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Surgery: The Primary Treatment for GIST

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2025 GIST Summit
March 1, 2025

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Surgery: The Primary Treatment for GIST

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Houston, TX

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March 1, 2025

Disclosures

- None

Warning

- This talk contains photography and video from anonymized cases, anyone with concerns seeing images of anatomy, tumors, etc please be mindful

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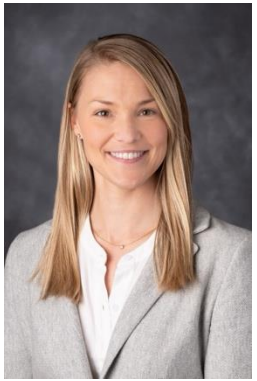
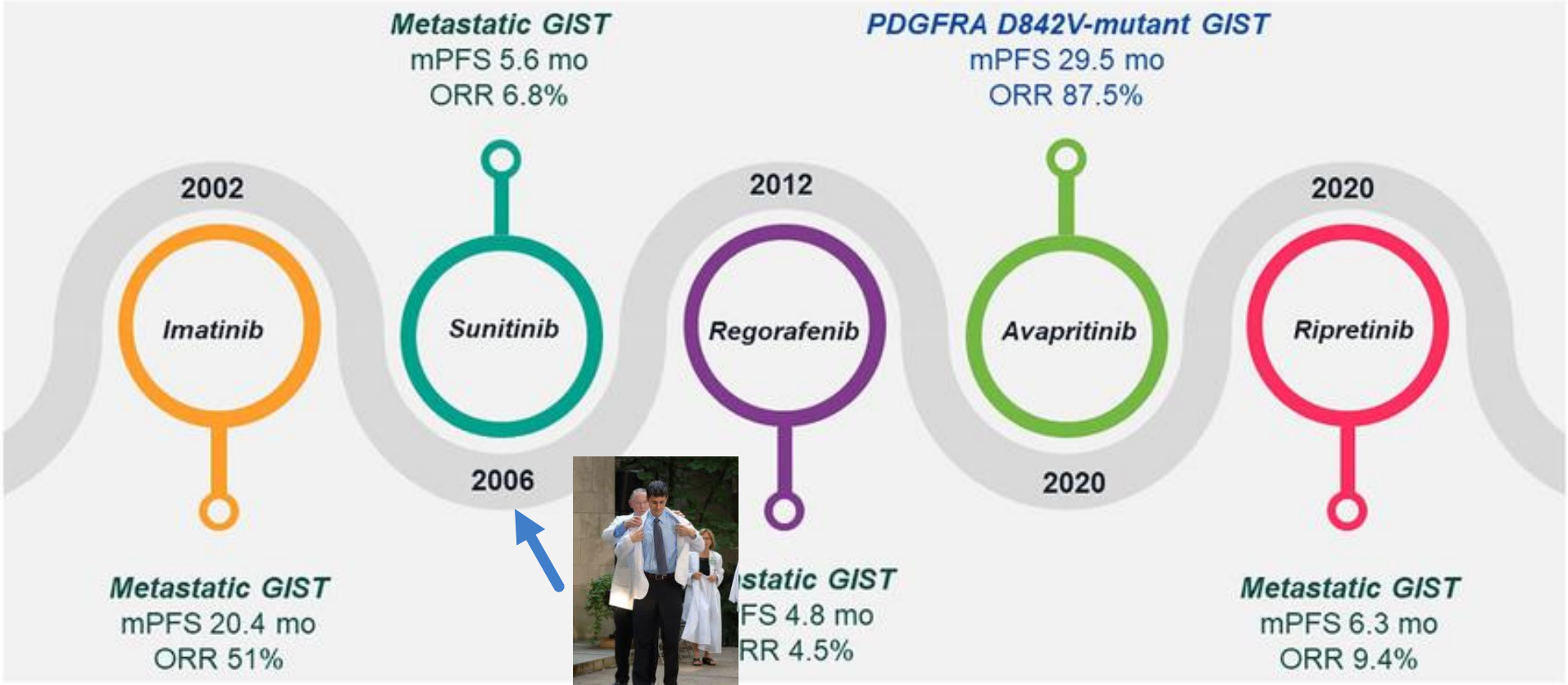


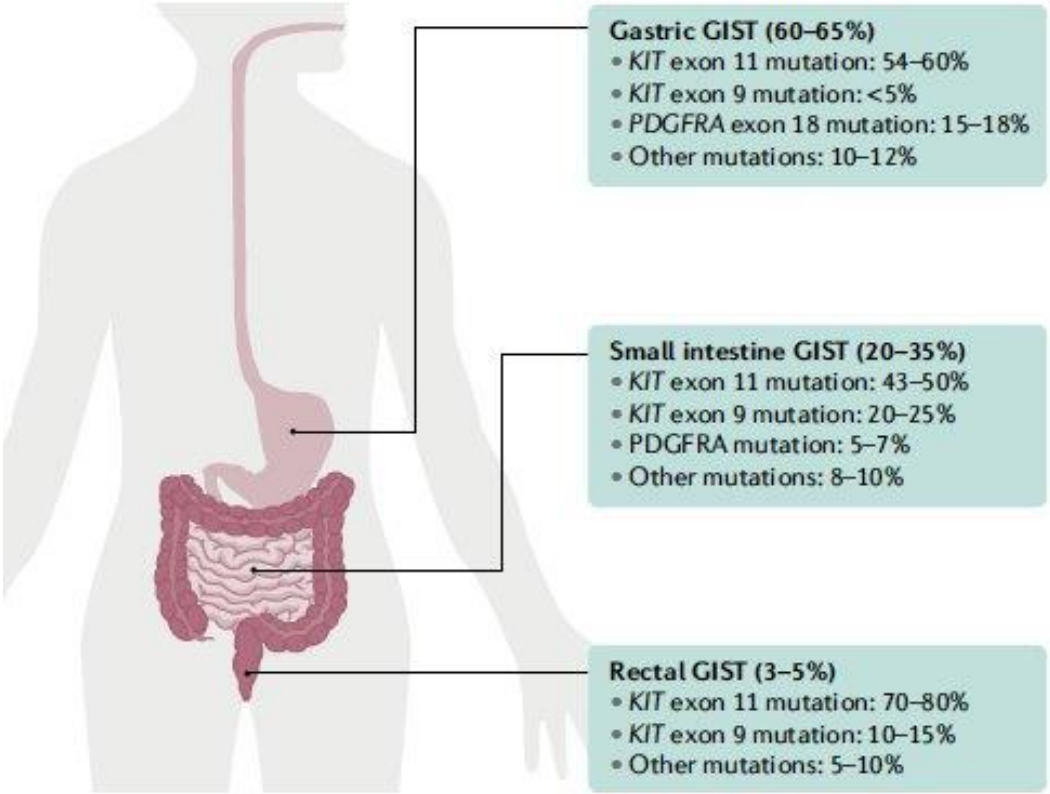
Heather Lillemoe

Christopher Scally

Why I like treating patients with GISTs



Why I like treating patients with GISTs



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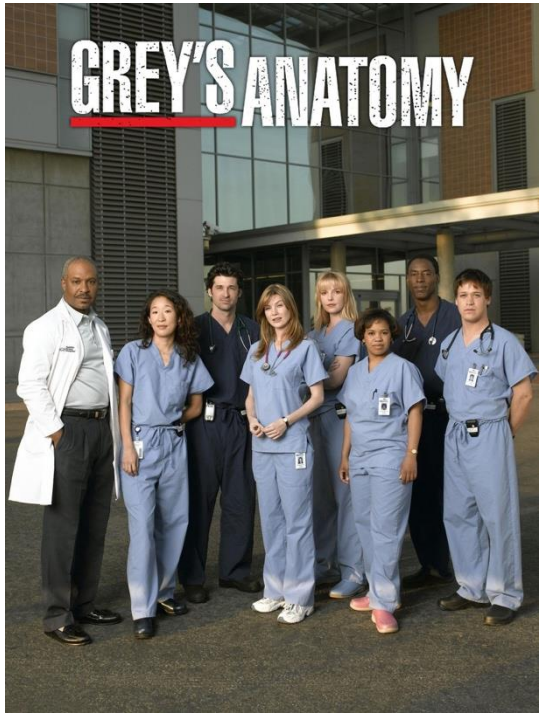
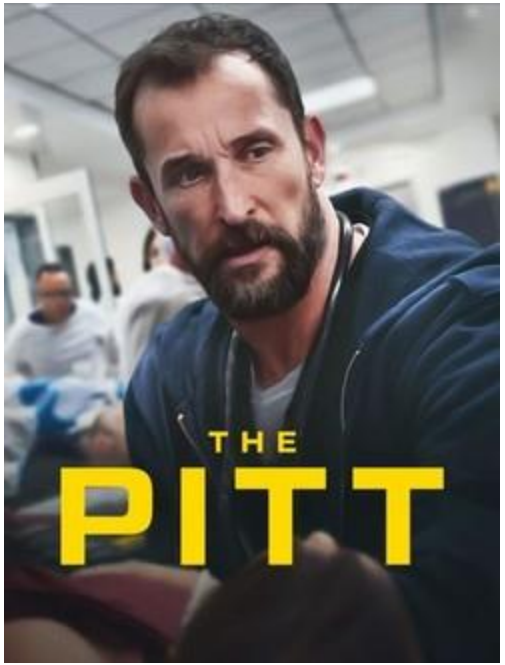
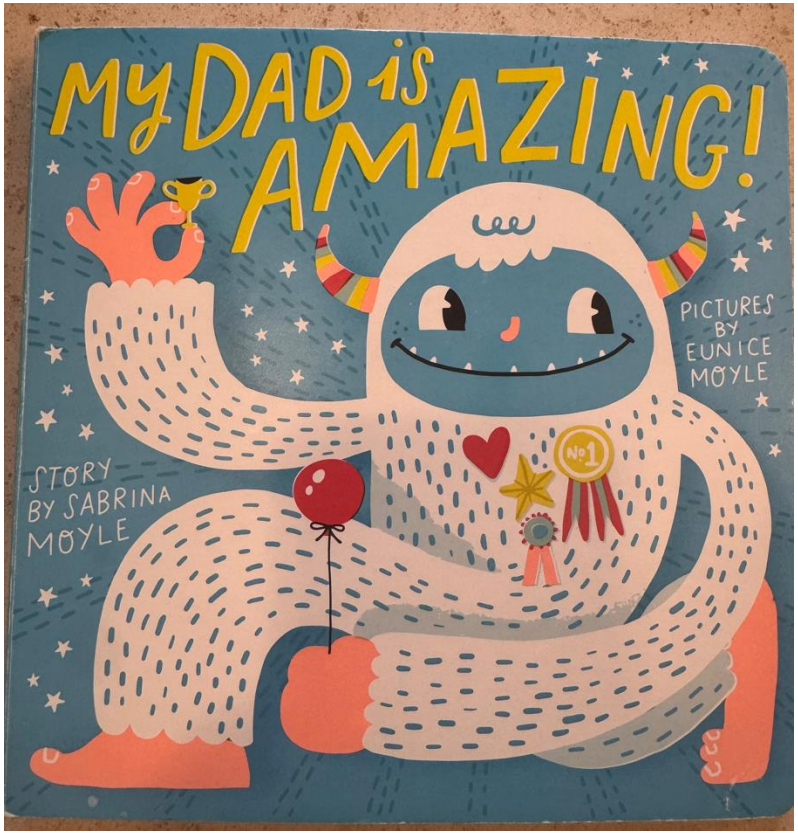
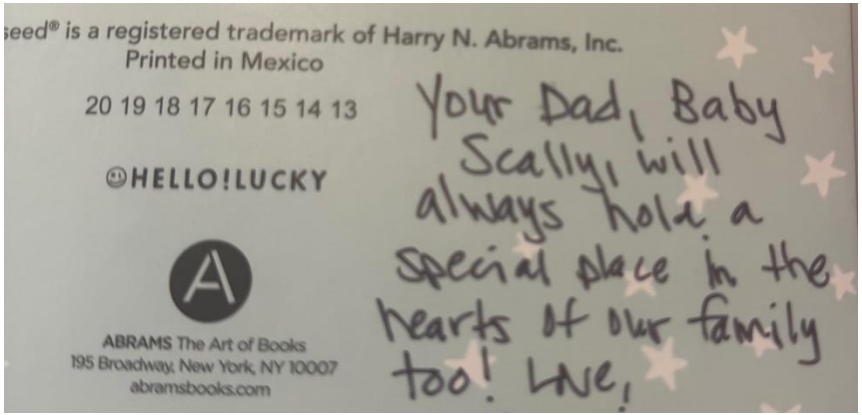




Why I like treating patients with GISTs





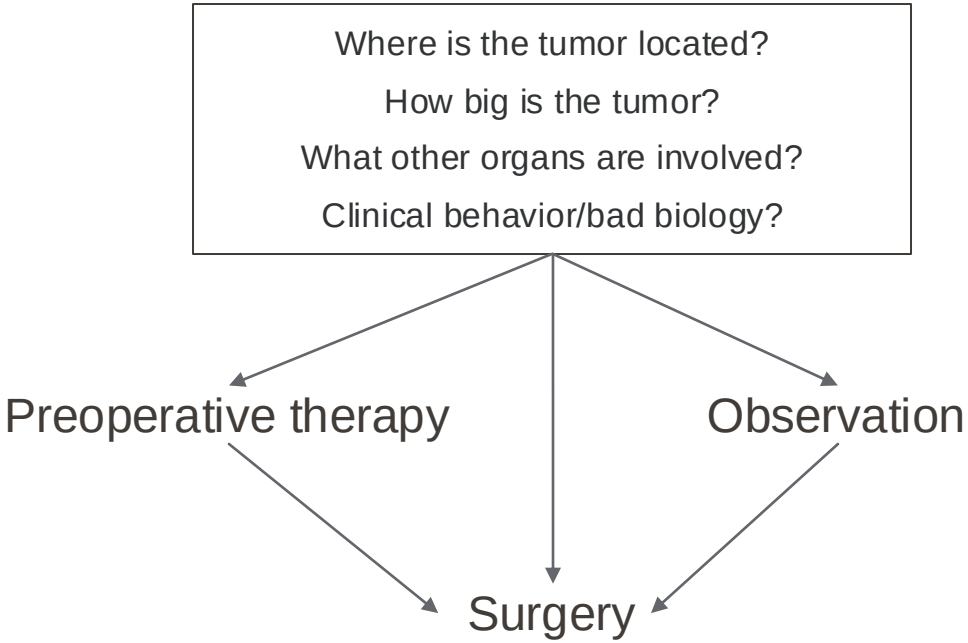
Overview

- How do surgeons think about GISTs?
- Gastric GIST Surgery Principles and Practices
- Treatment of non-Gastric GISTs
- Approach to neoadjuvant chemotherapy
- Management of Small GISTs
- Role for Surgery in metastatic disease

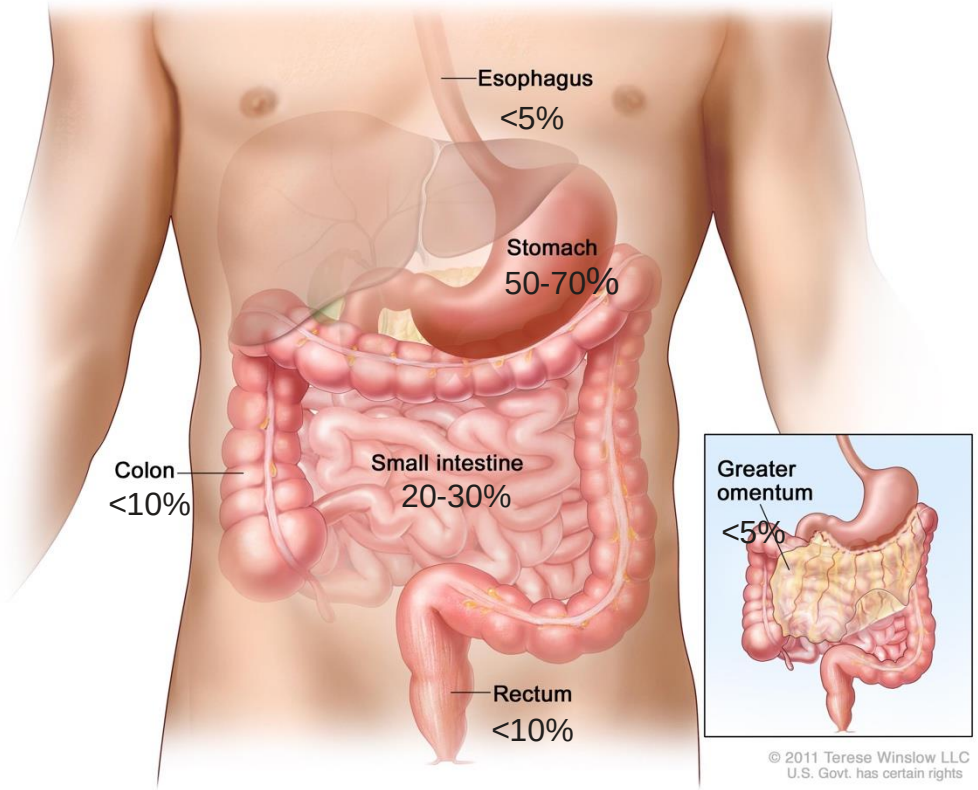
How do Surgeons Think About GISTs?

- Can it be removed? (Resectability)
- How “big” is the operation? (Morbidity)
- Can it be removed with a minimally invasive surgery? (Surgical approach)
- What other organs might have to be removed to take out the tumor? (Adjacent structures)

Surgical Approach to GISTs



Where is the tumor located?

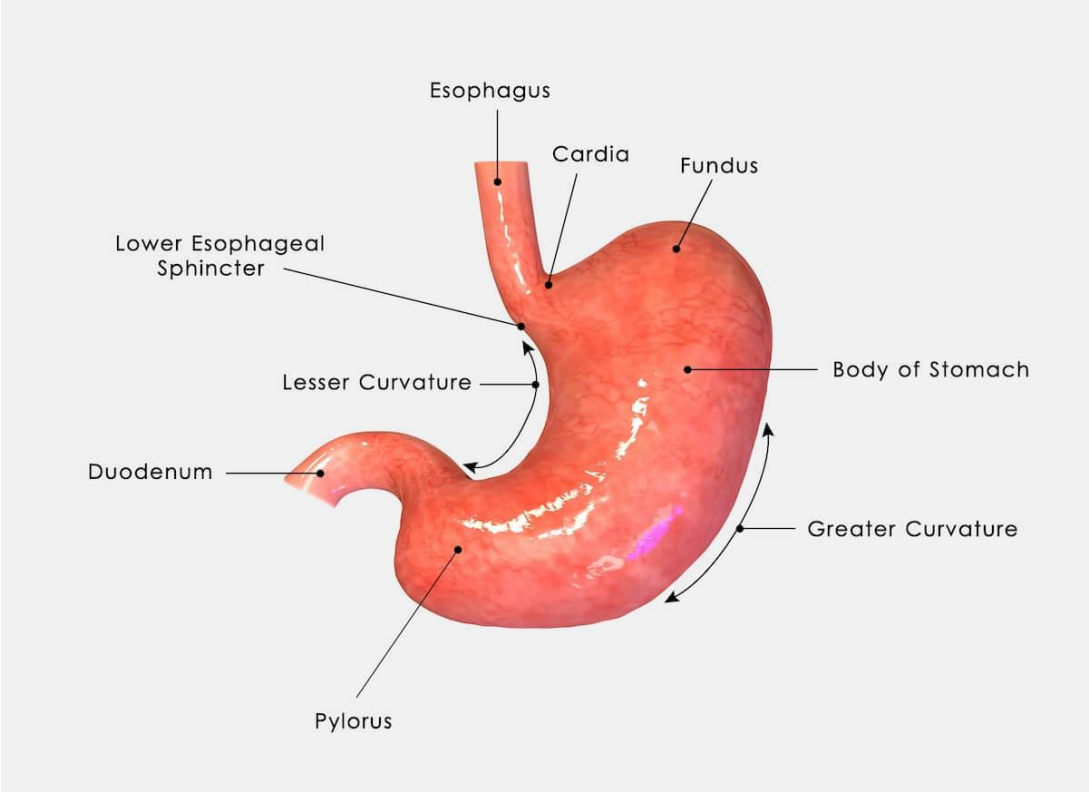


https://www.cancer.gov/types/soft-tissue-sarcoma/hp/gist-treatment-pdq

Gastric GIST: Where in the stomach is the tumor located?

Stomach

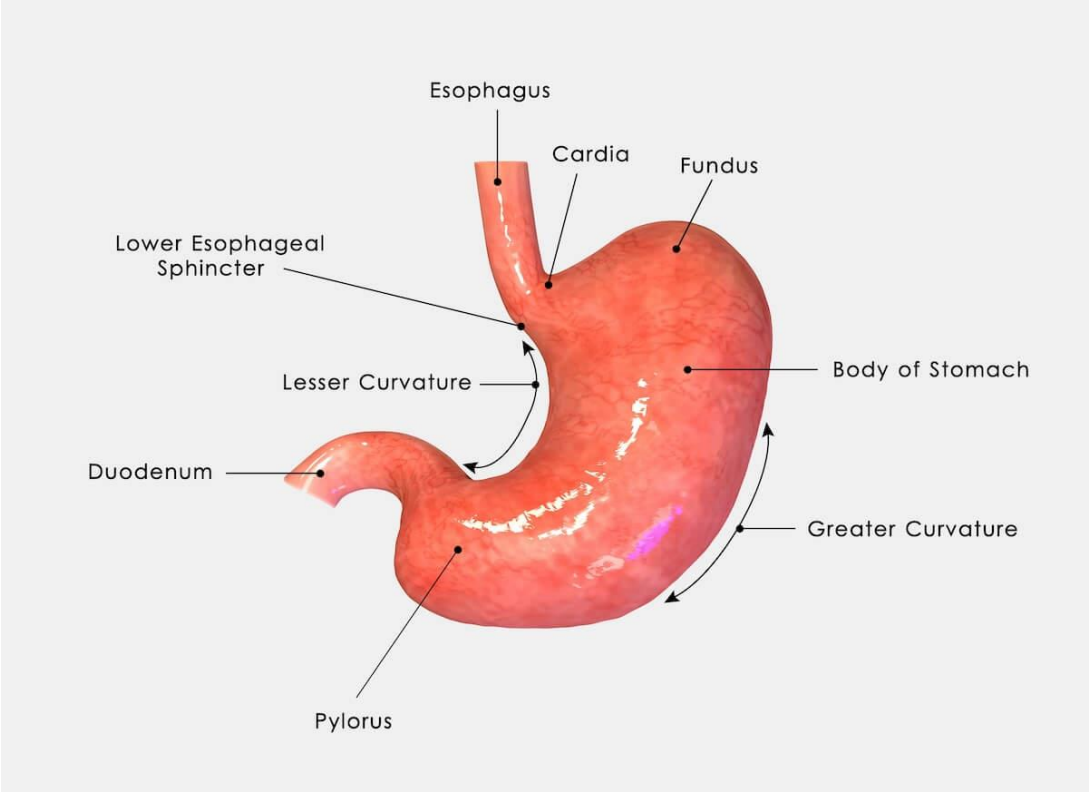
- Partial gastrectomy (“Wedge”)
- Total gastrectomy/subtotal gastrectomy
- Distal gastrectomy



Gastric GIST: Where in the stomach is the tumor located?

Cardia/Sphincter:

- Resection of all or part of lower esophageal sphincter (“gastroesophageal junction”) can lead to:
  - debilitating reflux
  - narrowing of the esophagus (stricture)
  - difficulty swallowing



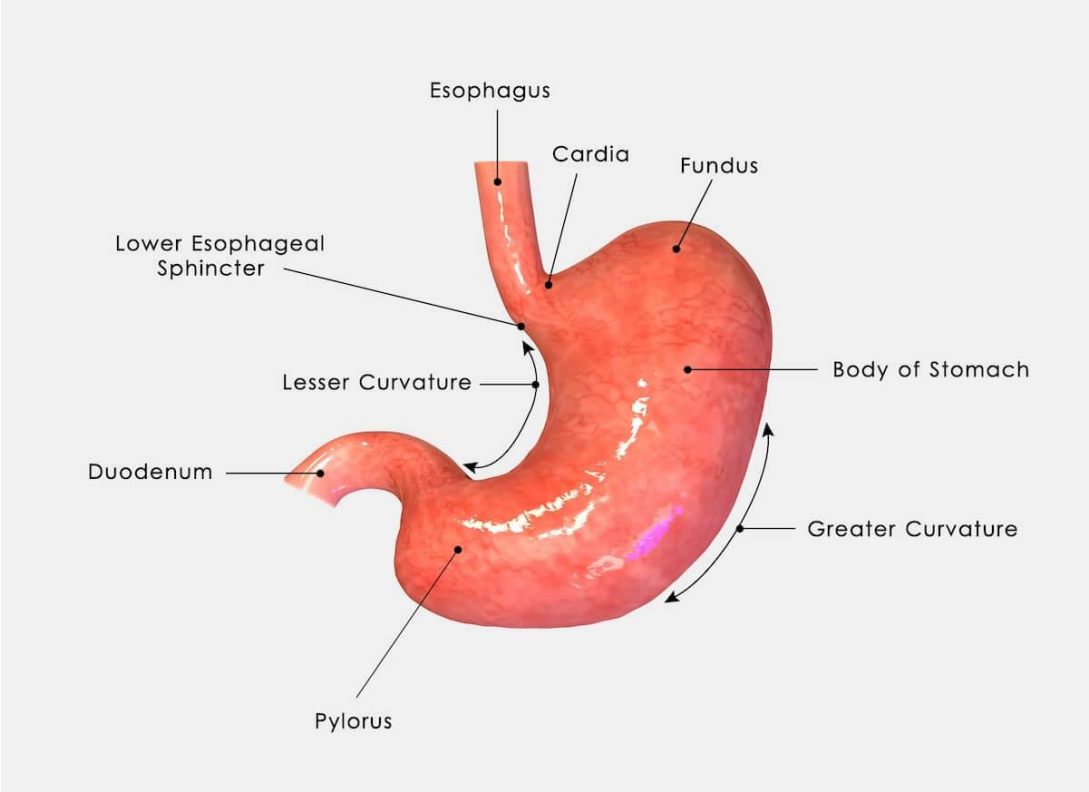
Gastric GIST: Where in the stomach is the tumor located?

Body of stomach:

- Resecting too much of the stomach can lead to problems with digestion and absorption of food

Lesser Curvature:

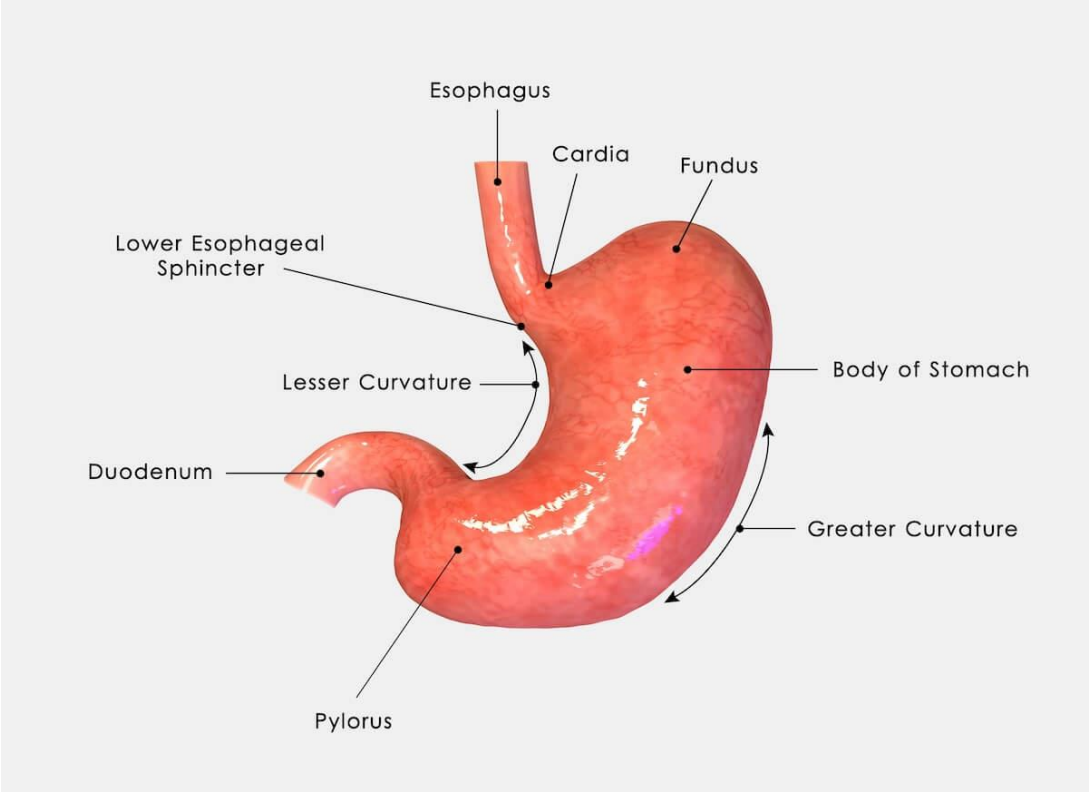
- Nerves in this area (vagus) control stomach emptying/digestion



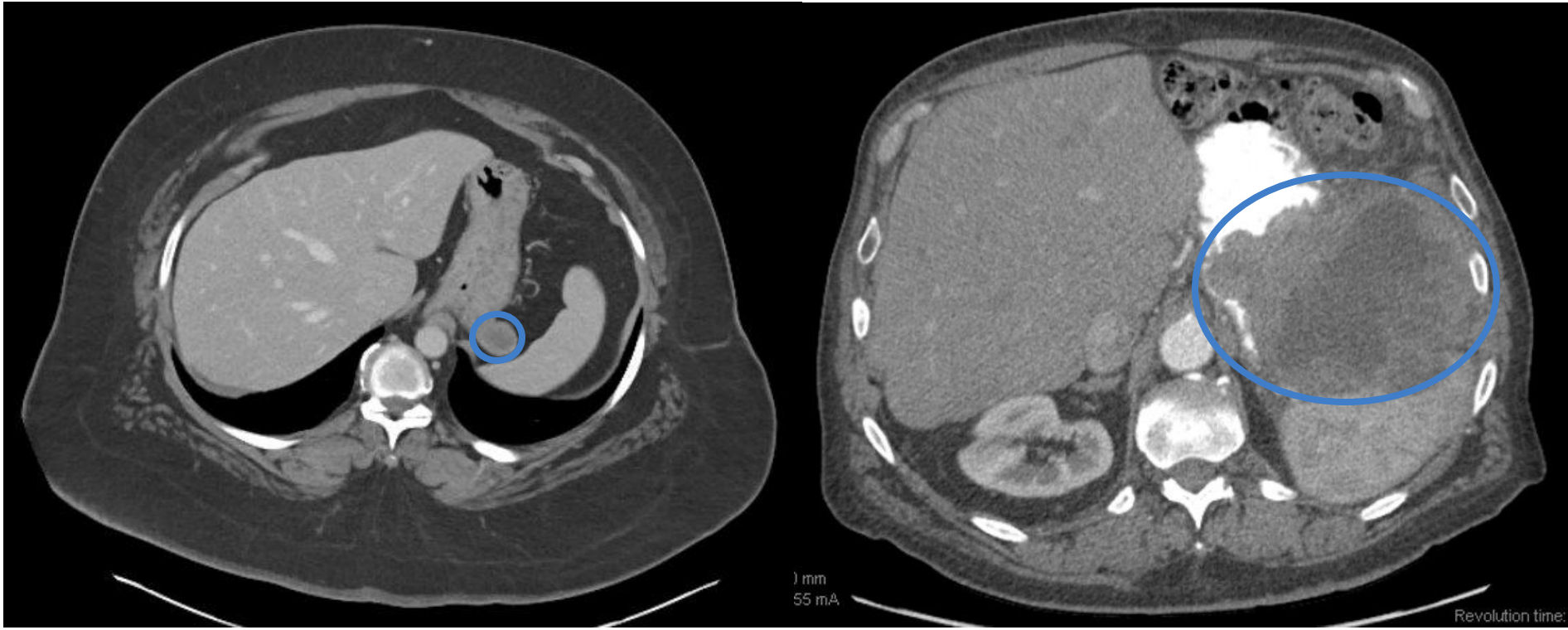
Gastric GIST: Where in the stomach is the tumor located?

Distal Stomach/Pylorus

- Resection in this area can narrow stomach, causing problems with food passage
- Pylorus sphincter helps prevent bile reflux



Gastric GIST: Example Cases

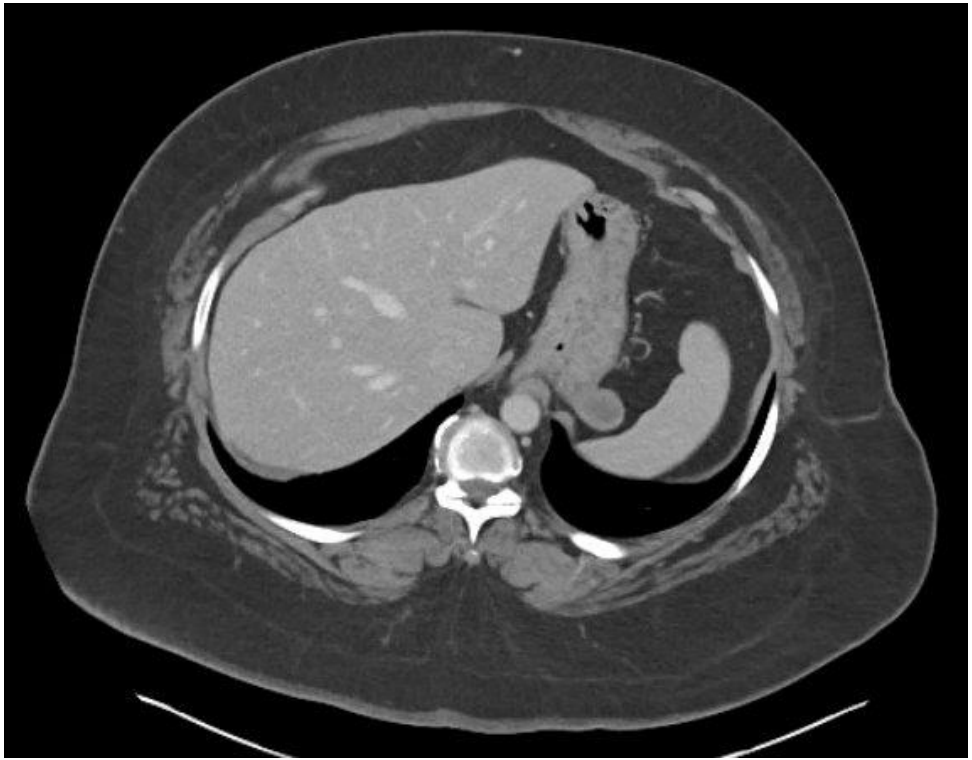


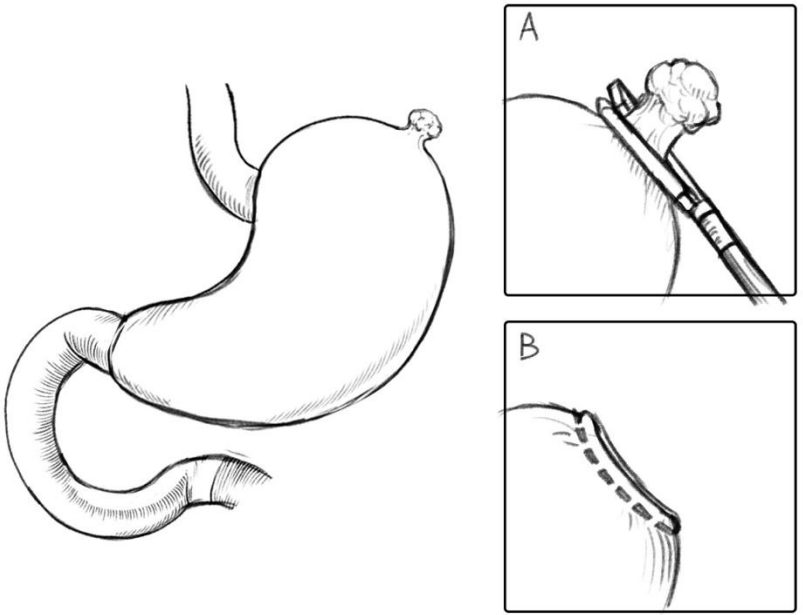
Gastric GIST: Minimally Invasive Approach

Laparoscopic surgery

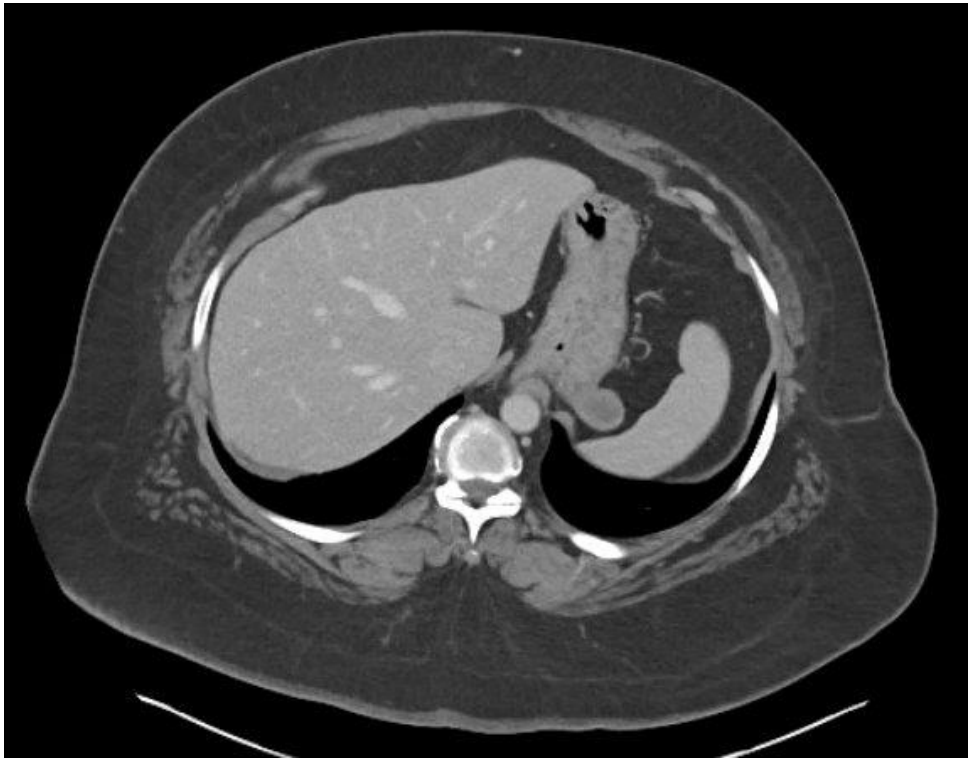
Robotic Surgery

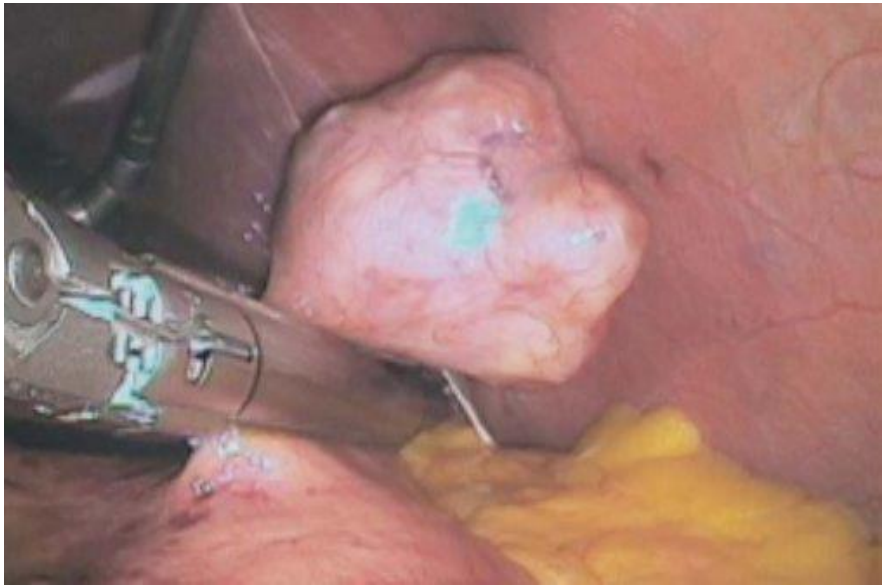
Gastric GIST: Minimally Invasive Approach





Gastric GIST: Minimally Invasive Approach





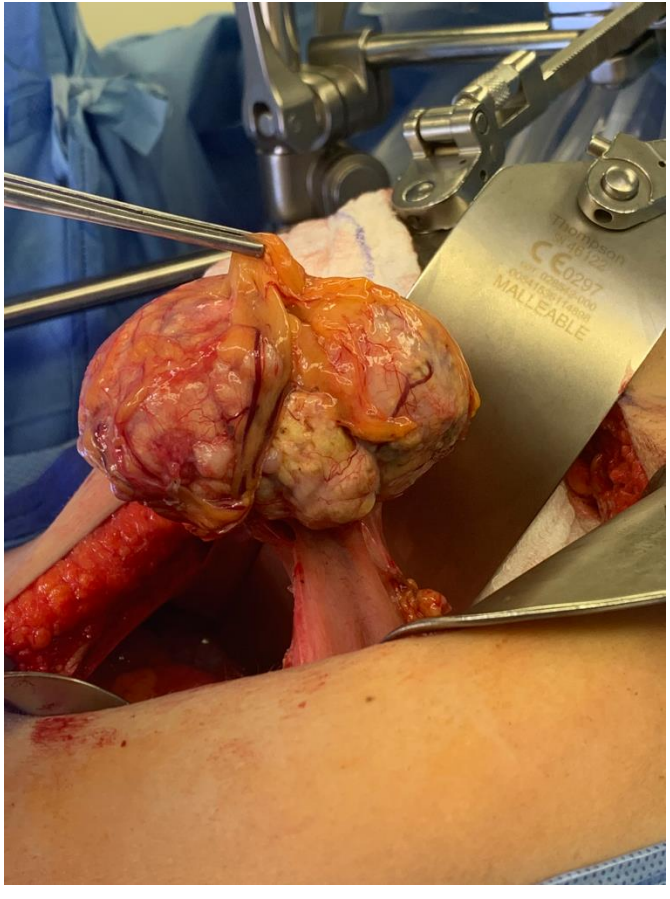
Gastric GIST: Minimally Invasive Approach

https://www.youtube.com/watch?v=h61kITw9TaU&list=PPSV

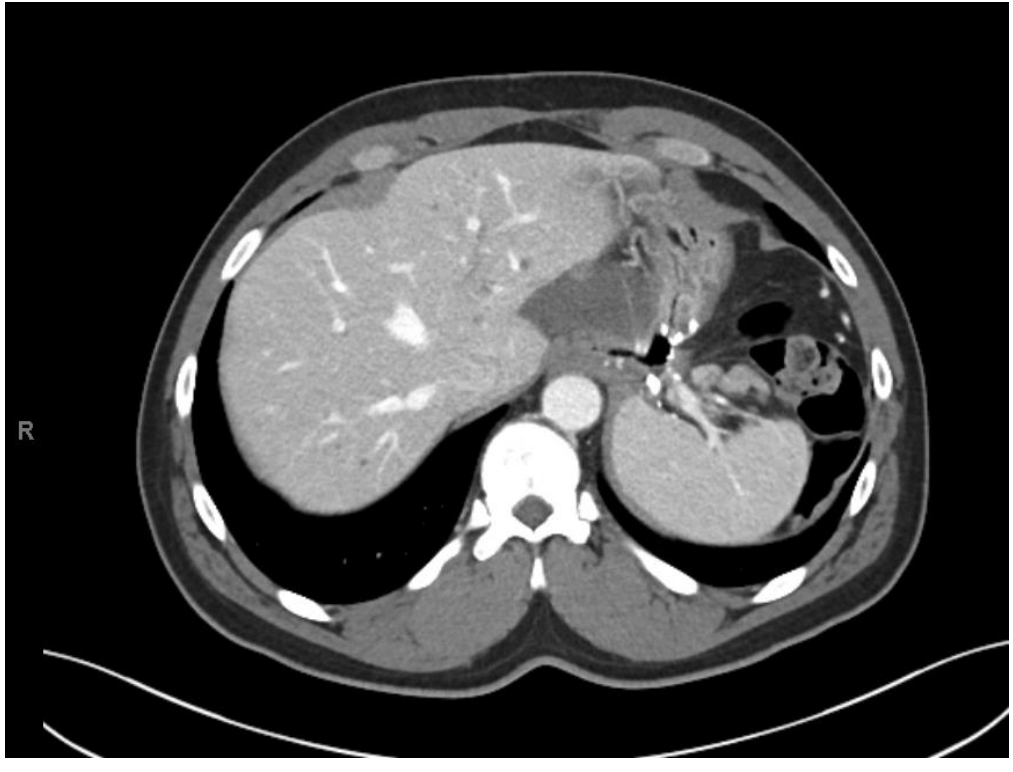
Gastric GIST: Open Approach

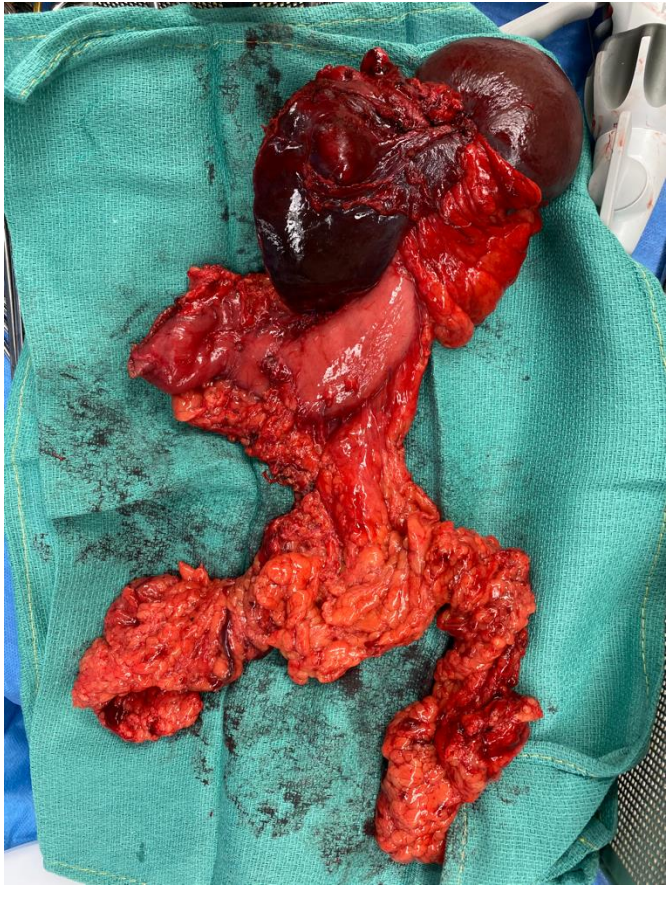
- Tumor size
- Involvement of adjacent organs (multivisceral resection)
- Complex anatomy
- Urgency (e.g. bleeding)
- Patient factors/comorbidities

Gastric GIST: Open Approach

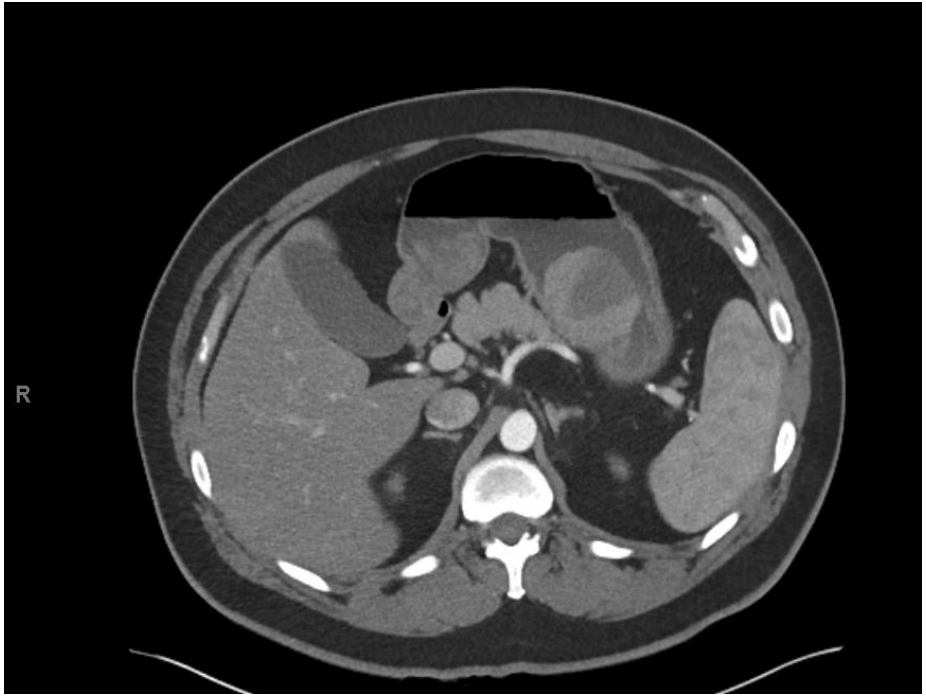


Gastric GIST: Open Approach





Gastric GIST: Open Approach



Treatment of Non-Gastric GIST

Small Bowel/Duodenum

- Partial small bowel resection
- Whipple operation

Colon

- Partial colectomy (right, left)

Rectum

- Low anterior resection (LAR)
- Abdominoperineal resection (APR)
  - Permanent colostomy

Esophagus

- Esophagectomy (different types depending on location along esophagus)

Treatment of Non-Gastric GIST

Gastric vs. non-gastric GIST:

PREDICTORS OF GIST BIOLOGIC RISK

Table 1: Gastric GIST: Guidelines for Assessing the Malignant Potential[1]

- This prognostic assessment applies best to *KIT*- or *PDGFRA*-positive GIST, whereas SDH-deficient GIST are more unpredictable.
- Risk stratification is determined without any prior exposure to TKI therapy.

Tumor Size	Mitotic Rate[2]	Risk	Risk Per CAP[2]
≤2 cm	≤5 mitoses/50 HPFs	Metastasis rate: 0%	None
	>5 mitoses/50 HPFs	Metastasis rate: 0%*	None
>2 cm to ≤5 cm	≤5 mitoses/50 HPFs	Metastasis rate: 1.9%	Very low (1.9%)
	>5 mitoses/50 HPFs	Metastasis rate: 16%	Moderate (16%)
>5 cm to ≤10 cm	≤5 mitoses/50 HPFs	Metastasis rate: 3.6%	Low (3.6%)
	>5 mitoses/50 HPFs	Metastasis rate: 55%	High (55%)
>10 cm	≤5 mitoses/50 HPFs	Metastasis rate: 12%	Moderate (12%)
	>5 mitoses/50 HPFs	Metastasis rate: 86%	High (86%)

CAP: College of American Pathologists; HPFs: High-power fields; *Predicted rate based on tumor category with very small numbers

Treatment of Non-Gastric GIST

Gastric vs. non-gastric GIST:

Table 2: Non-Gastric GIST (includes small bowel and colorectal GIST): Guidelines for Assessing the Malignant Potential[1]

- This prognostic assessment applies best to *KIT*- or *PDGFRA*-positive GIST whereas SDH-deficient GIST are more unpredictable. For anatomic sites not listed in this table, such as esophagus, mesentery, and peritoneum, or in the case of "insufficient data," it is best to use risk criteria for jejunum/ileum.
- Risk stratification is determined without prior exposure to TKI therapy.

Tumor Size	Mitotic Rate[2]	Risk	Risk
≤2 cm	≤5 mitoses/50 HPFs	Metastasis rate: 0%	Metastasis rate: 0%
	>5 mitoses/50 HPFs	Metastasis rate: 50%–54%	Metastasis rate: 0%*
>2 cm to ≤5 cm	≤5 mitoses/50 HPFs	Metastasis rate: 1.9%–8.5%	Metastasis rate: 1.9%
	>5 mitoses/50 HPFs	Metastasis rate: 50%–73%	Metastasis rate: 16%
>5 cm to ≤10 cm	≤5 mitoses/50 HPFs	Metastasis rate: 24%	Metastasis rate: 3.6%
	>5 mitoses/50 HPFs	Metastasis rate: 85%	Metastasis rate: 55%
>10 cm	≤5 mitoses/50 HPFs	Metastasis rate: 34%–57%	Metastasis rate: 12%
	>5 mitoses/50 HPFs	Metastasis rate: 71%–90%	Metastasis rate: 86%

CAP: College of American Pathologists; HP

Treatment of Non-Gastric GIST

- More frequent use of systemic therapy given higher risk of metastasis
- If using systemic therapy, typically trial of neoadjuvant treatment
  - Allows assessment of tumor response

Approach to neoadjuvant chemotherapy

- Primary goal to shrink tumor and make surgical resection less morbid
  - Large tumors
  - Involvement of adjacent organs
  - Particularly challenging anatomic locations
  - Decrease vascularity of tumor

Approach to neoadjuvant chemotherapy

- Patient questions:
  - Is it safe?
  - How long will it take before surgery?
  - How will we know if it's working?
  - How will it change the surgery?

Approach to neoadjuvant chemotherapy

- Safety:
  - Early Randomized Phase II Trial: 19 patients received preoperative therapy
    - no effects on surgical complications
    - 62% had positive disease response to treatment
  - RTOG 0132 Multi-institutional Study: 52 patients received 2 months preoperative therapy
    - no effects on surgical complications
    - Only 4.5% progressed while on treatment (but were still operable)
    - No metastases observed during neoadjuvant treatment
    - Effective: 85% had metabolic response on PET-CT

McAuliffe et al, *Ann Surg* Onc 2009
Wang et al, *Ann Surg Onc* 2012

Approach to neoadjuvant chemotherapy

- How long will neoadjuvant treatment take?
  - Typical approach is treatment until “maximum effect” – aka tumor stops shrinking
  - ~6-9 months average, sometimes longer if continued response
  - Re-evaluate at each visit – will further tumor shrinkage change the extent or approach to surgery in any way?
- How will we know it is working?
  - Early restaging with PET-CT
  - Routine 2-3 month visits with imaging to assess response

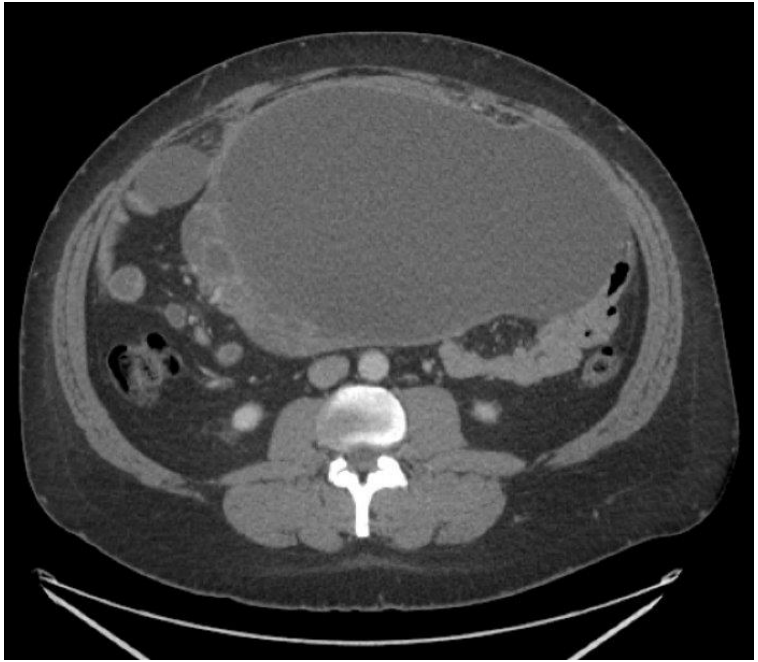
Approach to neoadjuvant chemotherapy

- How will we know it is working?
  - Early restaging with PET-CT
    - 70% with PET response within 8 weeks
    - If non-responsive, can consider change in treatment plan
  - Routine 2-3 month imaging
    - Evaluate for decrease in size
    - Evaluate for evidence of tumor necrosis/“metabolic” response

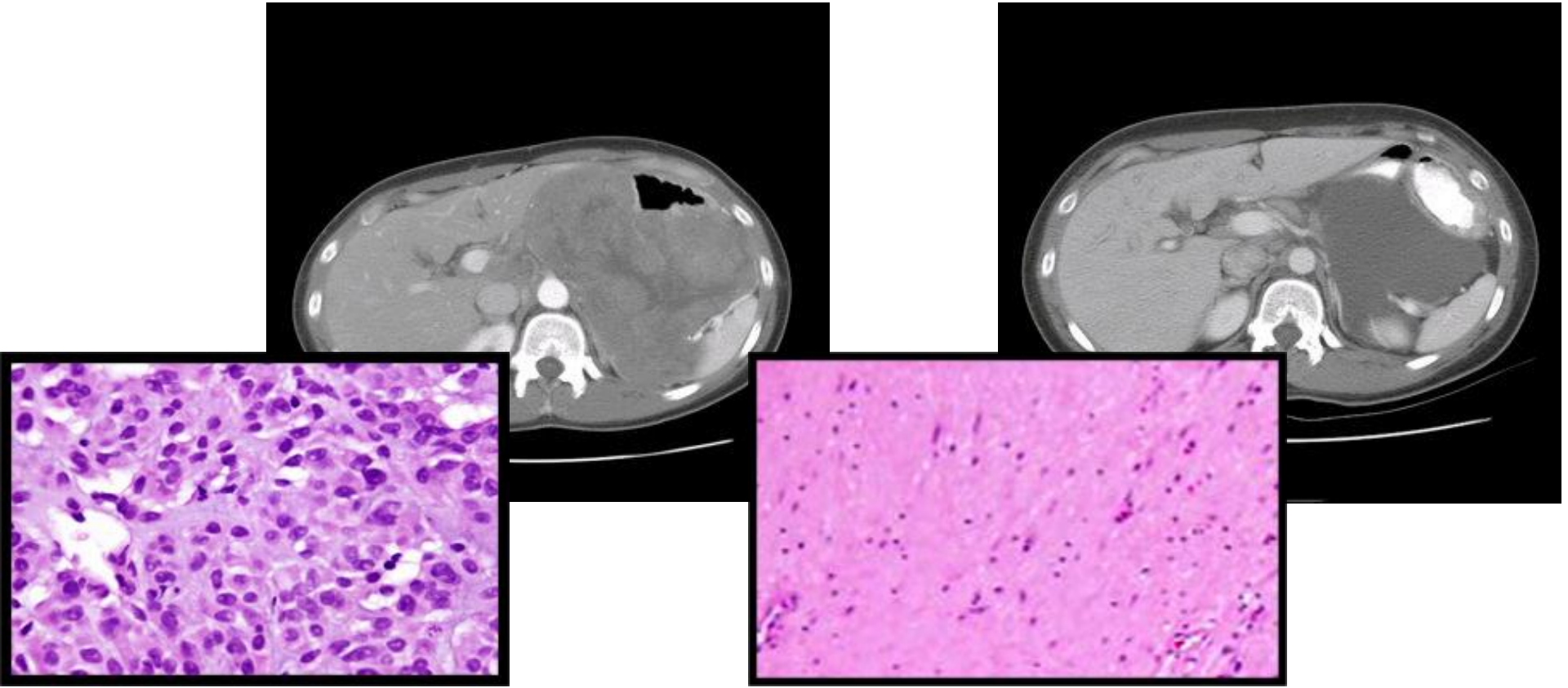
Approach to neoadjuvant chemotherapy

Approach to neoadjuvant chemotherapy

Approach to neoadjuvant chemotherapy



Approach to neoadjuvant chemotherapy



Approach to neoadjuvant chemotherapy

- How will it change the operation?
  - Decrease complexity/extent of surgery
  - 10 patients with tumors located at gastroesophageal junction
    → 6 able to avoid total gastrectomy
  - 29 other patients with gastric tumors
    --> None required total gastrectomy

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DOI: 10.1002/ijc.34052

CANCER THERAPY AND PREVENTION

IJC INTERNATIONAL JOURNAL of CANCER

The role of neoadjuvant imatinib in gastrointestinal stromal tumor patients: 20 years of experience from a tertial referral center

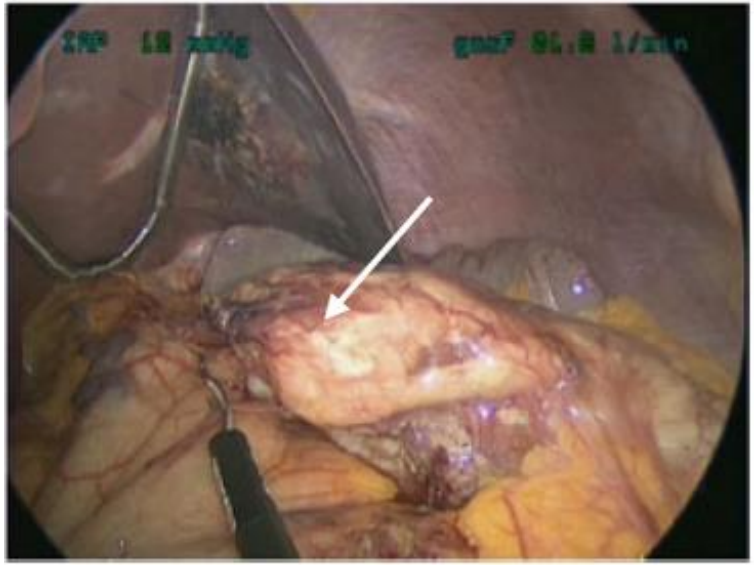
Sara Renberg[1] | Yifan Zhang[2,3] | Fredrik Karlsson[4,5] | Robert Bränström[4,5] | Jan Åhlen[4,5] | Li Jalmsell[4] | Christina Linder-Stragliotto[4,5] | Felix Haglund de Flon[2,3] | Andri Papakonstantinou[3,4]

Approach to neoadjuvant chemotherapy

- How will it change the operation?
  - Decrease complexity/extent of surgery

Approach to neoadjuvant chemotherapy

- How will it change the operation?
  - Make MIS approach possible



Management of Small GISTs

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Gastrointestinal Stromal Tumors

NCCN Guidelines Index
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Discussion

WORKUP AT PRIMARY PRESENTATION

- All patients should be evaluated and treated by a multidisciplinary team with expertise and experience in gastrointestional stromal tumors (GIST)
- For very small gastric GIST <2 cm[a]
  - Consider endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB)[b] or Endoscopic ultrasound-guided core needle biopsy (EUS-CNB)
  - Imaging[c]

MANAGEMENT BASED ON THE RESULTS OF INITIAL DIAGNOSTIC EVALUATION

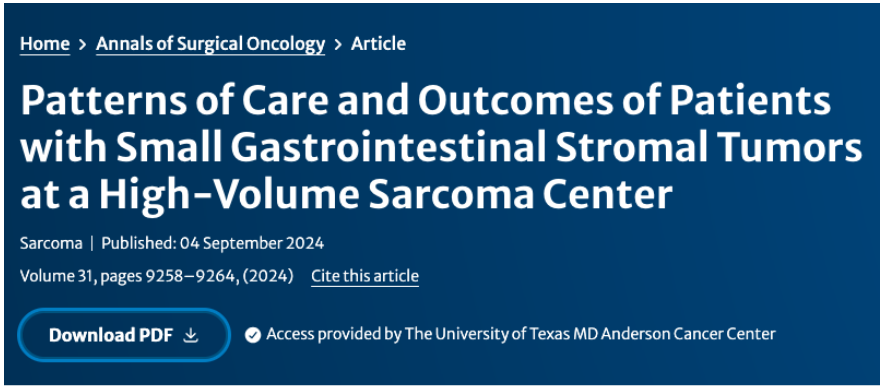
- No high-risk EUS features → Consider periodic endoscopic or radiographic surveillance[c,l]
- High-risk EUS[f] or biopsy features[g] → Complete surgical resection[m] → Postoperative Outcomes and Treatment (GIST-3)
- Resectable with minimal morbidity → Complete surgical resection[m] → Postoperative Outcomes and Treatment (GIST-3)

Management of Small GISTs

- 86 Patients with Small GISTs
  - 44 underwent upfront surgery (often not at MD Anderson)
  - 42 underwent active surveillance

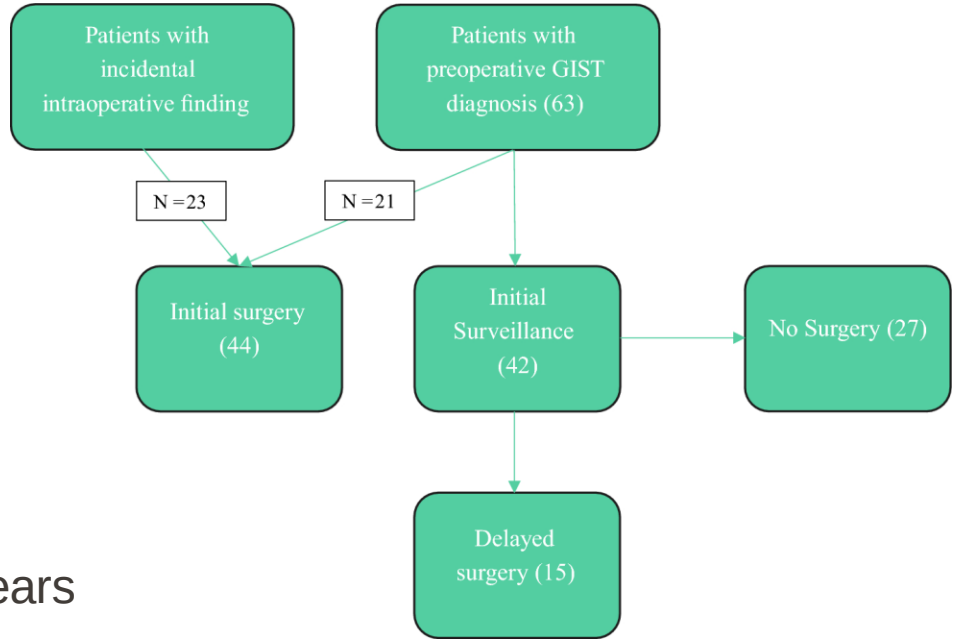
  → 27 Never underwent surgery

  → 15 eventually underwent surgery



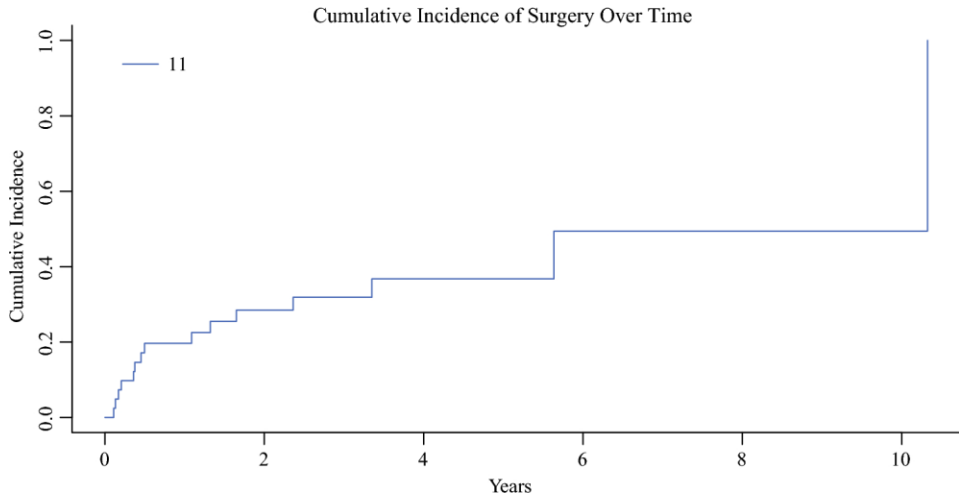
Management of Small GISTs

- 15 Patients eventually underwent surgery
  - 6 patients: Tumor growth
  - 4 patients: Patient preference
  - 1 patient: Tumor bleeding
  - 1 patient: Pain
  - 3 patients: Unknown
- Timeframe to surgery: Median 2 years



Management of Small GISTs

- Timeframe to surgery: Median 2 years
  - 1 patient: 40 days -> Presented to ER with pain
  - 1 patient: 11 years -> unknown



Management of Small GISTs

- Factors predicting who doesn't get surgery:
  - Age > 65
  - Multiple comorbidities
  - Presence of another cancer

Conclusions

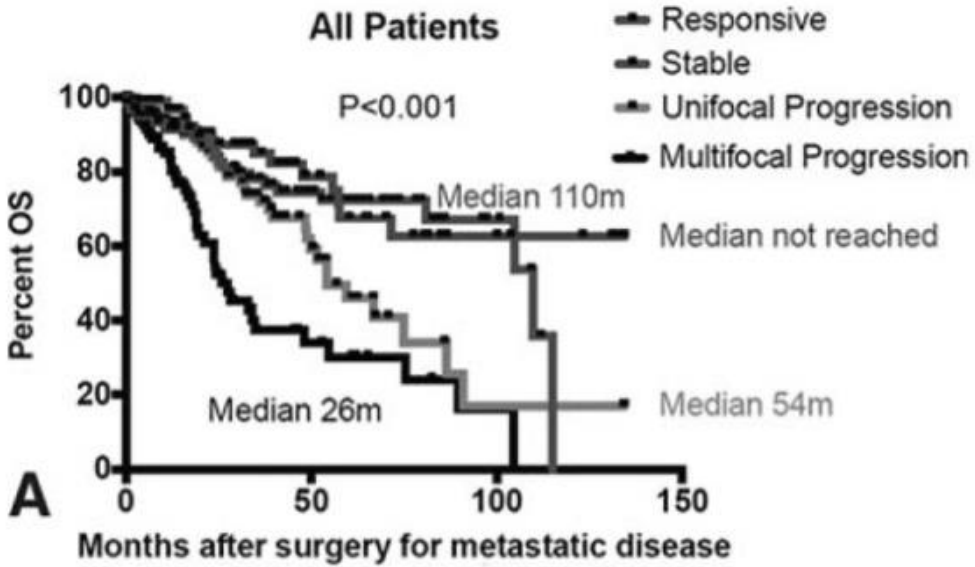
- Active Surveillance is safe (no differences in survival or risk of metastasis)
- Among young, otherwise healthy patients -> Majority eventually get resection
- My practical approach: Patient/physician discussion on preferences, low threshold to just remove

Role for Surgery in Metastatic Disease

Understanding who benefits:

Table 2 Retrospective studies of

Study
Raut, 2006 (35)
DeMatteo, 2007 (36)
Gronchi, 2007 (37)
Sym, 2008 (38)
Yeh, 2010 (39)
Mussi, 2010 (40)
Park, 2014 (41)
Rubió-Casadevall, 2015 (42)
Fairweather, 2018 (43)
Raut, 2010 (44)
Yeh, 2017 (45)

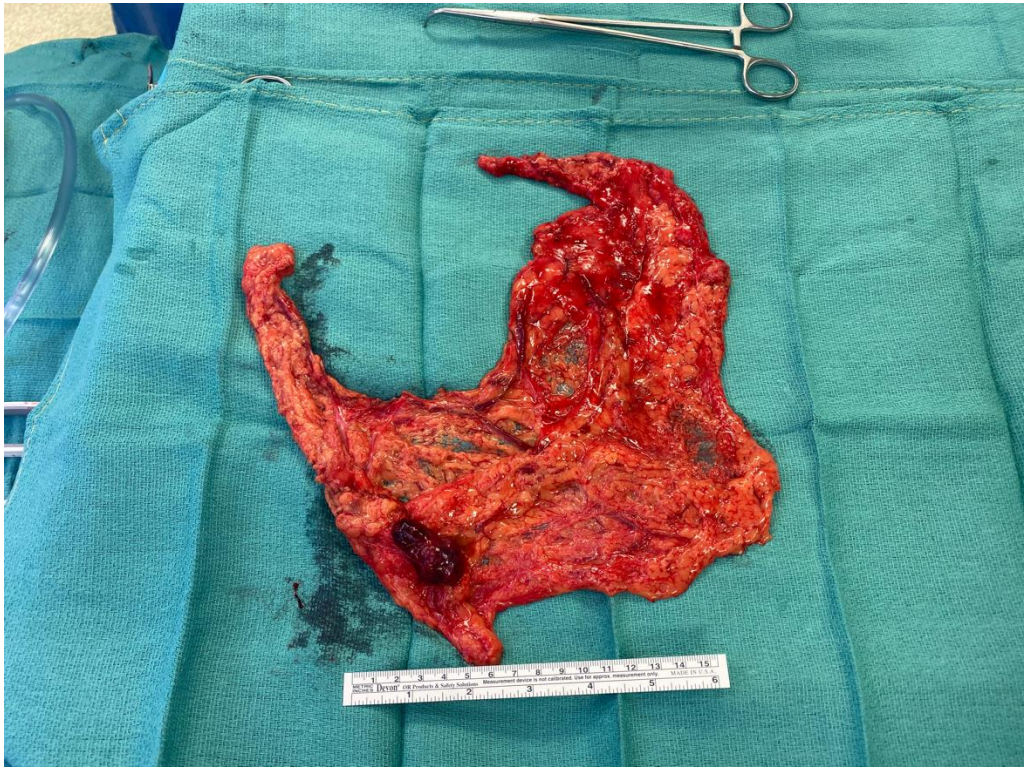


Role for Surgery in Metastatic Disease

Rationale for surgery:

- Palliation of symptoms
- Ability to clear all sites of disease
- Single site of progression (“oligoprogression”)
  - Avoid moving to next line TKI therapy
  - Evaluate tumor for secondary mutations
- Allow for treatment break?

Role for Surgery in Metastatic Disease



Role for Surgery in Metastatic Disease

52 year-old man

2001: Palpable abdominal mass → GIST Exon 11 mutation

2001-2002: ASWOG S0033 Trial of long-term imatinib in advanced GIST

5/2002: Resection (Pisters)

12/2002: Liver metastasis, resected

2002-2014: Adjuvant imatinib

2015: Treatment break → Peritoneal disease

Role for Surgery in Metastatic Disease

2015-2020: Resumes imatinib, near complete response in all sites of disease

2020: Progression of single right-sided peritoneal nodule

2020: Surgery (me)

Mutation analysis: Exon 13, confirmed sensitive to sunitinib, TSC mutation → Possible candidate for mTor inhibitor trial

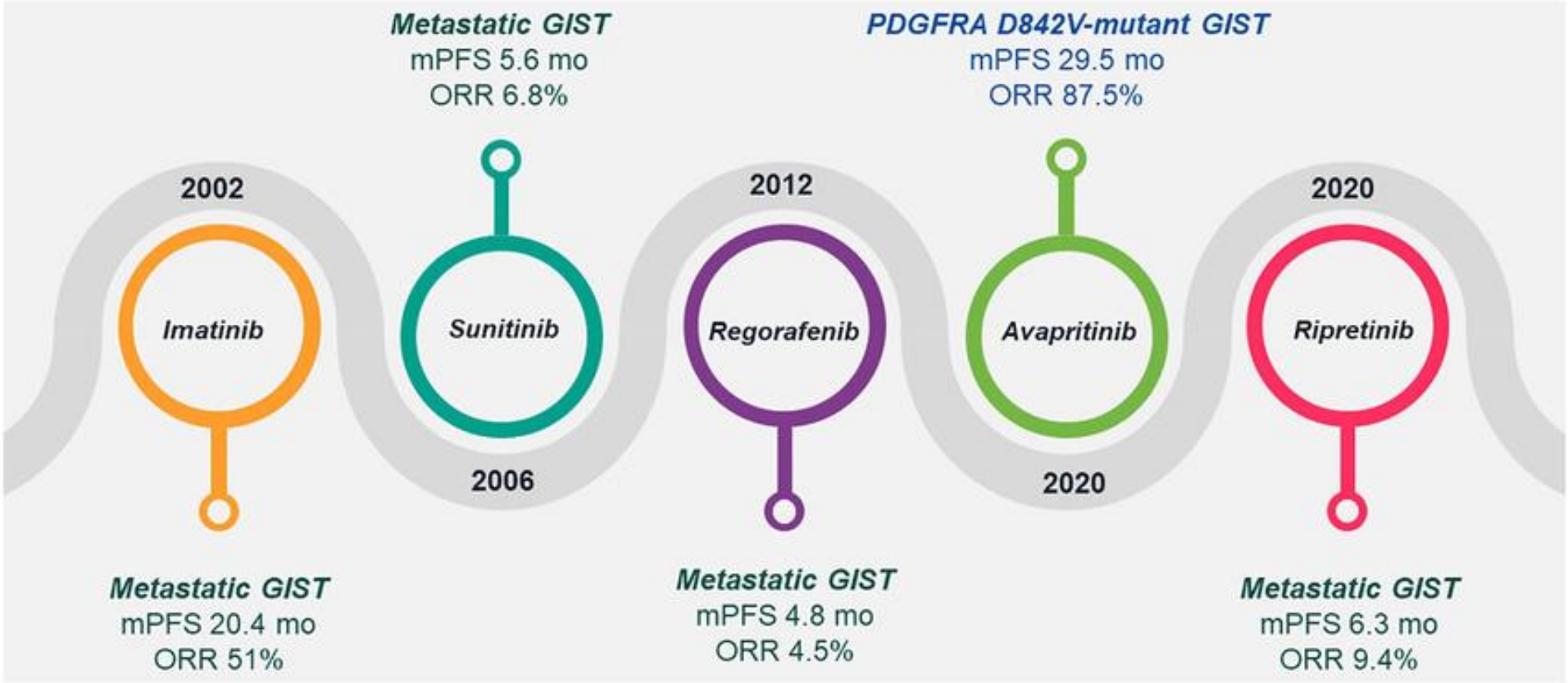
Role for Surgery in Metastatic Disease

2020-2021: Sunitinib

2021: Progression → Clinical trial

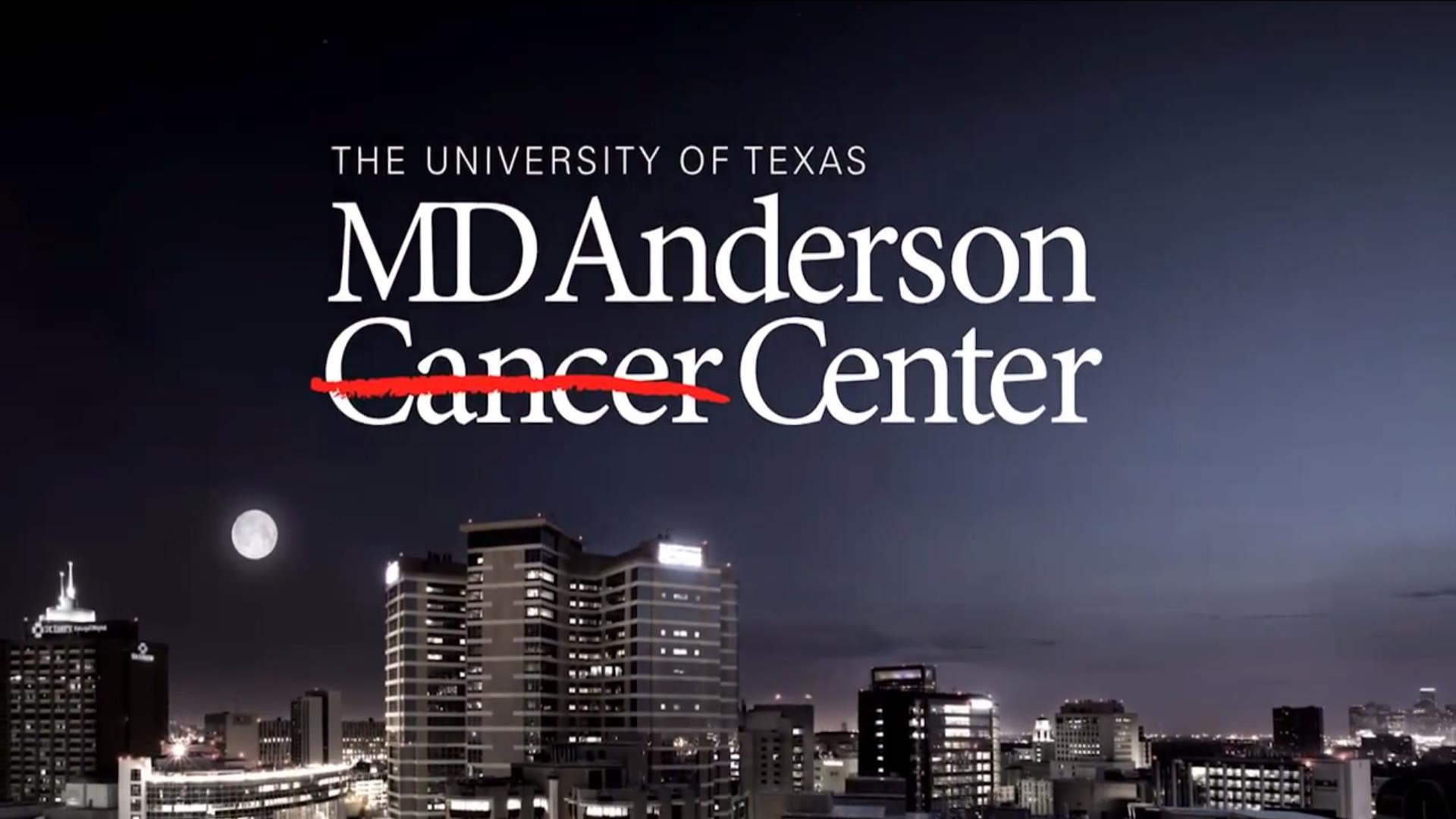
2022: Regorafinib

Role for Surgery in Metastatic Disease



What's next in GIST?

- Circulating tumor DNA
- Next generation TKIs
- Better understanding of role of surgery in metastatic setting
- Improving surgical technology → Expanded access to MIS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