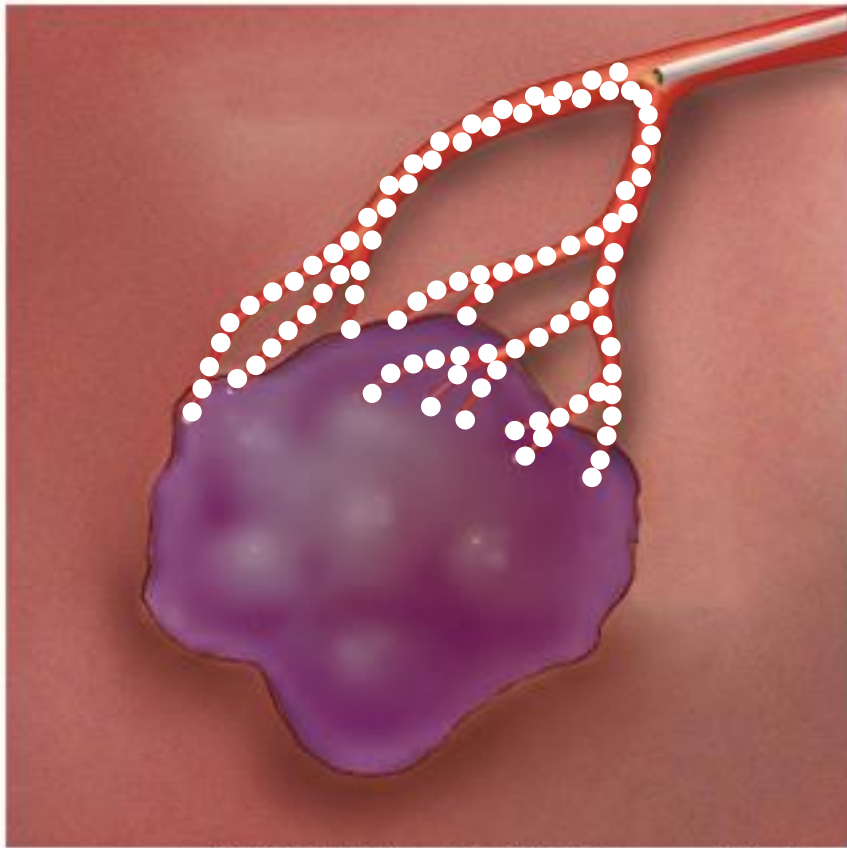
- Goal
 - Devitalize tumor via ischemic damage
 - Small particles for terminal vessel blockade
 - Endpoint of procedure
 - Stasis of flow in feeding blood vessels



© Society of Interventional Radiology, www.SIRweb.org

Hepatic Artery Embolization

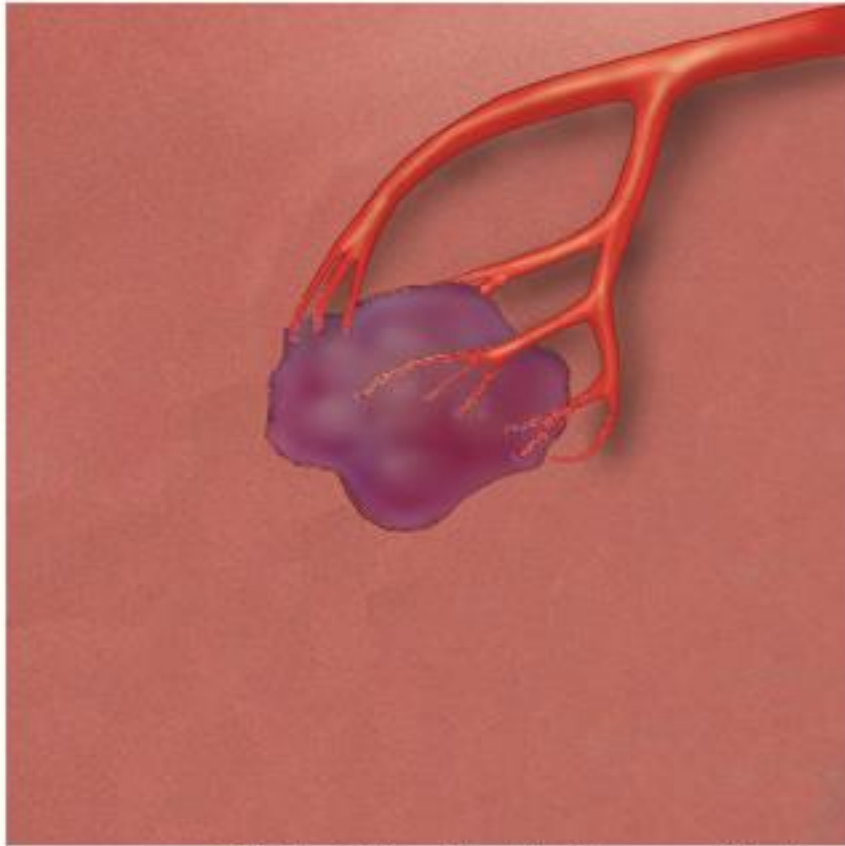
- Goal
 - Devitalize tumor via ischemic damage
 - Small particles for terminal vessel blockade
 - Endpoint of procedure
 - Stasis of flow in feeding blood vessels



© Society of Interventional Radiology, www.SIRweb.org

Hepatic Artery Embolization

- Goal
 - Devitalize tumor via ischemic damage
 - Small particles for terminal vessel blockade
 - Endpoint of procedure
 - Stasis of flow in feeding blood vessels



© Society of Interventional Radiology, www.SIRweb.org

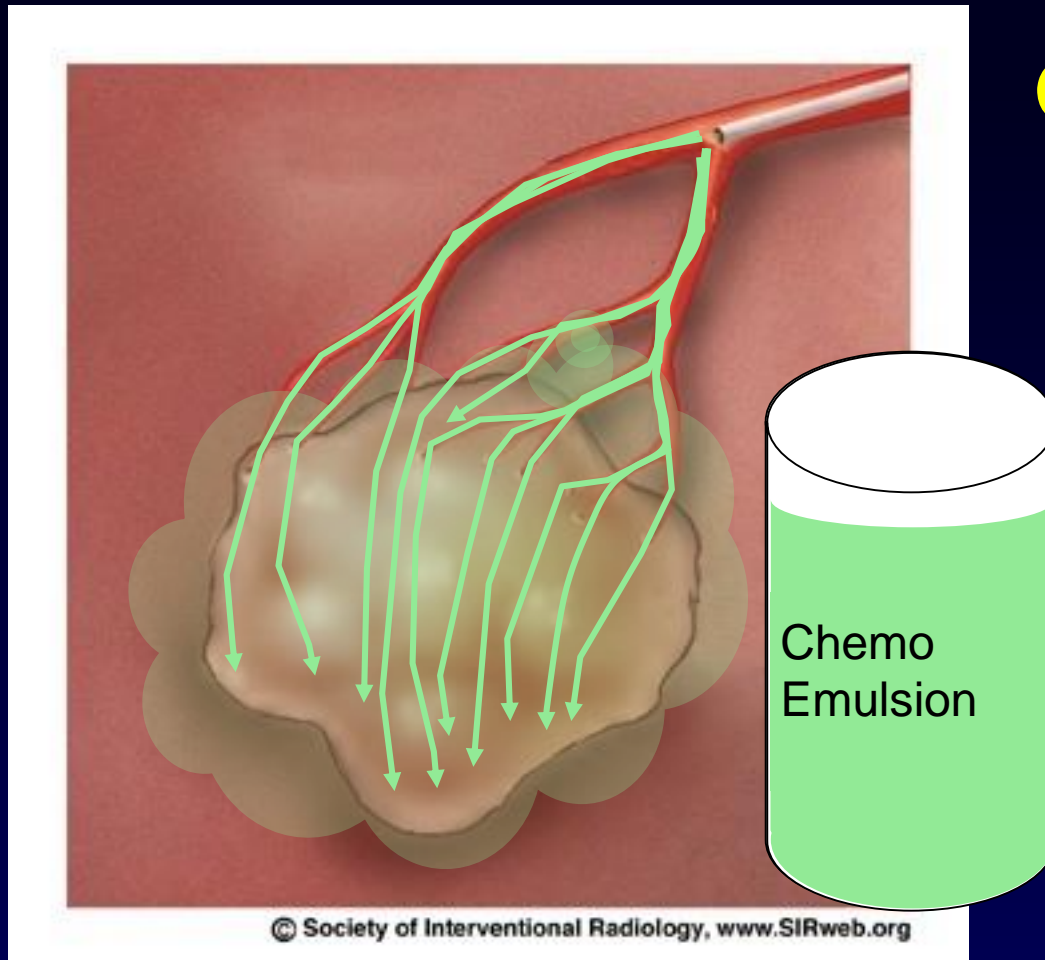
TACE

Goal

- Devitalize tumor via chemotherapeutic effect

Technical issues

- Chemo-emulsion delivered to tumor



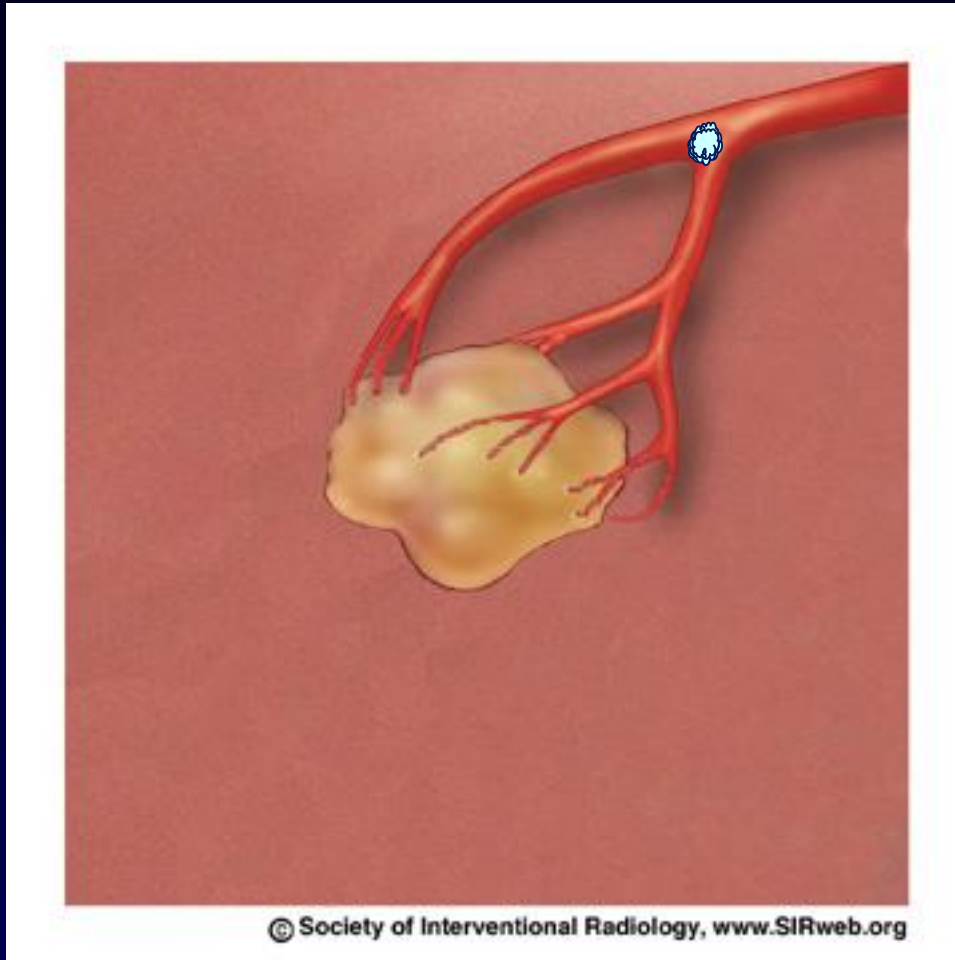
TACE

Goal

- Devitalize tumor via chemotherapeutic effect

Technical issues

- Chemo-emulsion delivered to tumor
- Large particle embolization
 - Gelfoam pledgets
- **NOT** performed to stasis
 - Slowed antegrade flow to tumor



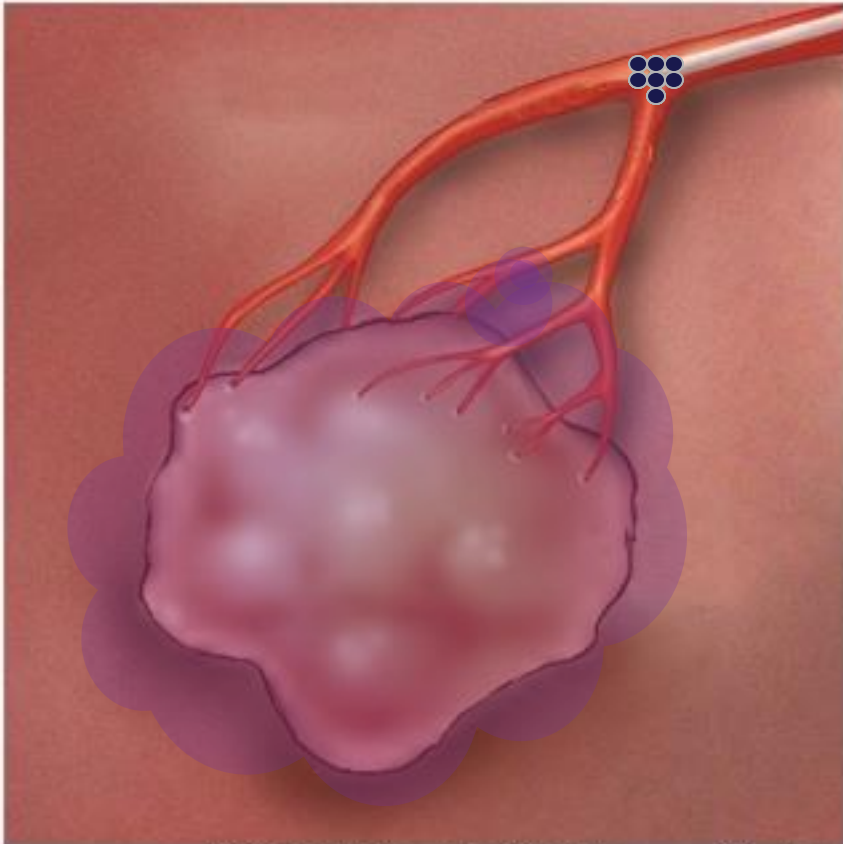
TACE

Goal

- Targeted delivery of chemotherapy

Technical issues

- Small particles for penetration of tumor
 - 100-300 micron
 - Drug is slowly eluted into tumor
- Complete occlusion of tumor vessels
- Avoid stasis in parent vessel



© Society of Interventional Radiology, www.SIRweb.org

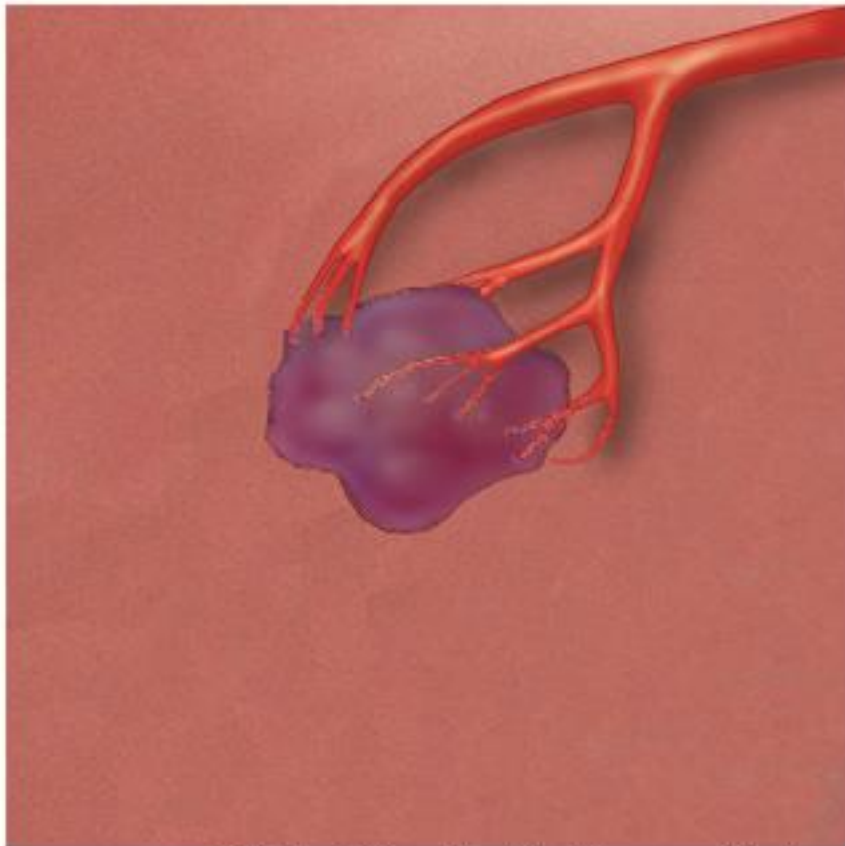
DEB-TACE

Goal

- Targeted delivery of chemotherapy

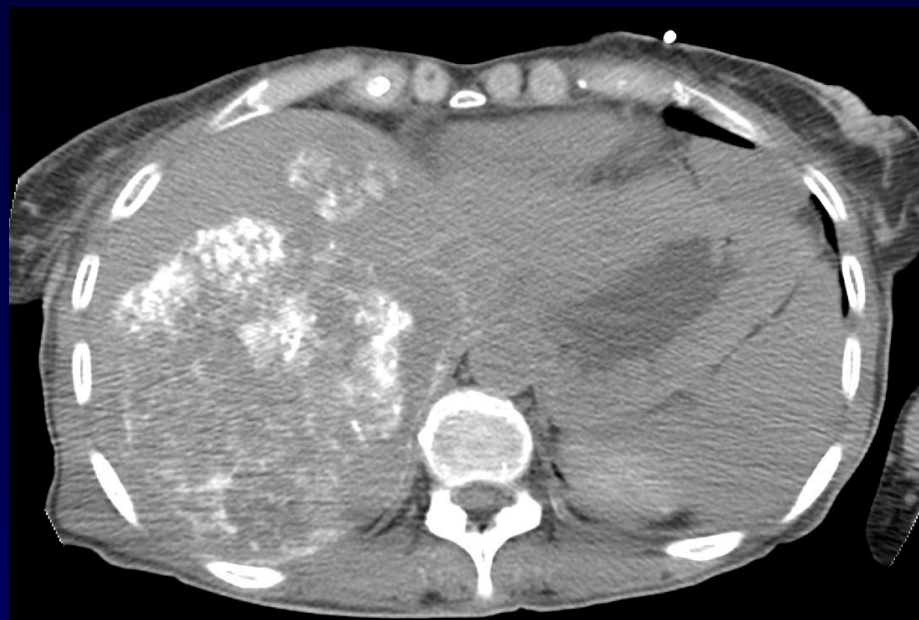
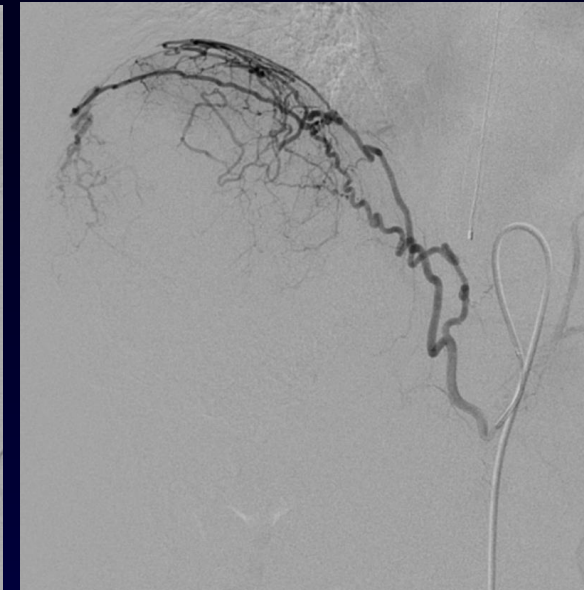
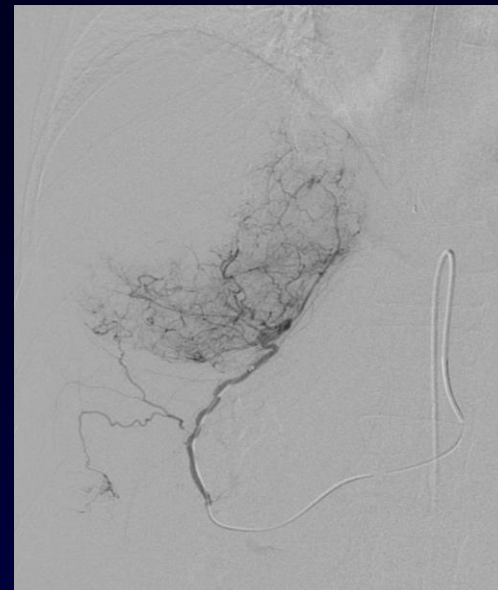
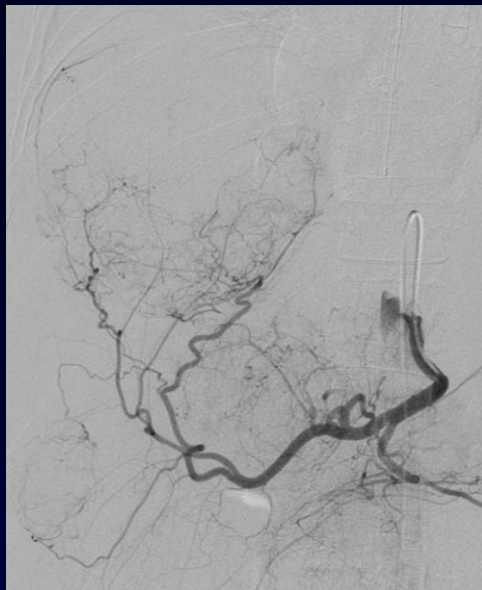
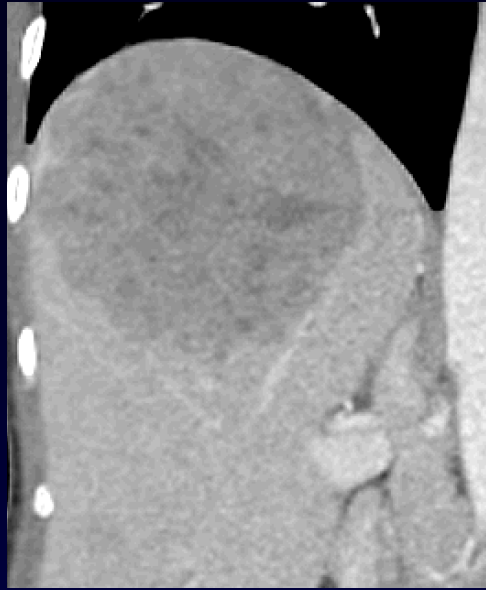
Technical issues

- Small particles for penetration of tumor
 - 100-300 micron
- Chemotherapy + ischemia results in tumor cell death

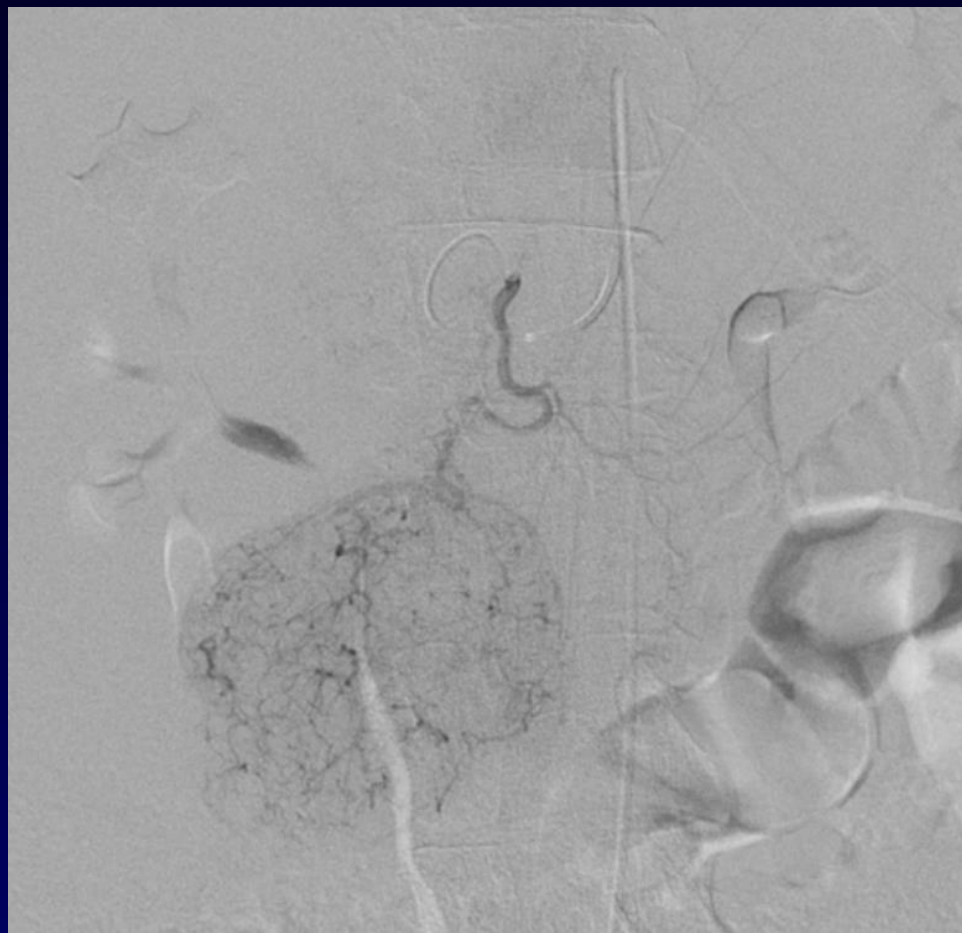


© Society of Interventional Radiology, www.SIRweb.org

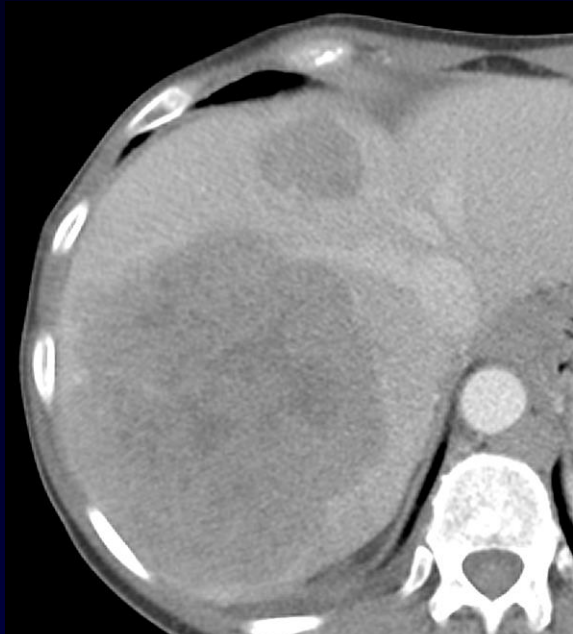
The blood supply to a sarcoma liver metastasis can be disrupted by identifying individual feeder vessel under realtime fluoroscopy



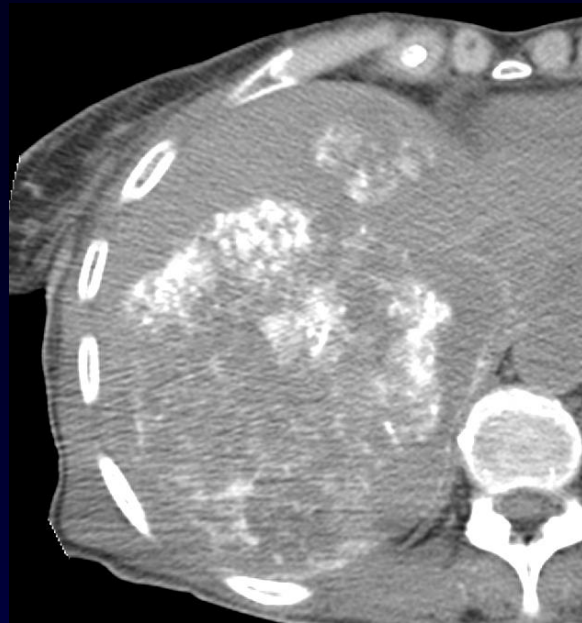
6 weeks later



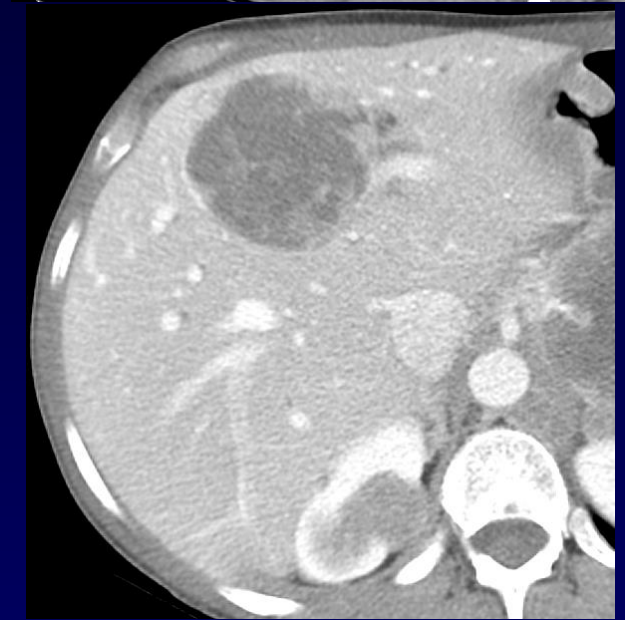
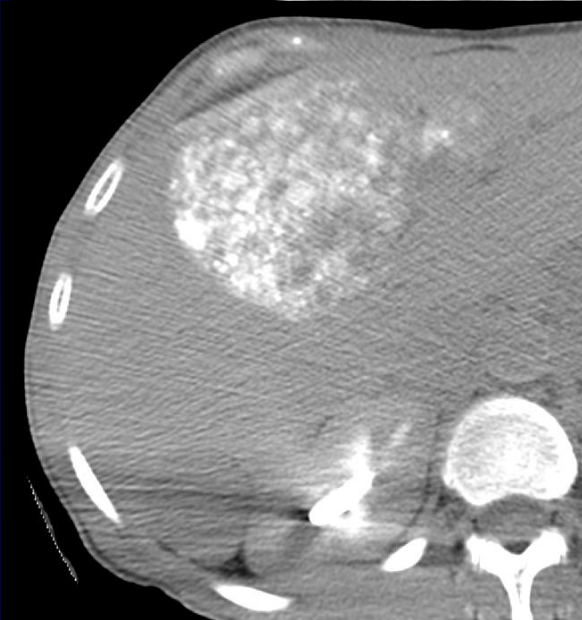
Pre



Immediate Post



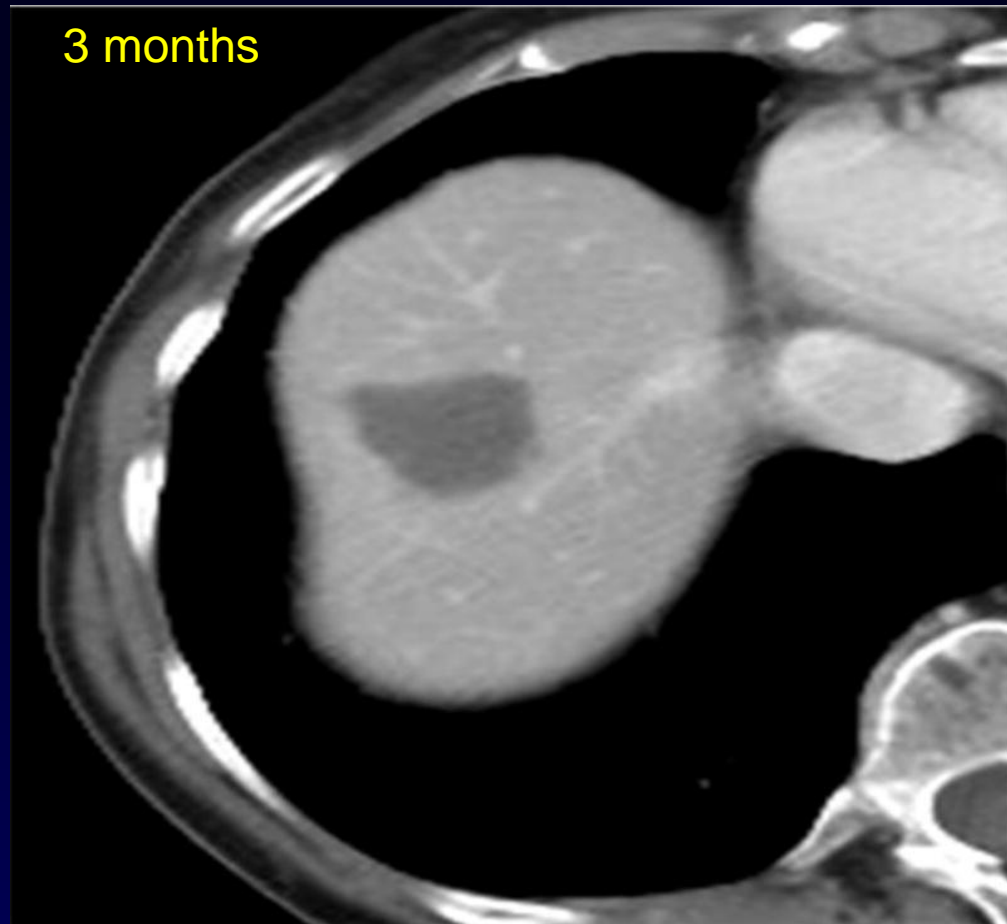
4 Months Post



76-yo with GIST metastatic to the liver

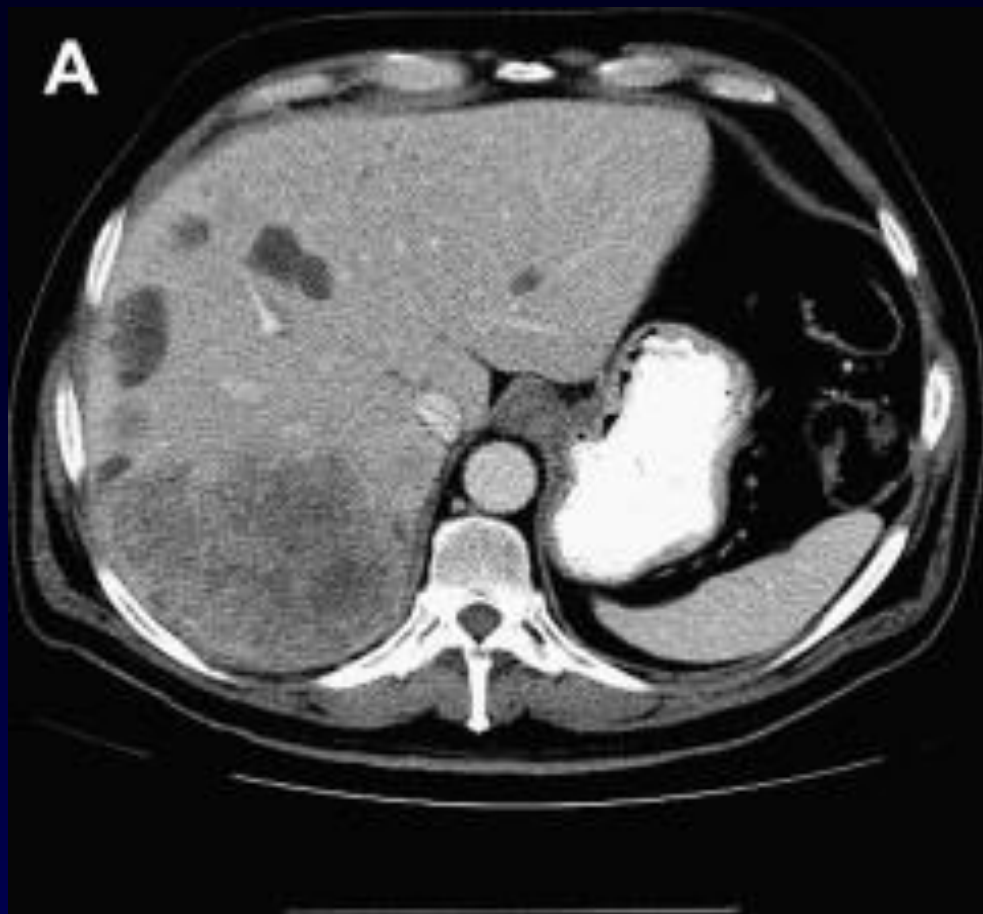


3.9 cm mass in anterior segment of the liver



After HAE, tumor size decreased and replaced to non-enhancing area

65-yo with GIST with progressive hepatic metastasis while receiving imatinib treatment

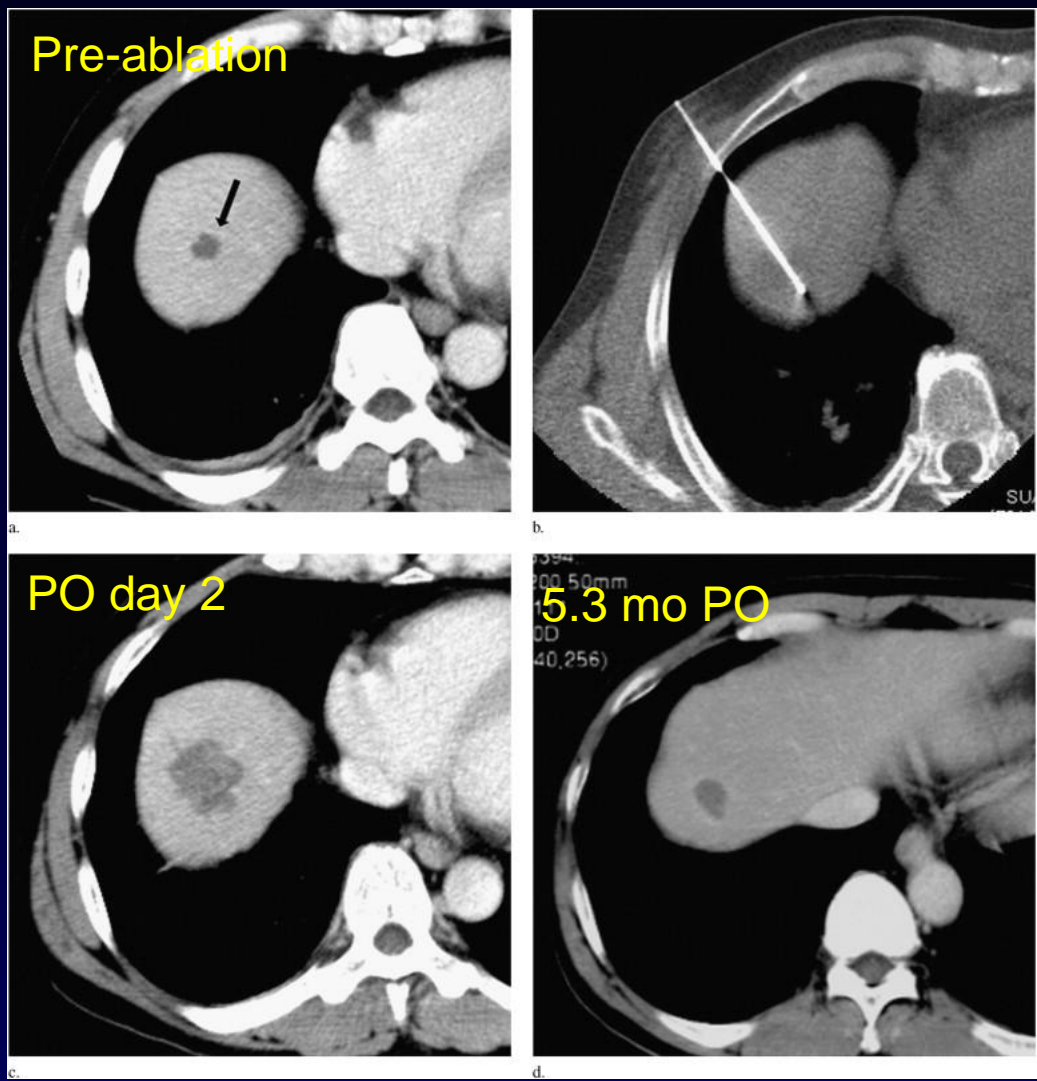


Avritscher et al, Hematology/Oncology Clinics; 23,1: 129-137

Large solid mass in posterior right liver

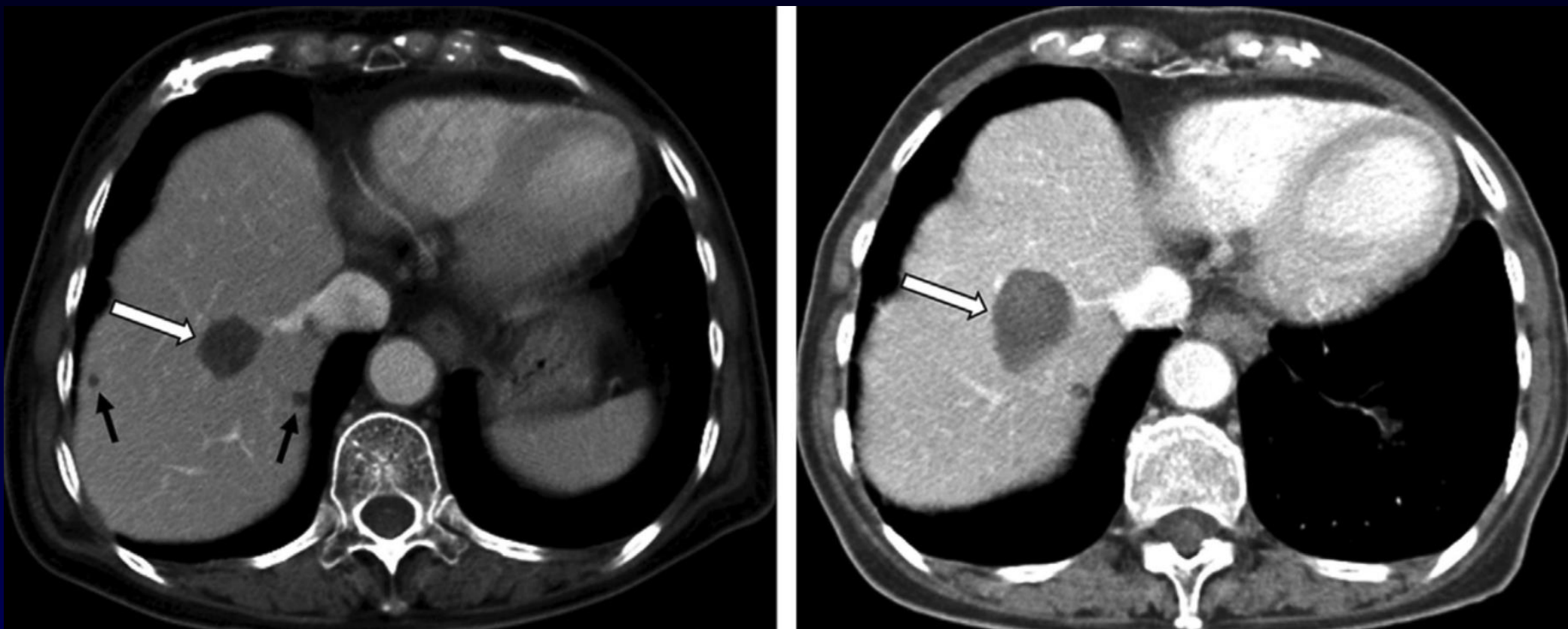
Decrease in density of mass post-HACE

55-yo with GIST metastatic to the liver



Yamanaka et al, JVIR; 2013; 24,3: 341-346

77 with with GIST and solitary hepatic metastasis while receiving imatinib treatment, s/p RFA



Jung et al, J Vasc Interv Radiol 2015; 26:1797-1802

40 year old with sarcoma, with solitary liver mass met

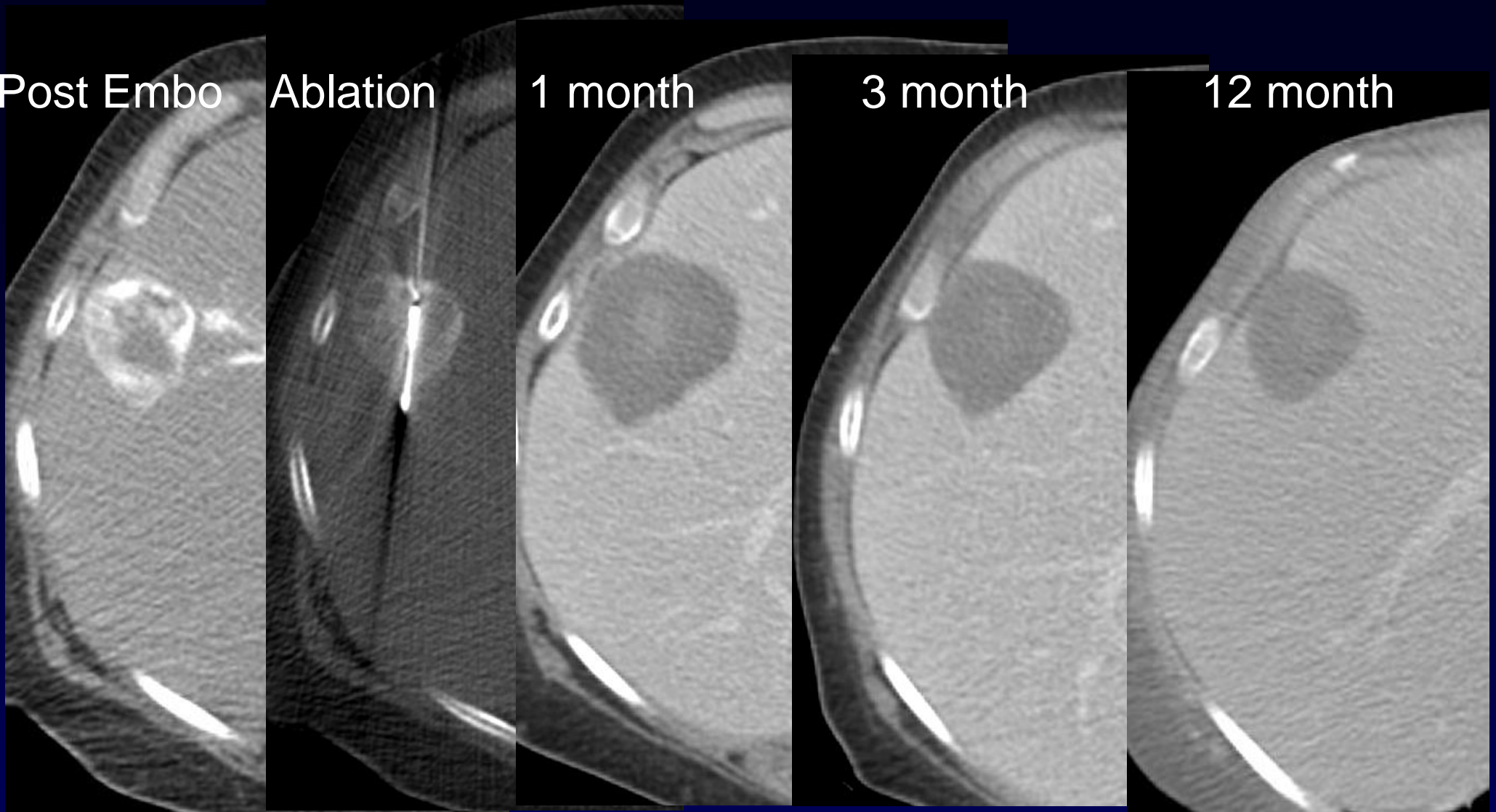
Post Embo

Ablation

1 month

3 month

12 month



Embolization + ablation provides a double kill effect, which can create a wider margin and less risk of recurrence.

Patient with ablation of livers metastases from GIST progress less and survive longer than patients with other sarcoma histologies

Progression at RFA site

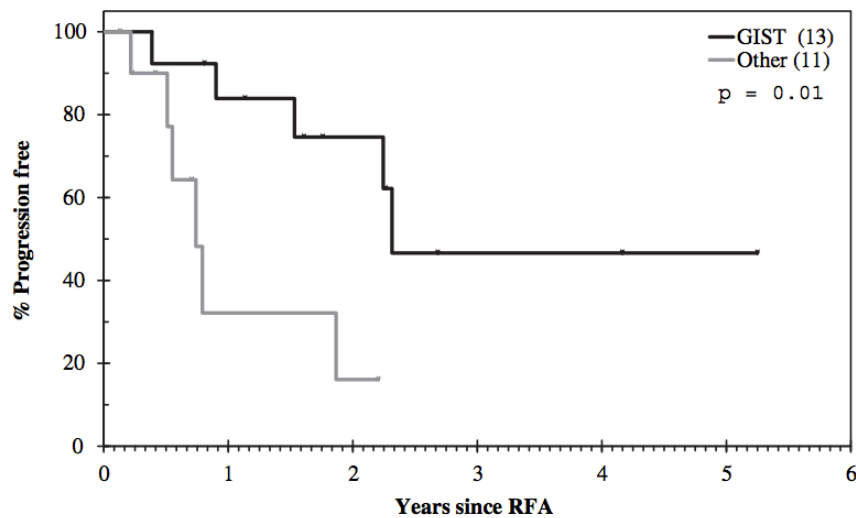


Figure 1. Time to progression at first radiofrequency ablation site for gastrointestinal stromal tumours and other histological subtypes.

Survival

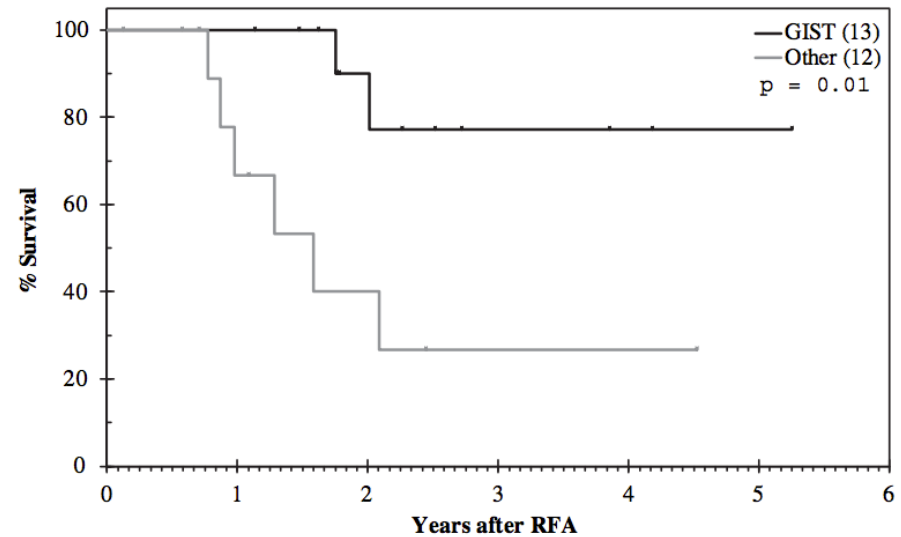
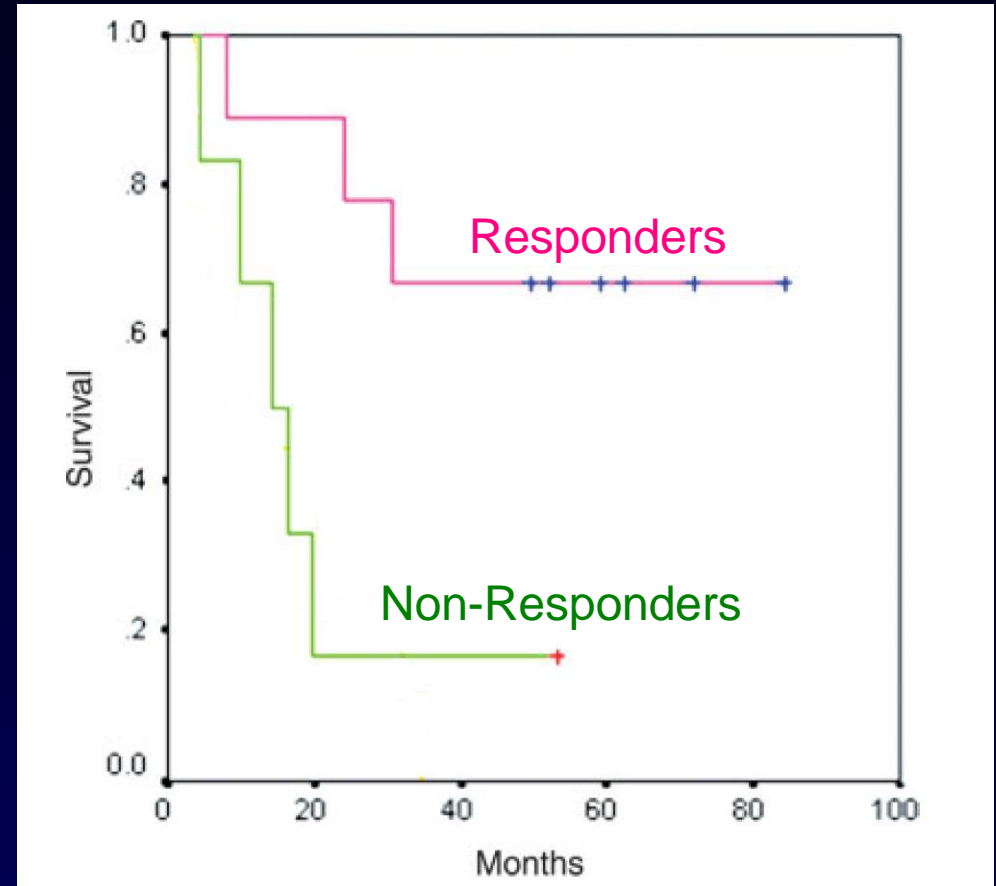
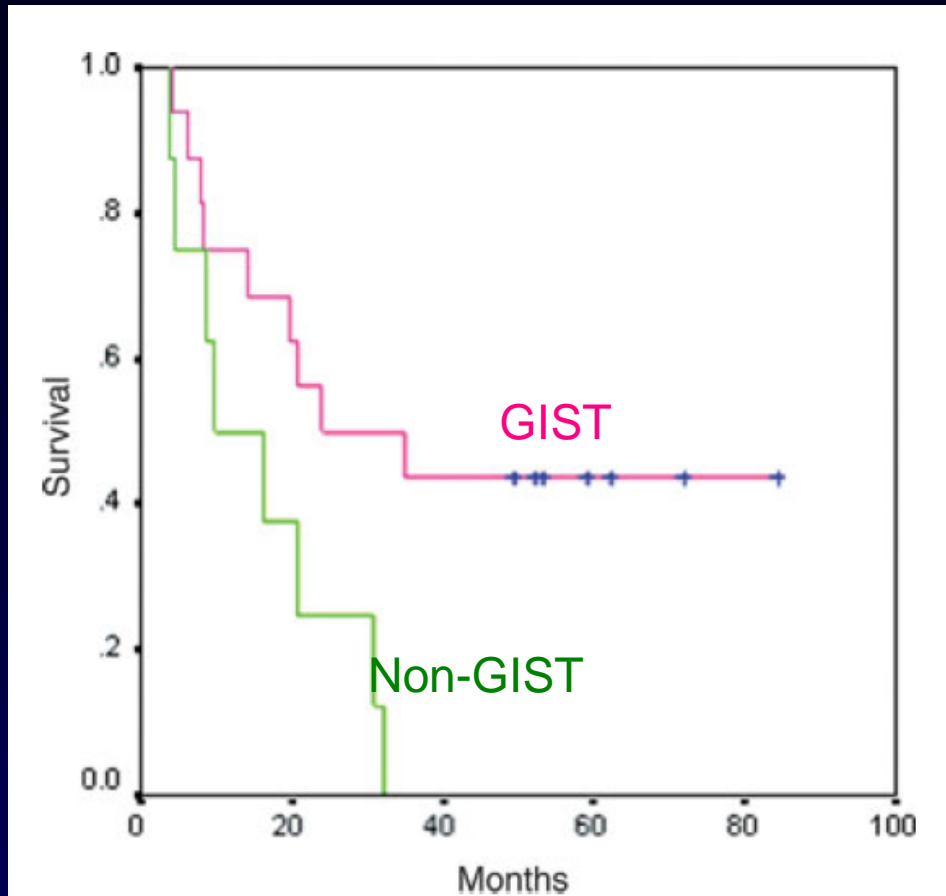
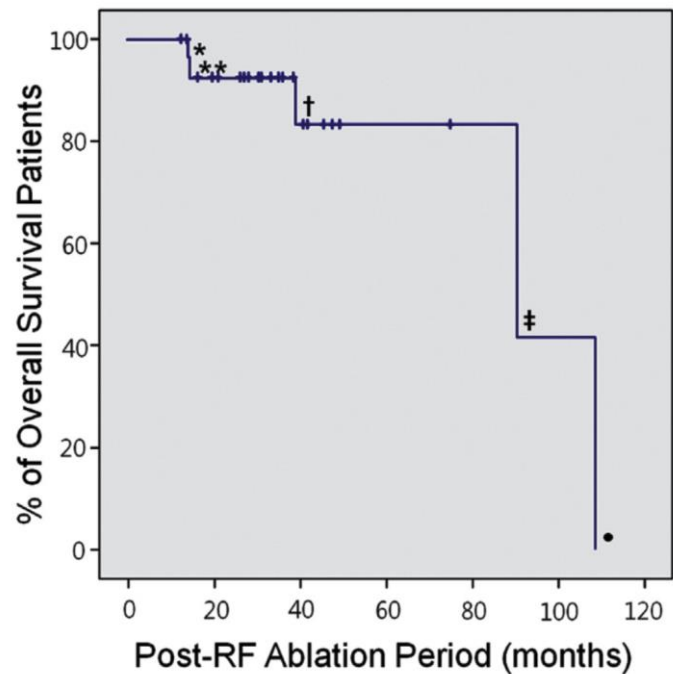


Figure 2. Overall survival from RFA for gastrointestinal stromal tumours and other histological subtypes.

Histology and initial radiographic response are strong predictors of overall survival after embolization of liver mets from sarcoma



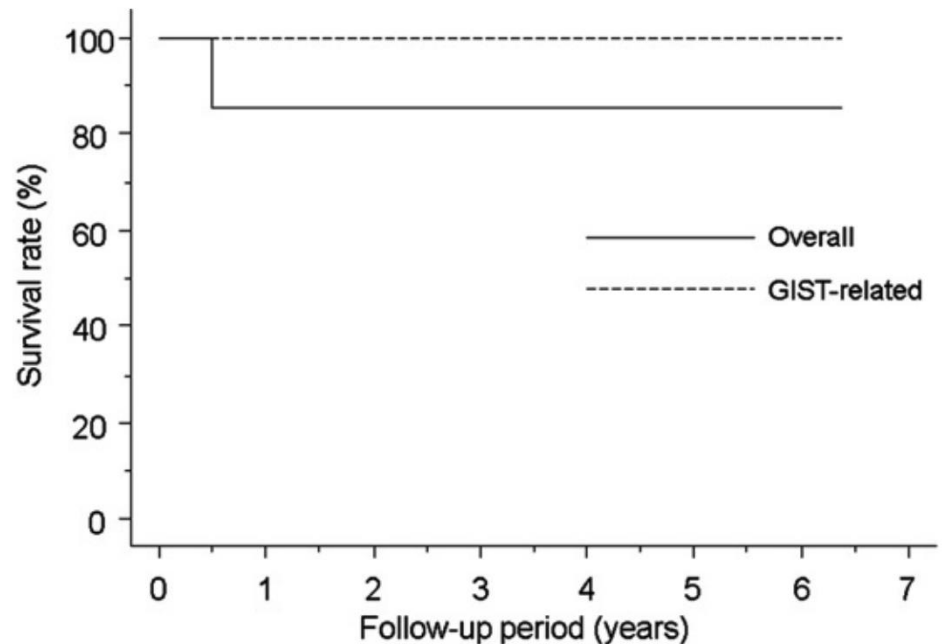
In well selected patients, RFA of GIST metastasis to liver results in overall survival of 90 months



* : 96.3 %, 14.1 months * * : 92.6 %, 14.3 months † : 83.3 %, 38.6 months
‡ : 41.7 %, 90.2 months • : 0%, 108.6 months

Figure 3. Graph of estimated overall patient survival rate after RF ablation in 29 patients.

5-year OS and GIST-related survival rates were 85.7% and 100%, respectively, following liver RF ablation of GIST



Patients at risk	7	4	3	3	2	1	1
------------------	---	---	---	---	---	---	---

Figure 2. Survival curves: the solid line shows overall survival and the dashed line shows GIST-related survival after liver RF ablation. The 5-year overall survival and GIST-related survival rates were 85.7% (95% confidence interval; 33.6%–97.8%) and 100%, respectively.

Median survival after hepatic artery embolization for GIST metastatic to the liver is 17 months

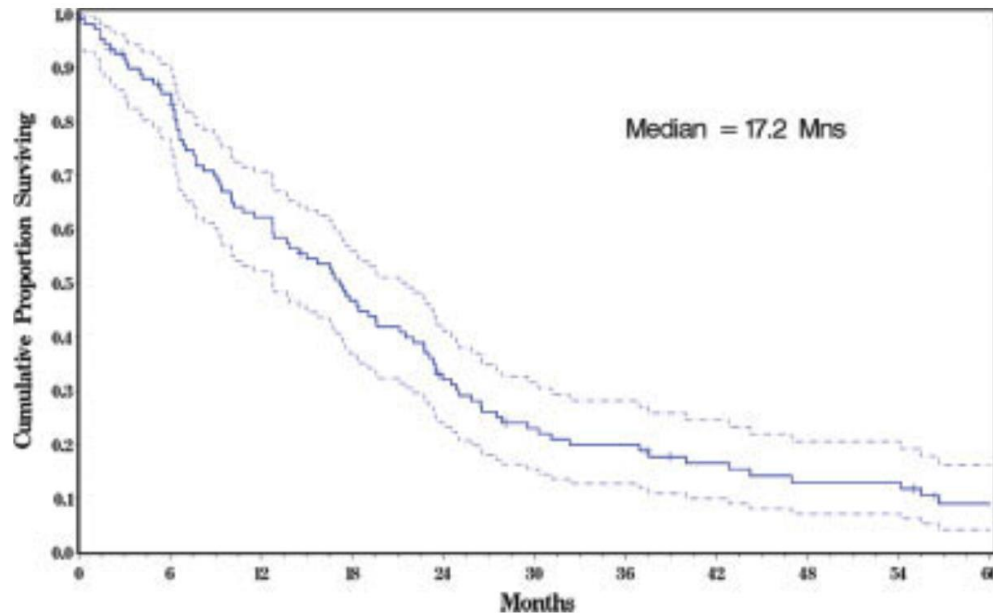


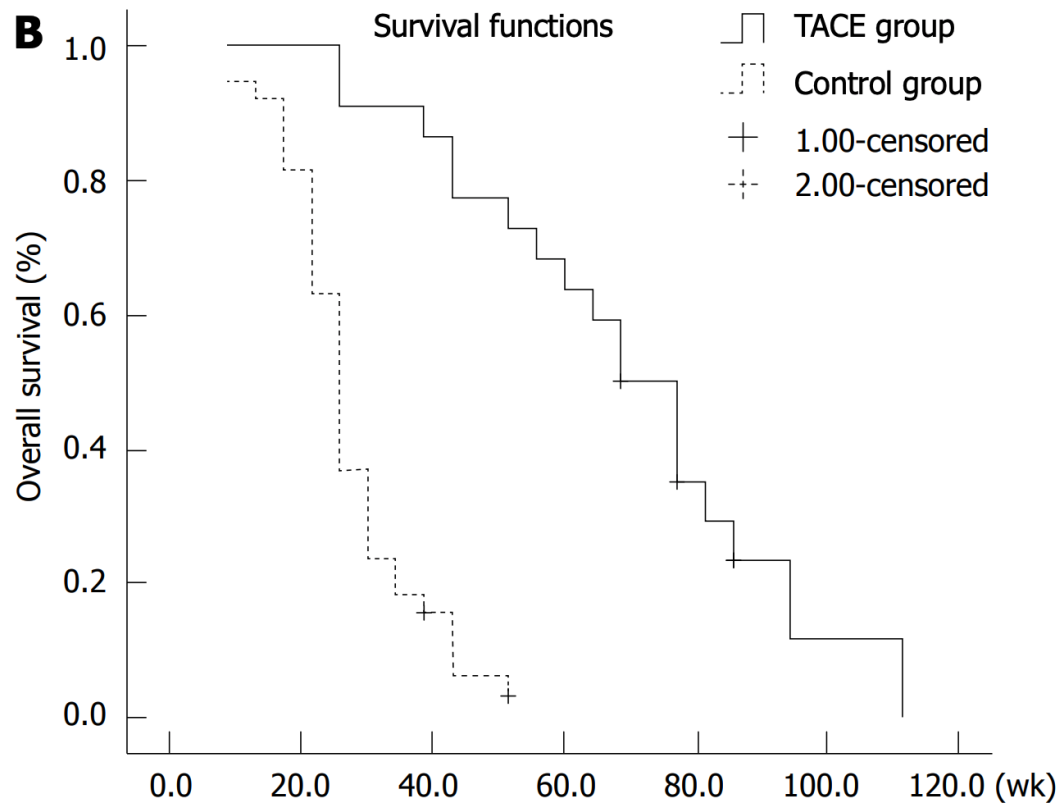
FIGURE 2. Kaplan–Meier survival curve for overall survival in all 110 patients from the time of first hepatic artery chemoembolization (HACE) with 95% confidence intervals. The median overall survival time was 17.2 months.

TABLE 5
Multivariate Analysis of Overall Survival

Variable	Hazards ratio	95% CI	<i>P</i>
Imatinib			
No	1.0		
Yes	0.126	0.041–0.390	.0003
No. of liver lesions			
1	0.279	0.098–0.797	.0172
2–5	0.616	0.346–1.097	.0997
>5	1.0		
Extent of liver disease			
≤50%	1.0		
>50%–75%	1.963	0.938–4.106	.0733
>75%	7.097	1.957–25.741	.0029
Extrahepatic metastases			
No	1.0		
Yes	5.619	2.758–11.448	<.0001
RECIST response			
PR+SD	1.0		
PD	8.403	3.373–20.935	<.0001

95% CI indicates 95% confidence interval; RECIST, Response Evaluation Criteria in Solid Tumors; PR, partial response; SD, stable disease; PD, progressive disease.

Chemoembolization for GIST metastasis to liver has a similar survival to hepatic artery embolization

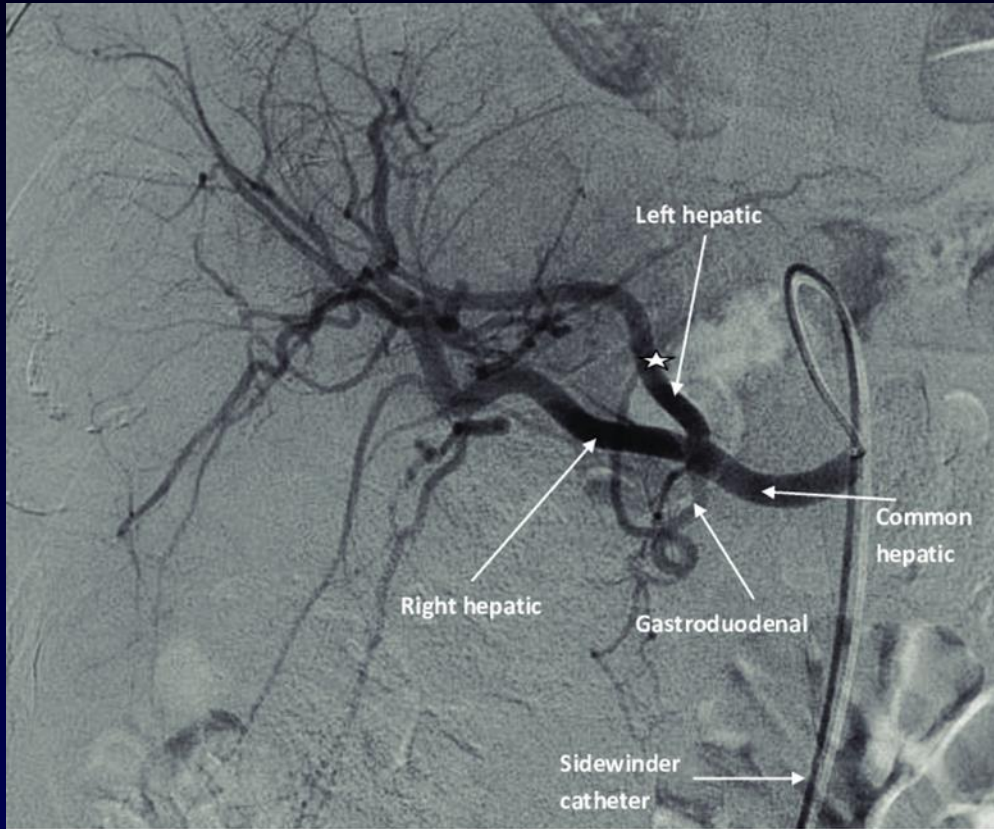


Median overall survival was 68.5 weeks = 17 months

Figure 1 The median progression-free survival (A) and overall survival (B) were longer in transcatheter arterial chemoembolization group than in control group ($P = 0.0001$). TACE: Transcatheter arterial chemoembolization.

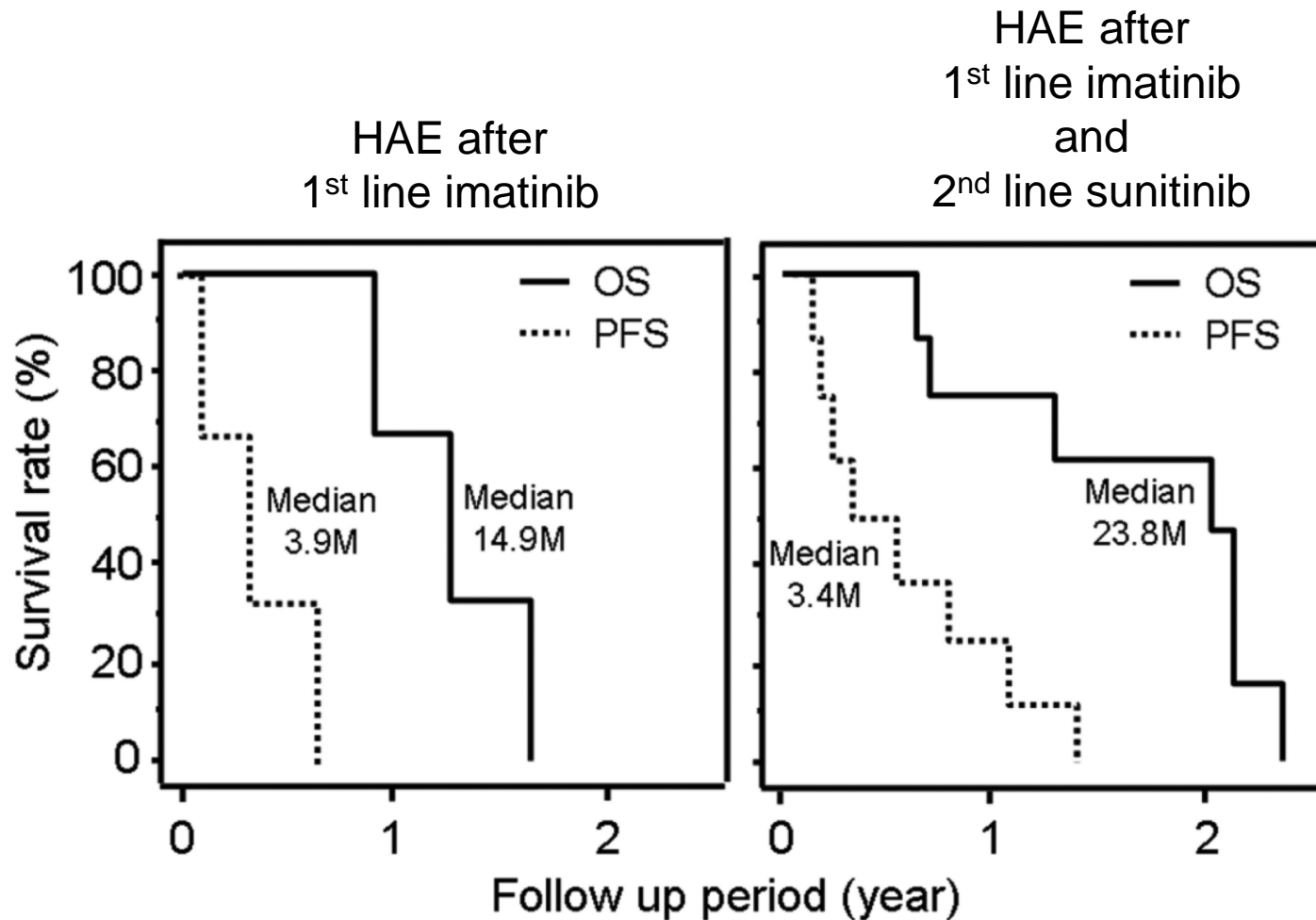


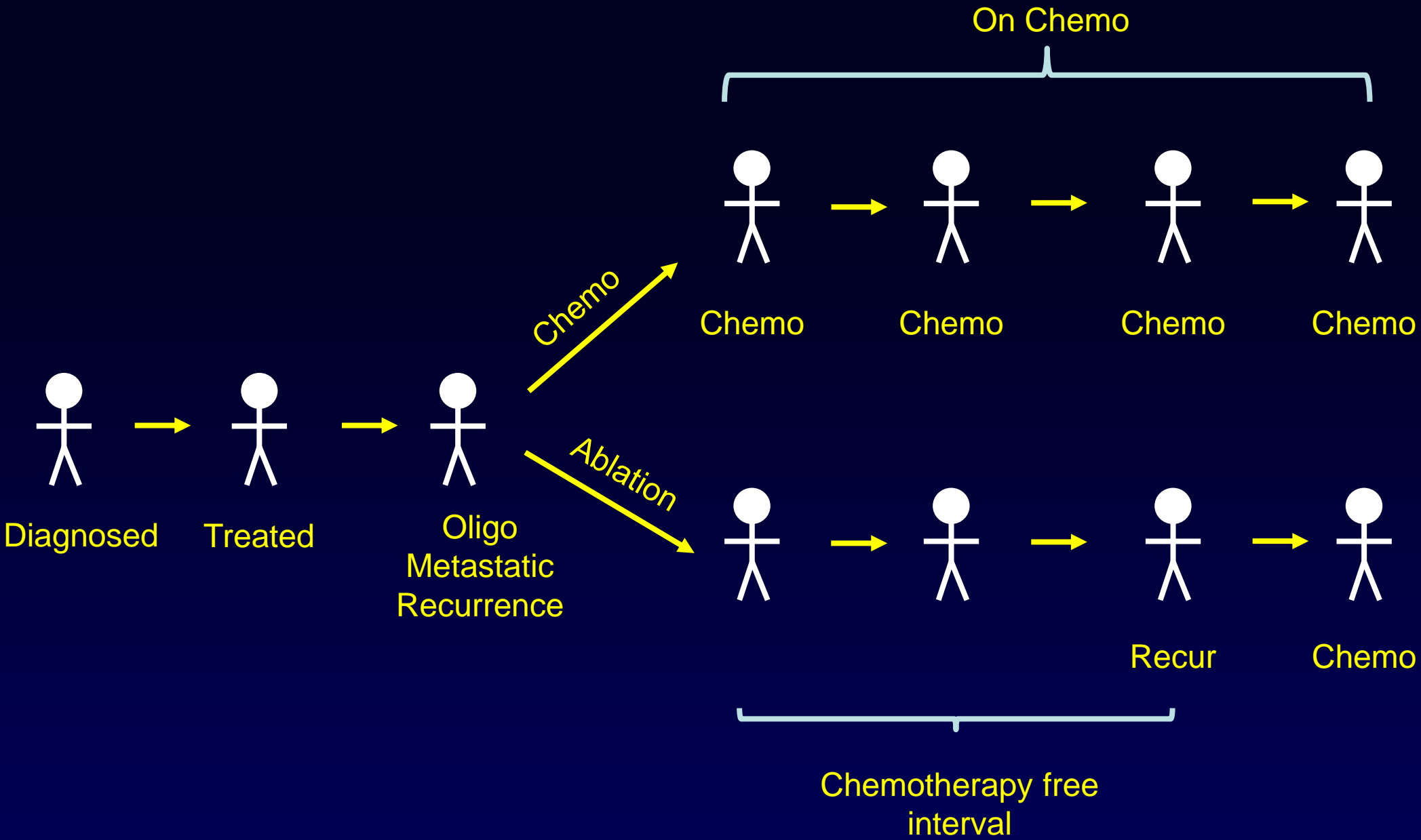
Purpose



- To determine the efficacy of hepatic artery embolization (HAE) as a therapy for gastrointestinal stromal tumor (GIST) in patients who are refractory to imatinib +/- sunitinib

HAE is useful as both 2nd and 3rd line treatments





Despite ultimately recurring, and requiring chemotherapy, ablation of GIST metastases can delay the need for chemotherapy, providing an extended chemotherapy free interval

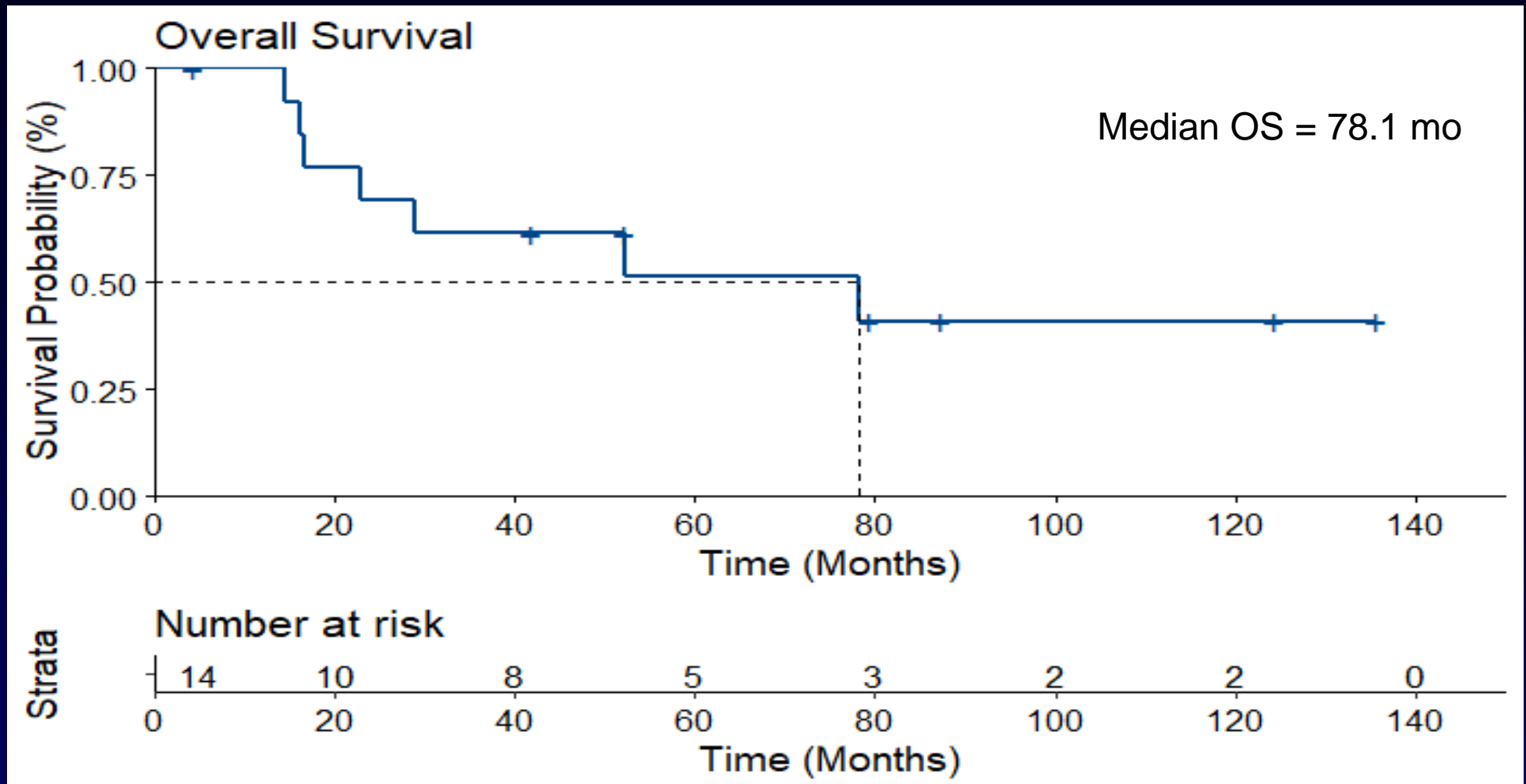
Purpose

- To determine the chemotherapy free interval in comparison to overall survival and progression-free survival in GIST patients who undergo ablation procedures

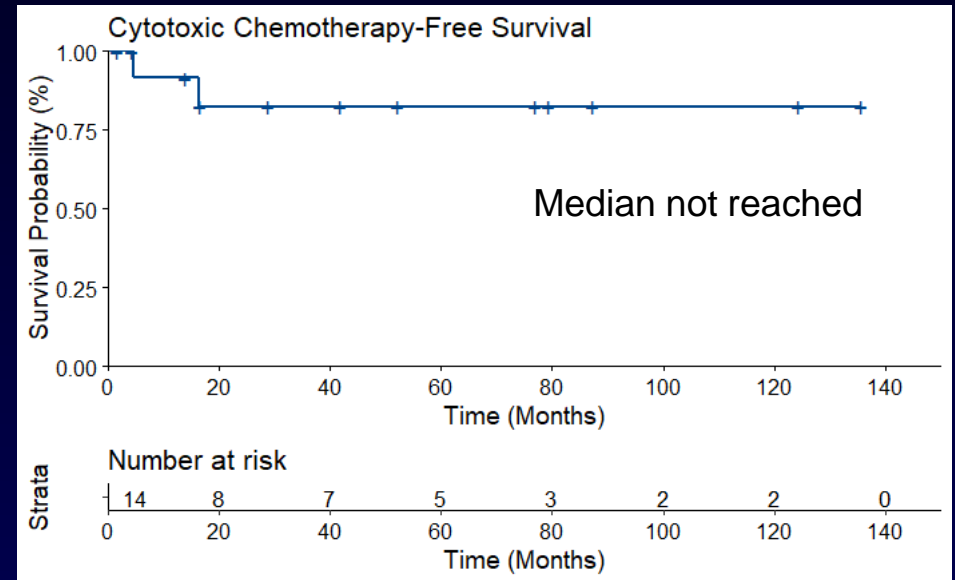
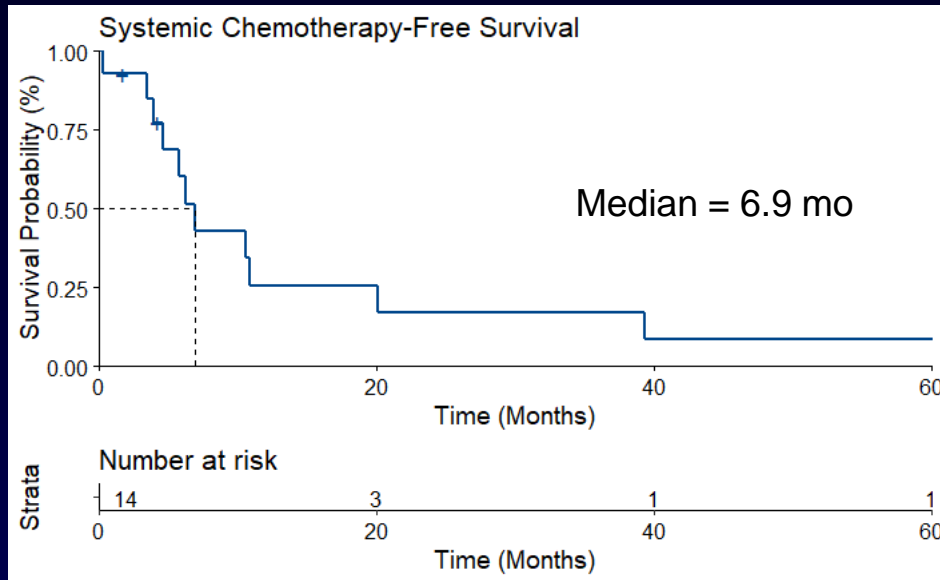
Methods

- 14 patients with GIST who underwent image guided ablation
- Computed the time-to-event post-ablation
 - Death
 - Local recurrence
 - Distant recurrence
 - Administration of systemic chemotherapy
 - Administration of cytotoxic chemotherapy
- Performed Kaplan-Meier analysis

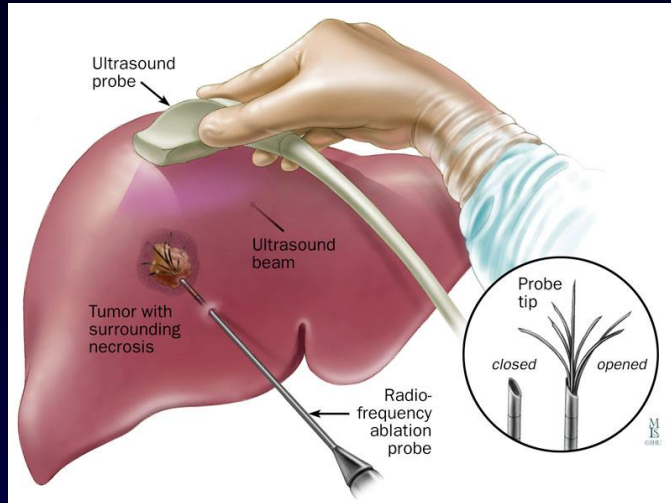
Median overall survival was 78.1 months after ablation of GIST metastases



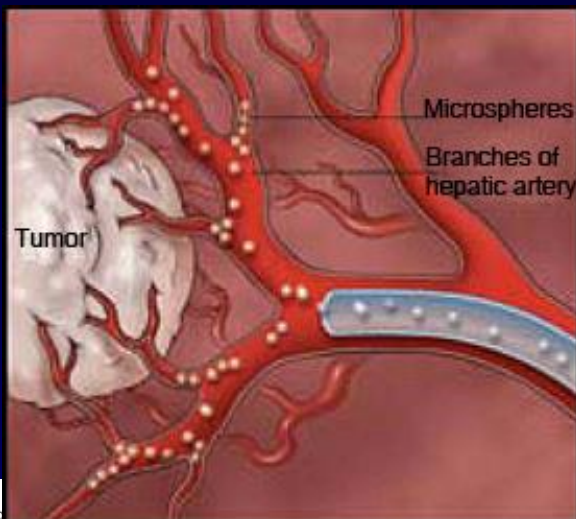
Locoregional therapy, with ablation or embo-ablation can result in extended periods off cytotoxic chemotherapy



Conclusions



- Ablation and embolization are viable treatment options for the treatment of GIST metastatic to the liver



- Image guided locoregional therapy can be considered in the 2nd line in well selected patient populations

