



How surgery fits into the care and the challenges for NETs patients

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Overview

- What's the role of surgery in NETs?
 - *Digestive system NETs*
 - *Metastatic NETs*
- Why is a *multidisciplinary clinic* the best way to navigate decisions regarding surgery?
- *What do I need to ask* the surgeon before and after my NETs surgery?



What's the Role of Surgery?





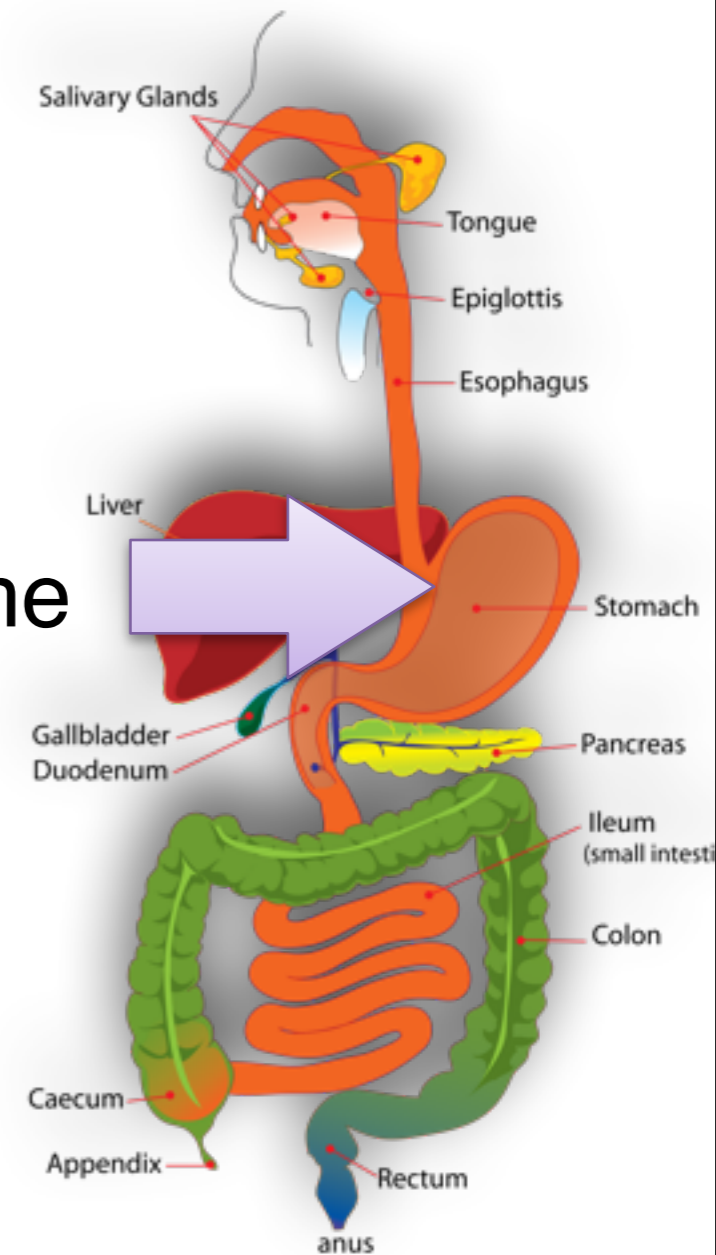
What's the Role of Surgery?

- Surgery is the **PRIMARY** modality of cure ... but surgery means different things for different NETs!



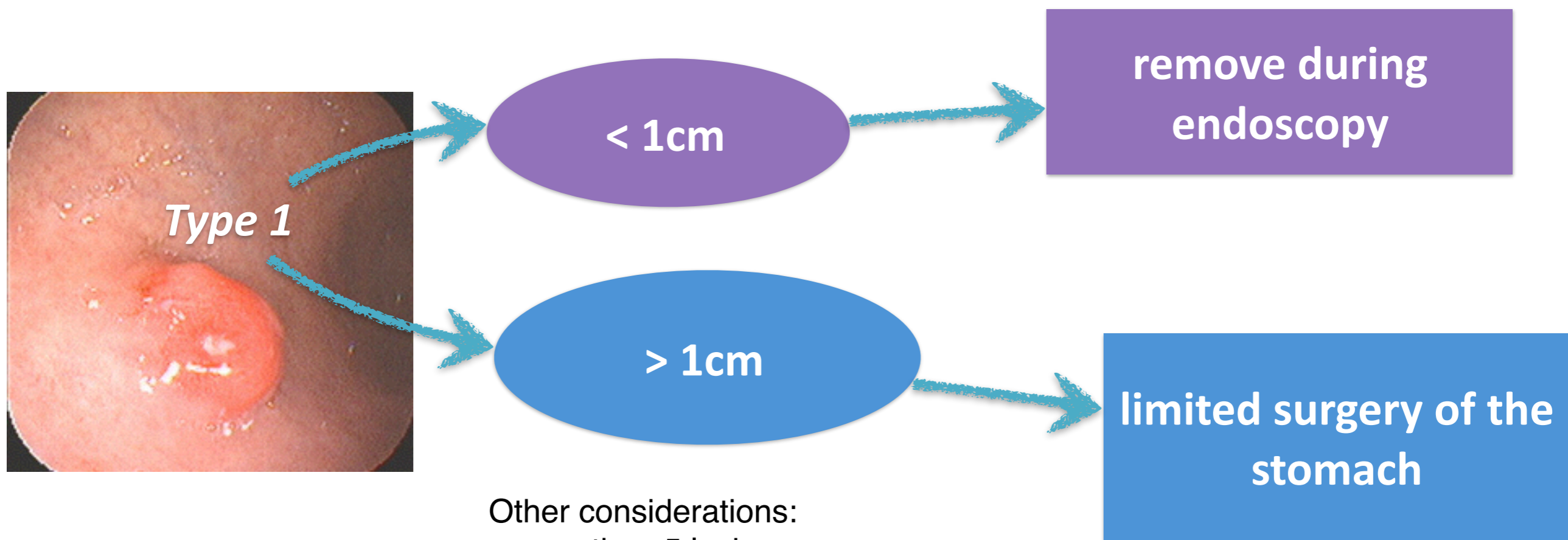
There are 4 types of stomach NETs

- Less than 1% of all gastric neoplasms
- Four main groups:
 - Associated with chronic atrophic gastritis type A (CAG-A)
 - Associated with Zollinger-Ellison Syndrome (ZES)
 - Sporadic Gastric NETs
 - Small Cell Gastric NETs



Type I Gastric NETs

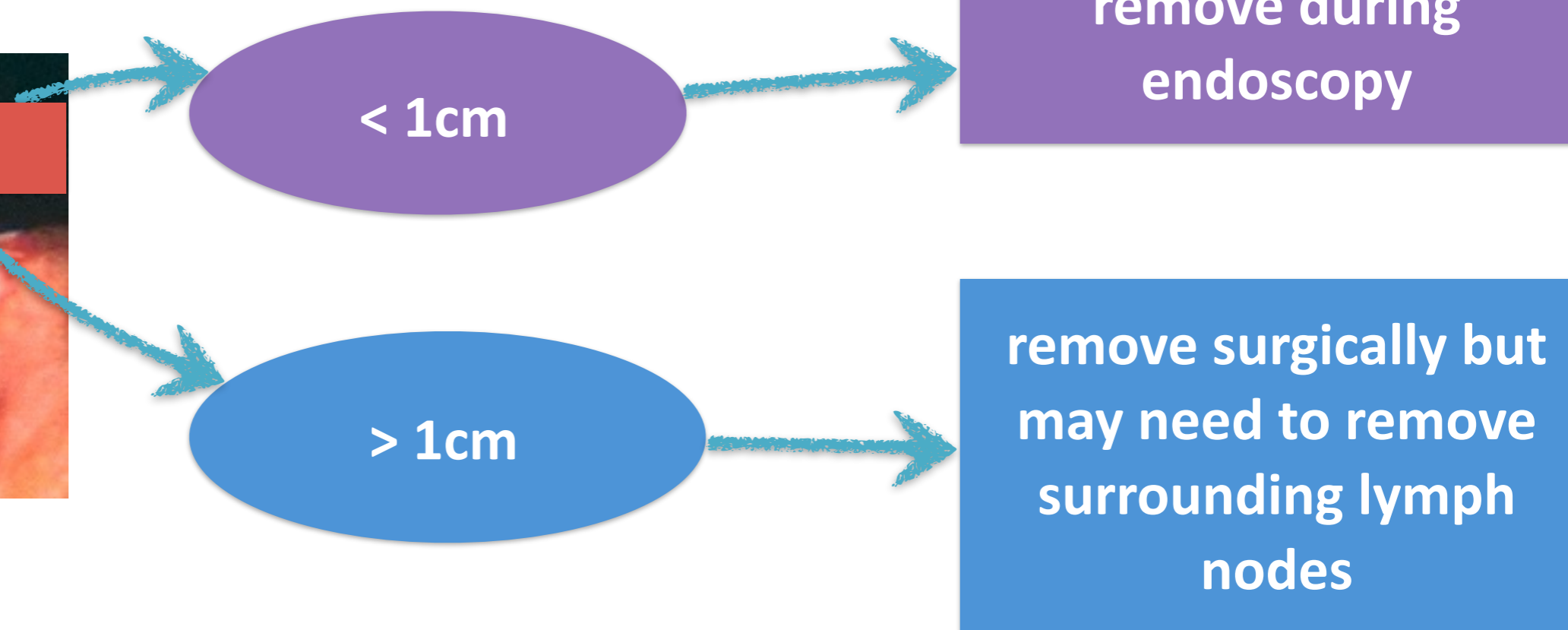
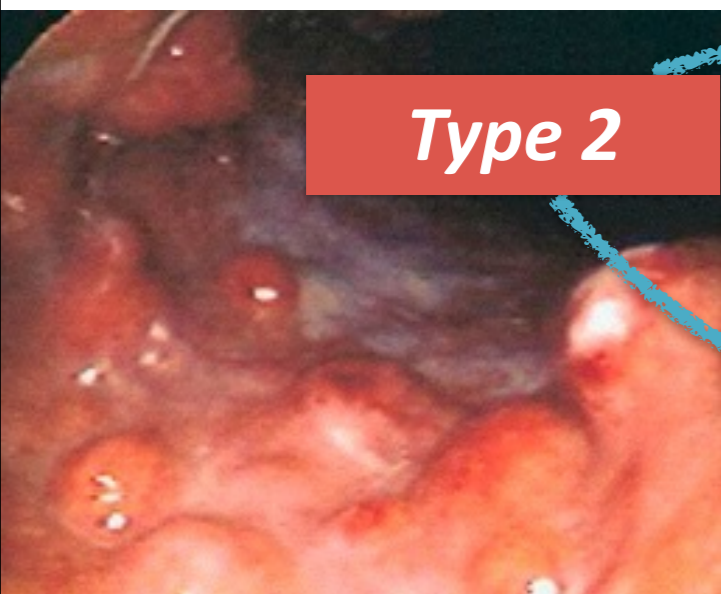
- Good prognosis, likely related to indolent nature
- Surrounded by “chronic atrophic gastritis”



Other considerations:
- more than 5 lesions
- refractory anemia

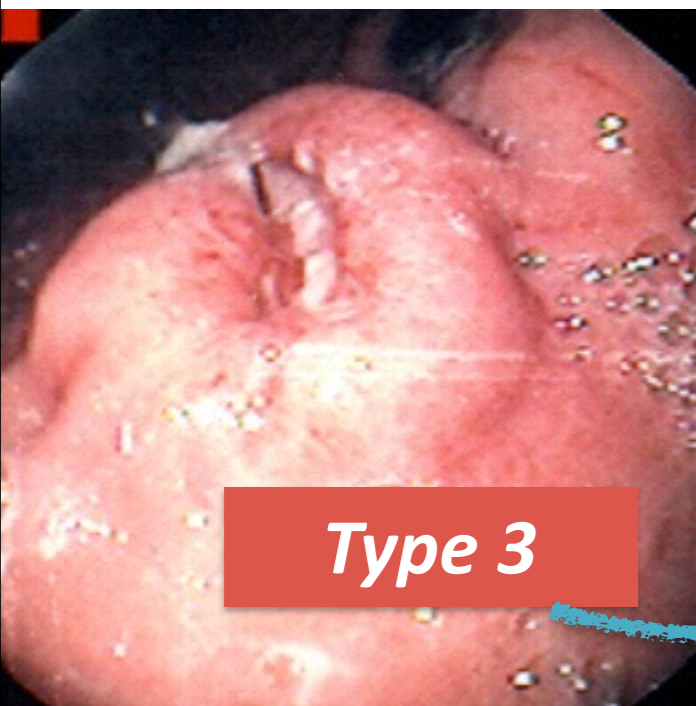
Type II Gastric NETs

- Think “Family History”
- *Usually* behaves less aggressively, similar to Type I but needs more thought



Type III Gastric NETs

- much more aggressive than Type I and Type II
- is not surrounded by 'chronic atrophic gastritis' - so it means your endoscopist *has to biopsy the NORMAL tissue*

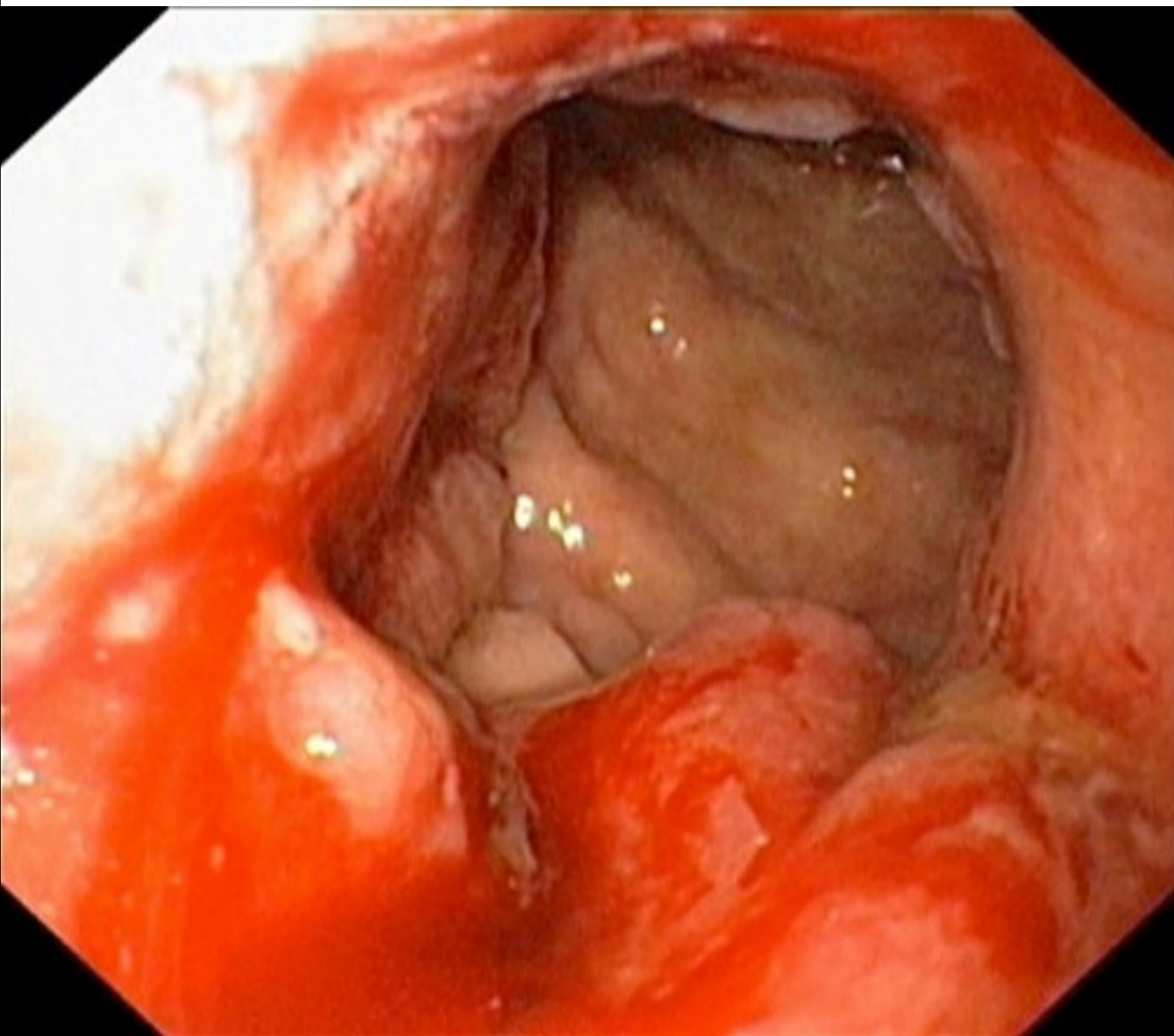


Any size

Surgery that involves a reconstruction, and all surrounding lymph nodes



Type IV Gastric NETs



- the most aggressive stomach NET - usually presents as a large lesion and not usually operable
- often called ‘small cell’ or ‘poorly differentiated’
- needs team plan ASAP



Characteristics and Considerations

Gastric NETs Type	Key Diagnostics	Surgical considerations?
ALL	<ul style="list-style-type: none"> - EUS: occurs in layers 1,2 or 3 - homogenous, well demarcated, mildly hypoechoic 	
I	<ul style="list-style-type: none"> - occurs in setting of chronic atrophic gastritis type A <ul style="list-style-type: none"> - in the fundus or body, often multicentric - small, typically lower Ki-67 <5% - increased gastrin 	<ul style="list-style-type: none"> ● very indolent disease in general ● > 1cm lesion may be better with surgical excision ● rare patient has refractory anemia
II	<ul style="list-style-type: none"> - MEN 1 history - otherwise similar characteristics as type I including increased gastrin 	<ul style="list-style-type: none"> ● not so indolent, higher rate of LN + ● > 1cm should be excised with nodal clearance.
III	<ul style="list-style-type: none"> - sporadic, not in association with CAG A - normal gastrin - may over produce histamine as well as serotonin - histamine causes itching, bronchospasm and flushing 	<ul style="list-style-type: none"> ● over 3/4 patients will present with LN+ so needs surgery with nodal clearance ● interface with medical oncology required to optimize care
IV	<ul style="list-style-type: none"> - poorly differentiated large lesions - normal gastrin 	<ul style="list-style-type: none"> ● often not resectable, but we need to help obtain good tissue for diagnosis ● interface with medical oncology ASAP



Surgical Planning

Gastric NETs Type	Surgical considerations?	Laparoscopic considerations
I	<ul style="list-style-type: none"> • very indolent disease in general • > 1cm lesion may be better with surgical excision • rare patient has refractory anemia 	<ul style="list-style-type: none"> • select patients • < 1 cm lesions should go for EMR first • solitary lesions best inked prior to surgery • multiple lesions need special consideration - antrectomy?
II	<ul style="list-style-type: none"> • not so indolent, higher rate of LN + • > 1cm should be excised with nodal clearance. 	<ul style="list-style-type: none"> • NO ROLE FOR ANTRECTOMY - cause of hypergastrinemia is NOT antrum • role of laparoscopy unclear due to need to address gastrinomas at same time as gastric NETs
III	<ul style="list-style-type: none"> • over 3/4 patients will present with LN + so needs surgery with nodal clearance • interface with medical oncology required to optimize care 	<ul style="list-style-type: none"> • may be the ideal case for laparoscopy in select cases • requires high laparoscopic skill set as most patients have locally advanced disease that may require subtotal or total gastrectomy
IV	<ul style="list-style-type: none"> • often not resectable, but we need to help obtain good tissue for diagnosis • interface with medical oncology ASAP 	<ul style="list-style-type: none"> • unlikely role for laparoscopy for resection

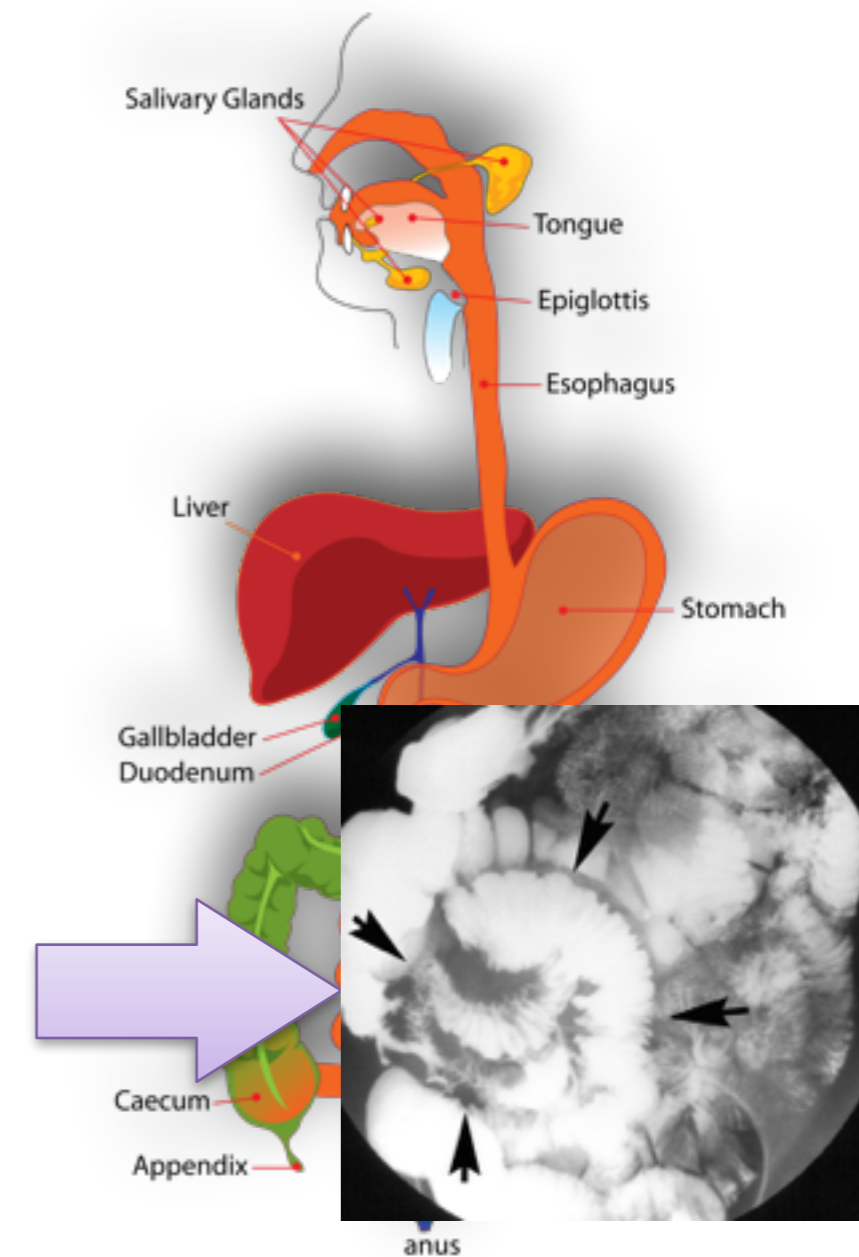


So what are the challenges for our Gastric NETs patients?

- Getting the diagnosis right
- Making a good decision re: observation versus endoscopic surveillance/management versus surgery
- If surgery - then you need to understand what it means from limited surgery to losing part of your stomach - different impacts on your life after

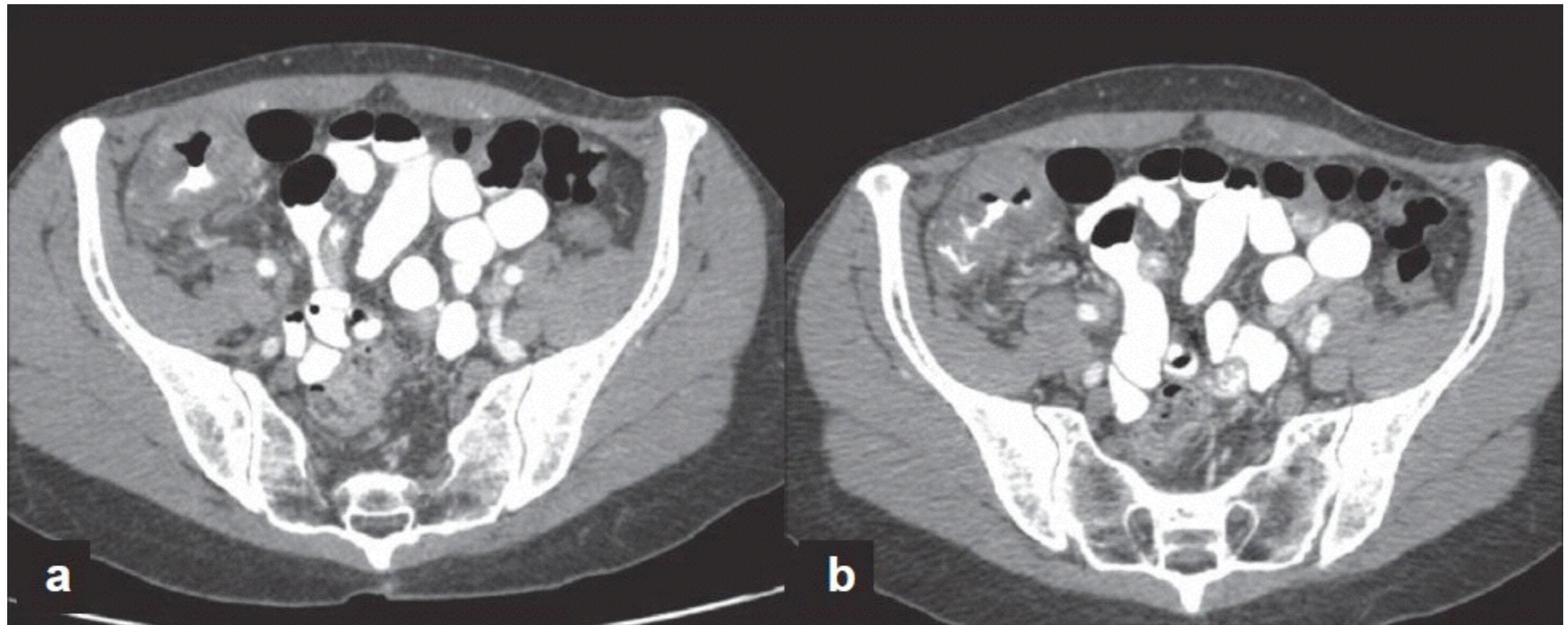
Small Bowel NETs

- Up to 1/3 of small bowel neoplasms
- Typically present in 60-70s
- Standard imaging techniques limited
- Mesenteric buckling and fibrosis
- MRI /CT enteroclysis
- Often history of years of vague abdominal discomfort



Imaging is Key!

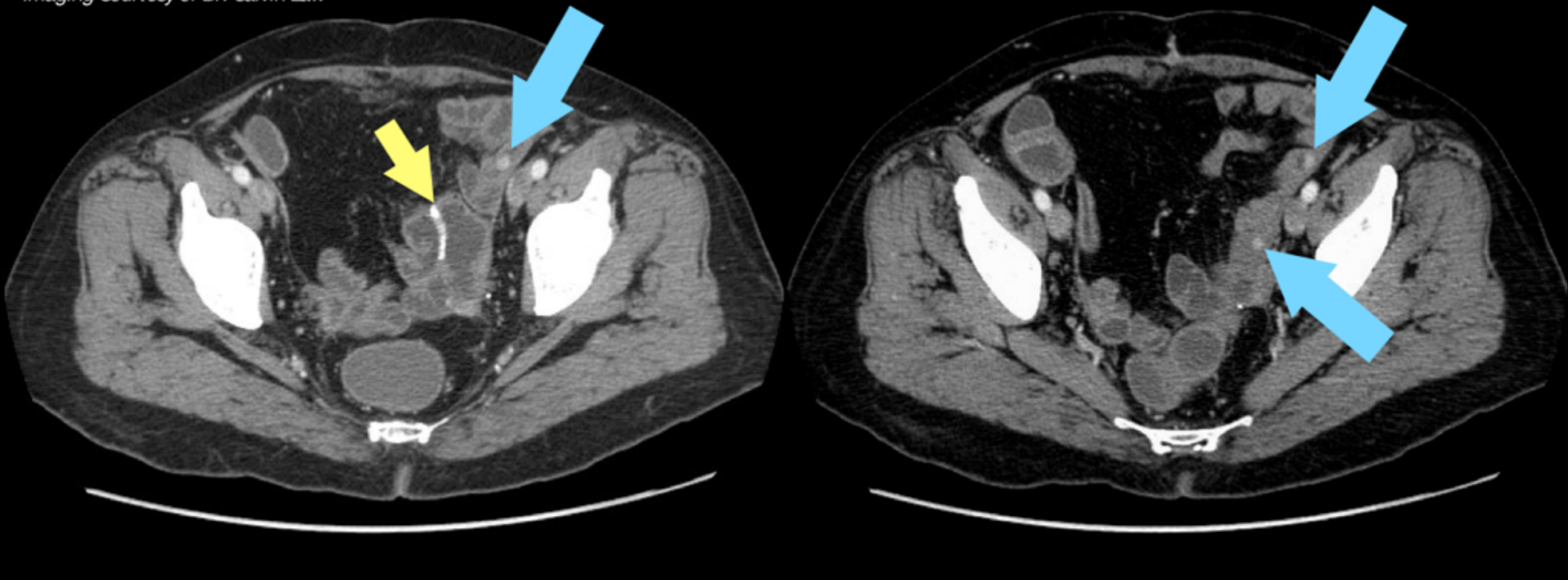
Standard CT Abdomen with oral contrast



The right imaging!

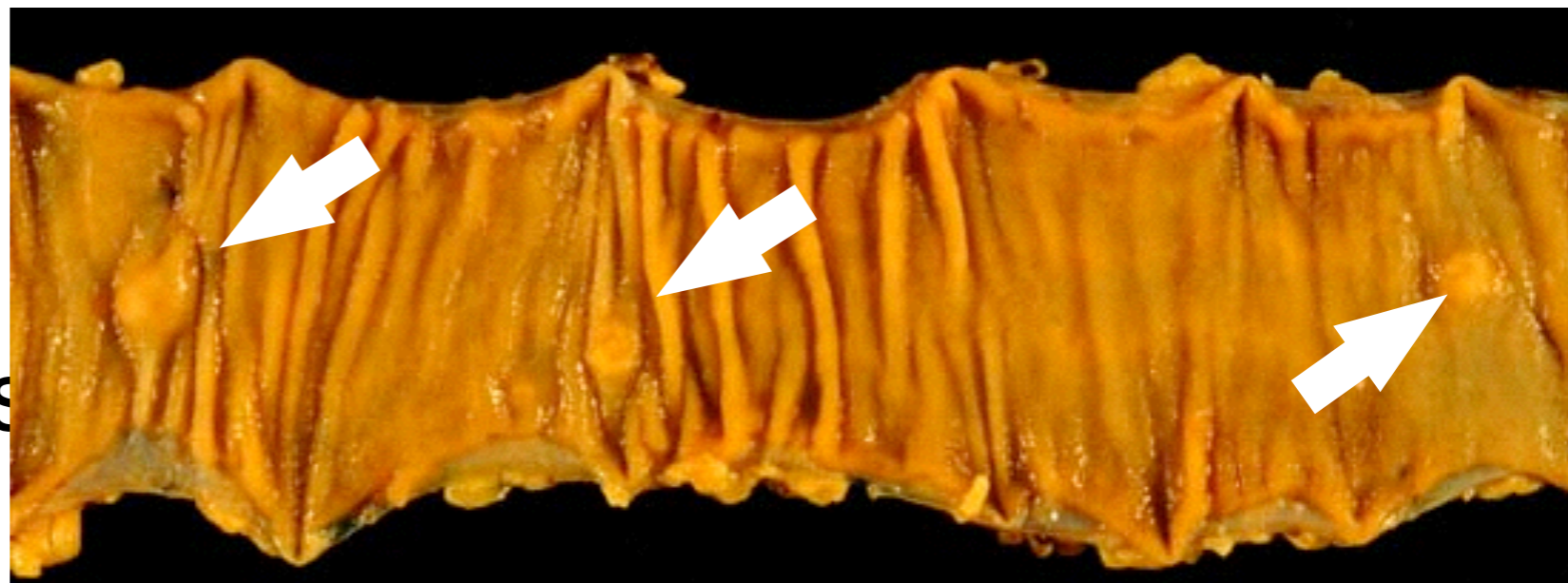
CT Enterogram with “negative” contrast

Imaging Courtesy of Dr. Calvin Law

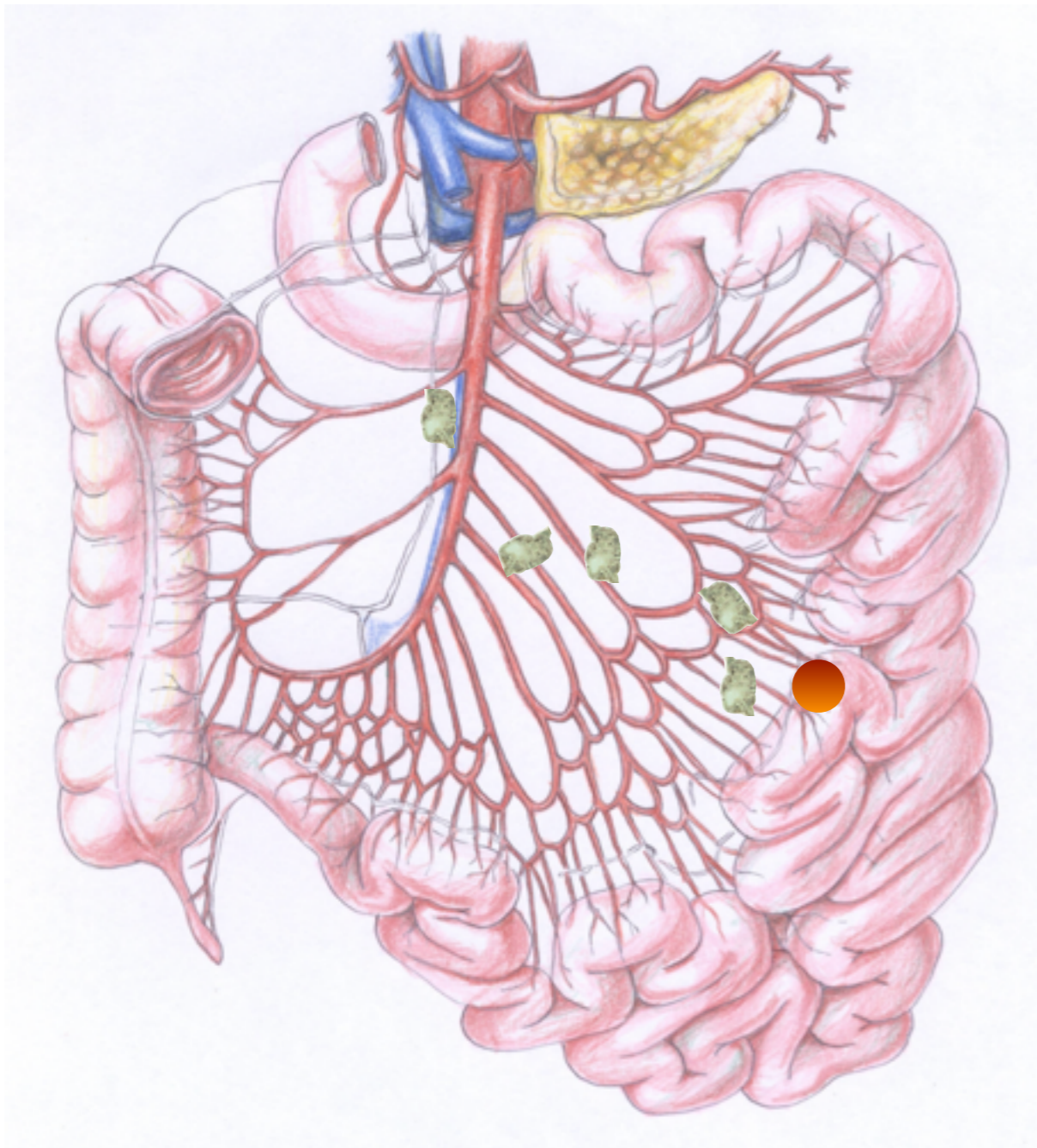


What makes the small bowel different?

- Most frequently in terminal ileum
- Can present as **dozens** of lesions
- Typically have **nodal metastases**
- Origin: **serotonin** producing intra-epithelial cells
- Tumour size not a predictor for nodal or distant metastases

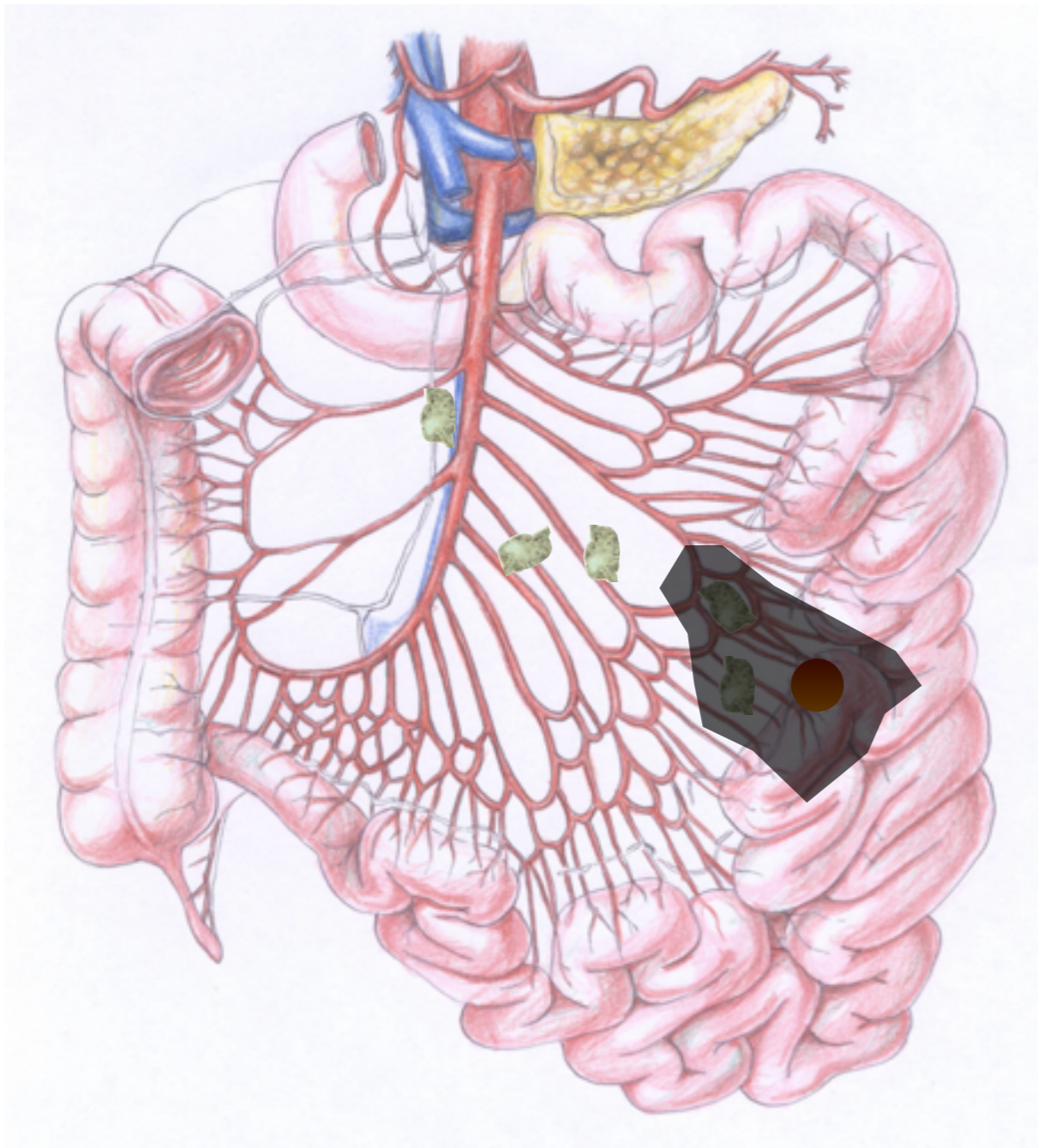


Questions during surgery for Small Bowel NETs



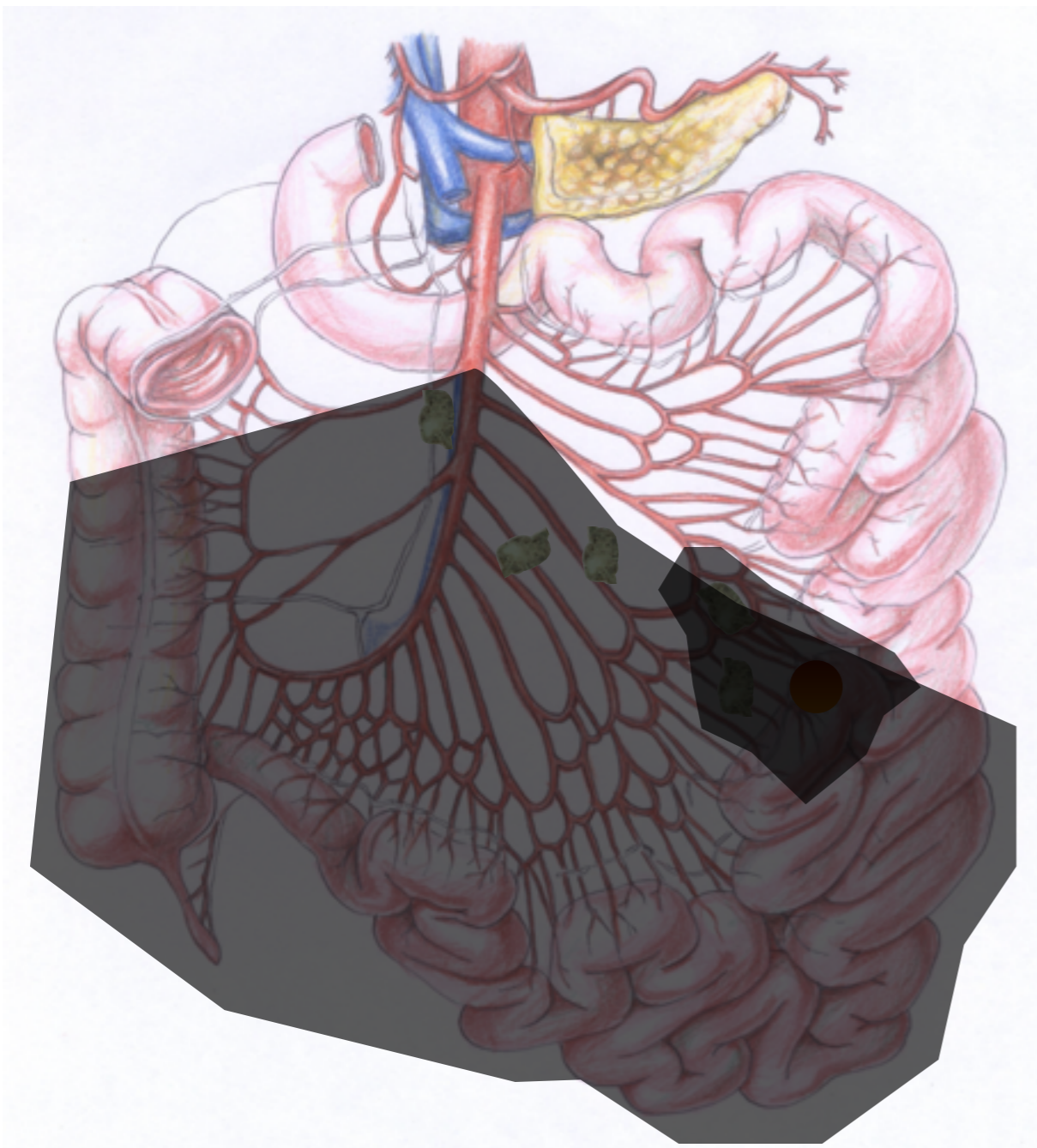
- Small Bowel NET
- Wide distribution of involved LNs

Option 1: small Surgery



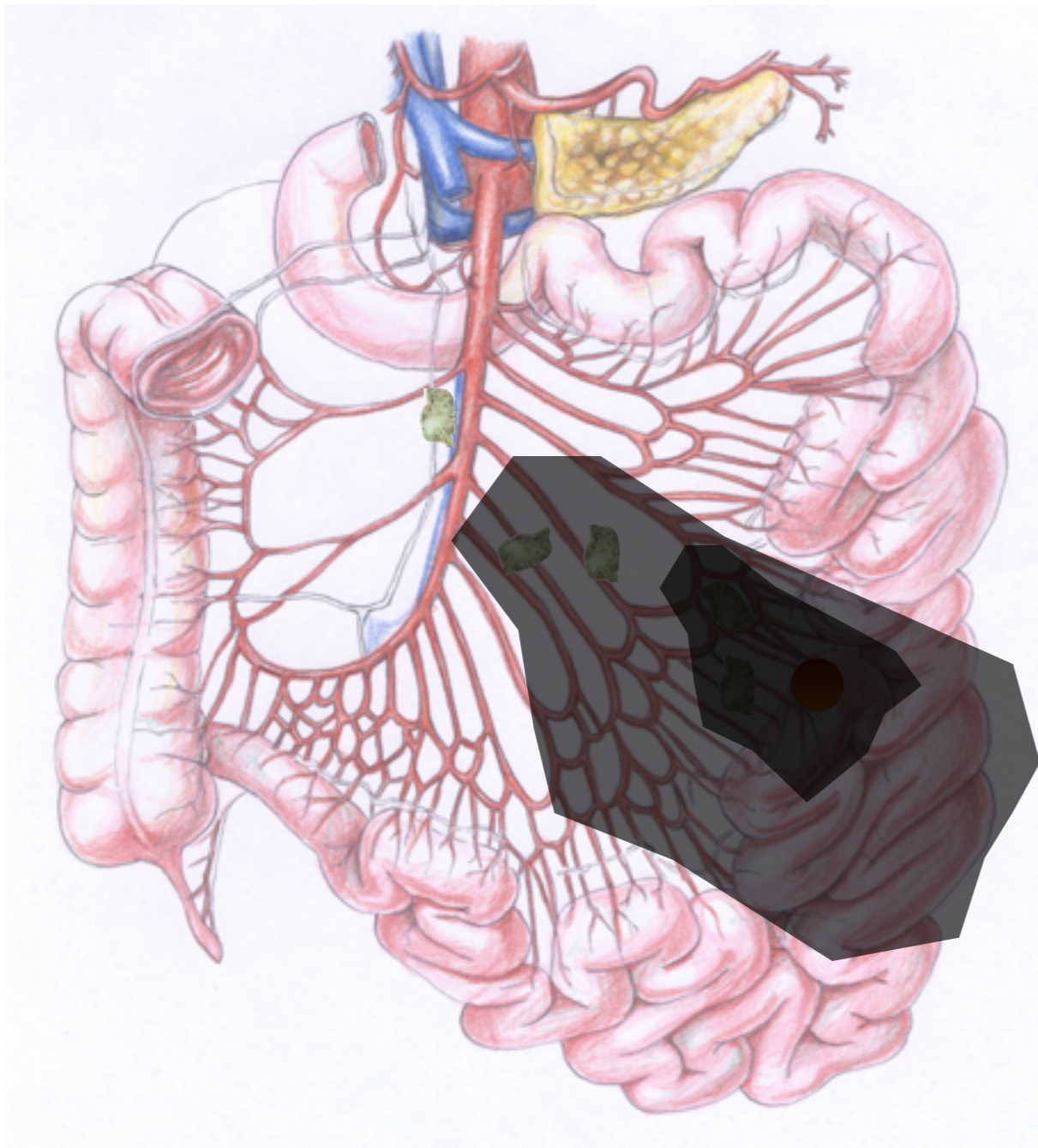
- Very conservative surgery
- Problems:
 - **larger residual volume of disease left behind than necessary**
 - **Residual mesenteric disease could lead to further disease related complications**

Option 2: BIG surgery



- Very radical surgery
- Problems:
 - **Complications!**
 - Quality of life for patient?
 - does not take into consideration the synergism of medical therapy to surgical resection

Option 3: The *optimal* surgery



- Appropriate surgery
- Key Points:
 - Maximal disease volume reduction balanced with patient functional considerations
 - allows the use of *multiple multi-disciplinary options* to achieve best patient results

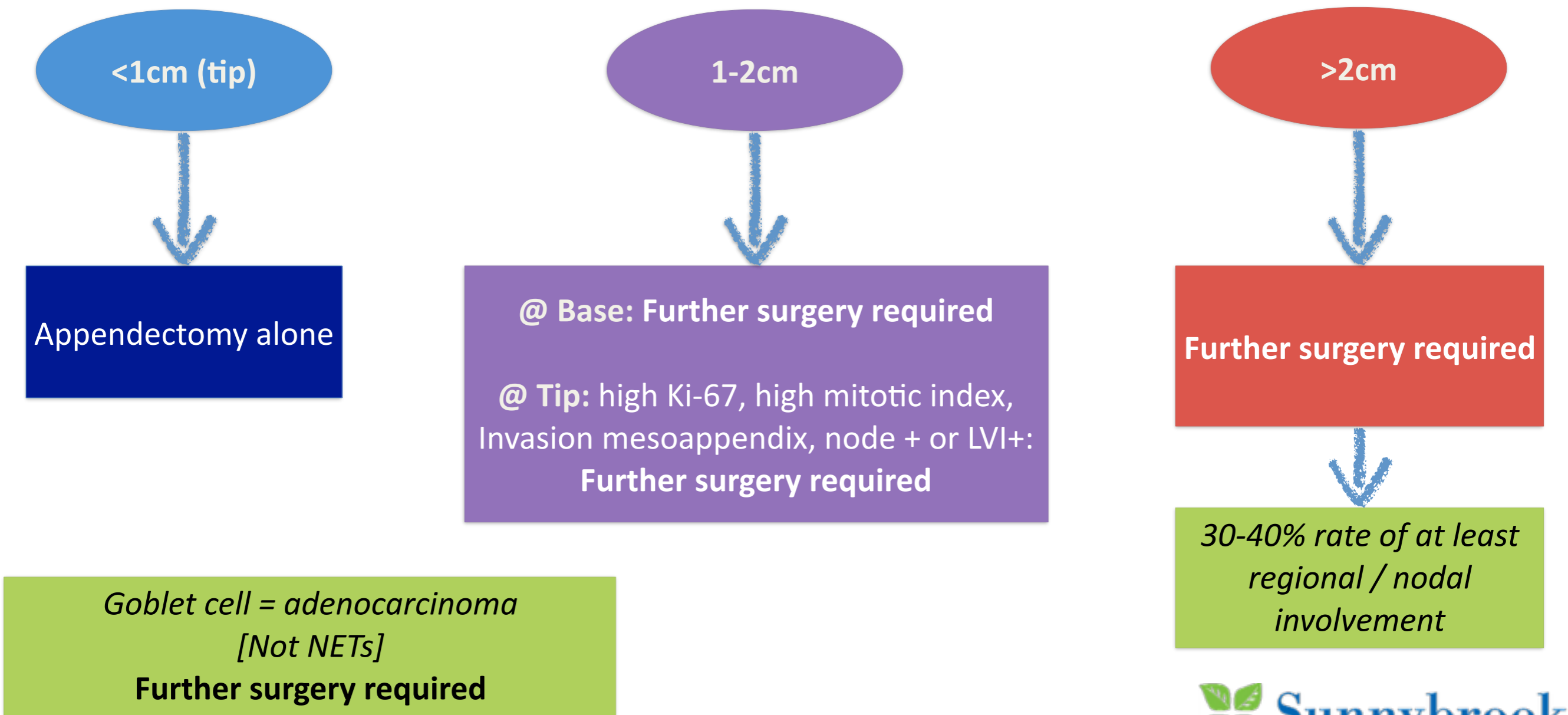


Appendiceal NETs

- Most common neoplasm of the appendix
- Present in the 40-50s
- ?regress with age
- Parallels with studies of subepithelial endocrine cells
- < 10% symptomatic



Strategies for Appendiceal NETs



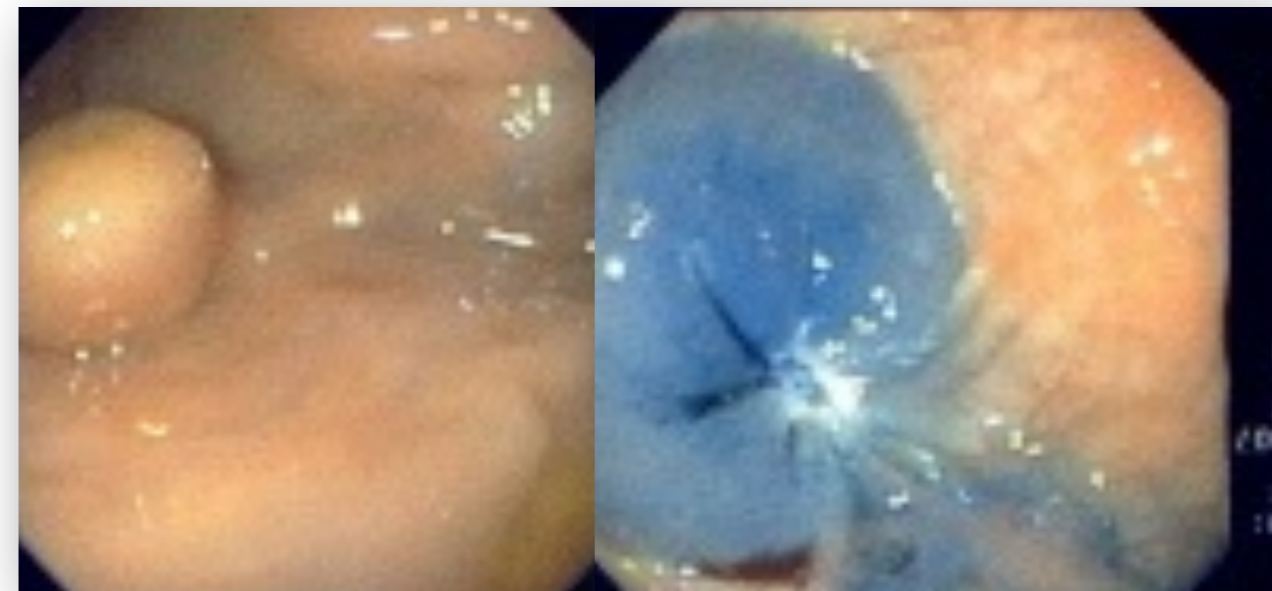
Rectal NETs

- 1-2% of rectal tumours
- Presentation in the 60s
- 50% asymptomatic, found on routine endoscopy
- NOT associated with serotonin or histamine: carcinoid syndrome rare



Rectal NETs - Size Matters!

- 2/3 are < 1cm
- Endoscopic or Transanal resection
- Caveats: muscular invasion, symptoms, ulceration
- > 2cm
- LAR or APR
- Cavetas: do careful workup for regional and systemic disease





What about “spread”?

- There are options to help our patients
- Surgical Options for Liver METs:
 - Requires sophisticated imaging
 - Requires different surgical techniques
 - Requires huge amount of planning - especially with the patient!

Intra-operative Octreotide Protocol

Patients well controlled on Octreotide LAR (Sandostatin) 30mg im

- additional dose of Octreotide LAR 60mg 2-3 weeks prior to procedure
- supplementary dose of Octreotide immediate release 250mcg-500mcg SC 1-2 hours before procedure
- intra-operative Octreotide for carcinoid crisis with hypotension 500mcg-1000mcg IV q5min, may need infusion 50mcg-200mcg/hr, in addition to fluids
- patients who have required supplemental doses intra-operatively should have 50mcg-200mcg/hr infusion for 4 - 24 hours post-operatively

Patients poorly controlled on Sandostatin LAR

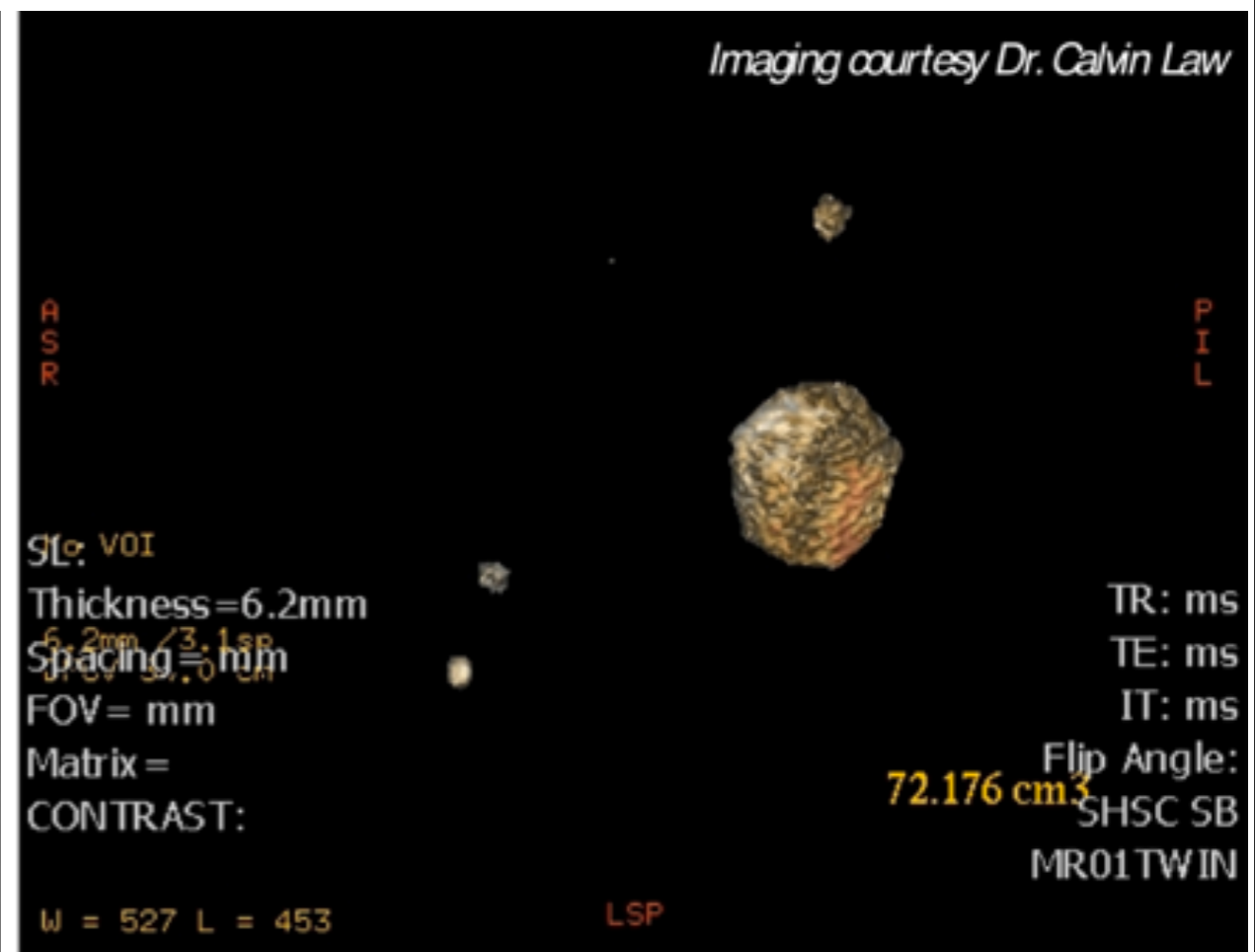
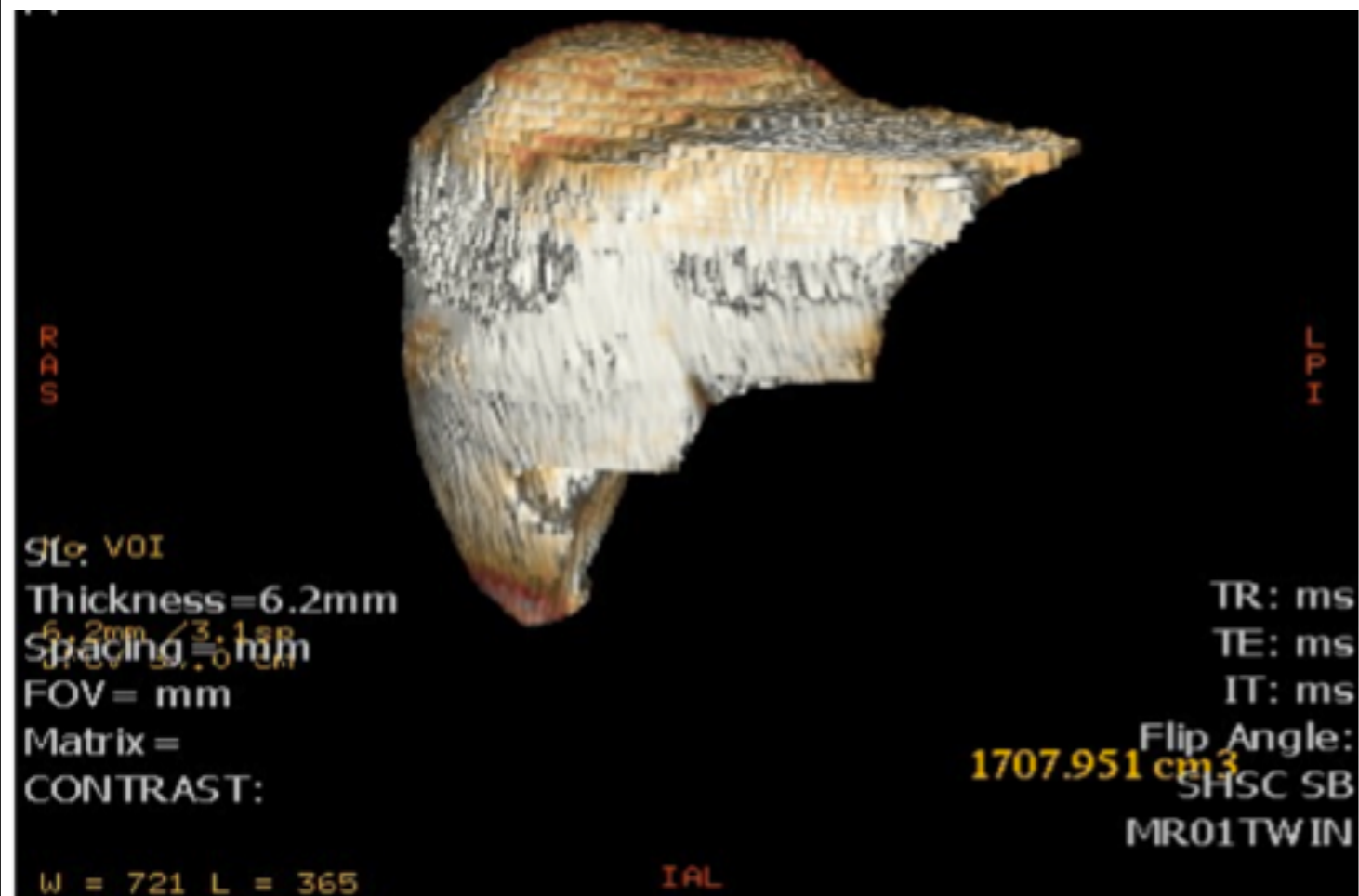
- additional dose of Octreotide LAR 60mg 2-3 weeks prior to procedure
- supplementary dose of 500mcg-1000mcg SC 1-2 hours before procedure
- infusion of 100mcg-250mcg/hr starting 1 hour before procedure and continue 12-24 hours after surgery and wean as tolerated

Patients not on therapy or for emergency Surgery

- 500mcg-1000mcg SC 1-2 hours before procedure
- consider post-operative infusion 100mcg-250mcg/hr
- ***Octreotide immediate release is available in the OR in vials of 100mcg/mL or can be ordered from Pharmacy in vials at a concentration of 500 mcg/mL***



Making technology work for our patients!





Find your way





It takes work for all of the team!



Imaging Courtesy of Dr. Calvin Law

How can a patient navigate this all?

Feinberg Y, Law CHL, Singh S, Wright FCW. *Eur J Onc N ePub 2013*

- At the start of establishing the clinic:
 - Qualitative study
 - In-depth interviews, analyzed for themes
 - 39 invitations; 18 interviews
 - Interview time range: 9 min – 2h 8min
 - 8 Female : 10 Males
 - Median age was 63 [range: 45-77]
 - In-depth, iterative approach based on grounded theory





Themes / Perspectives

- Difficulty with obtaining a diagnosis
- Difficulty in obtaining appropriate information about NETs from health care providers
- Difficulty finding treatment centers with knowledge of NETs
- Difficulty in finding disease specific support
- No clear disease pathway identified

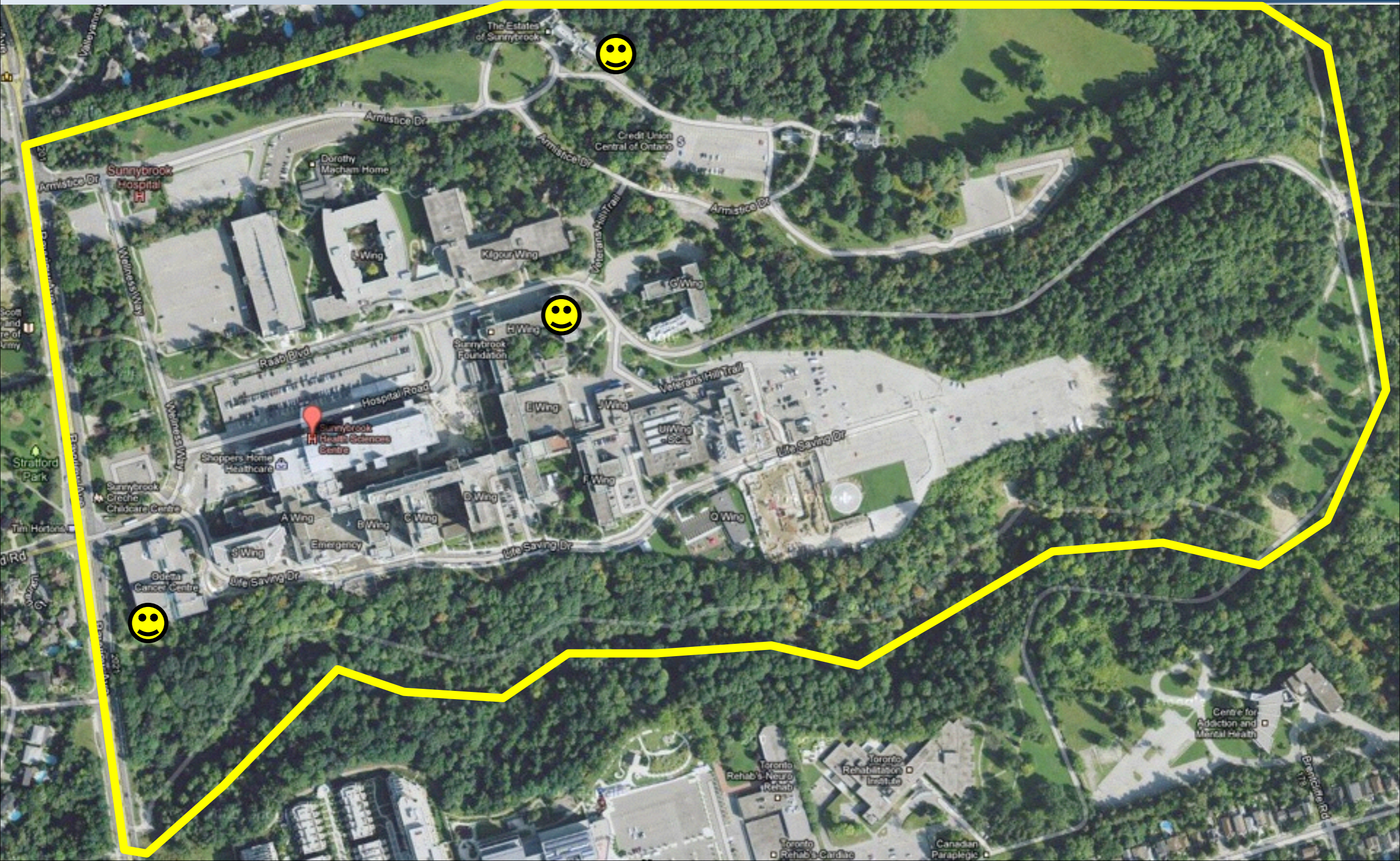


Sunnybrook Health Sciences Centre

- Sunnybrook at a glance:
 - has several campuses including this main campus, the Holland Centre, and St. John's Rehabilitation Centre
 - has over 11,000 employees
 - runs over 1,200 beds
 - performed over 16,000 surgeries last year



Just having interested MDs was not enough



Creating a safety NET



Institute of Clinical Evaluative Sciences

- Population based health services research
- Epidemiology research

Inpatient Wards and Diagnostic Units

- Inpatient – surgical, medical and radiation oncology
- Endoscopy Unit
- Cardiology, Angiography and Echo Units Unit

S-Wing

- Basic Science Research Labs
- Research Admin and Finance



Outpatient Diagnostic/Clinical Unit

- Gastroenterology
- Endocrinology

M-Wing

- Surgical Suites – dedicated OR suites for multiple sites/function such as Minimally Invasive Surgery and Hepatobiliary Surgery
- Diagnostic Radiology & Nuclear Medicine
 - Multi-detector Helical CTs
 - 1.5 and 3T MRIs
 - Contrast Enhanced U/S
 - Octreotide/MIBG Scanning
- Interventional Radiology
 - Angiography
 - Embolization
 - RFA/Microwave Ablation

Odette Cancer Center:

- Outpatient oncology clinics – Home of the Susan Leslie Clinic for NETs
- Clinical Trials Resources
- Clinical Research Space
- Chemotherapy Unit
- Radiation / Brachytherapy Unit



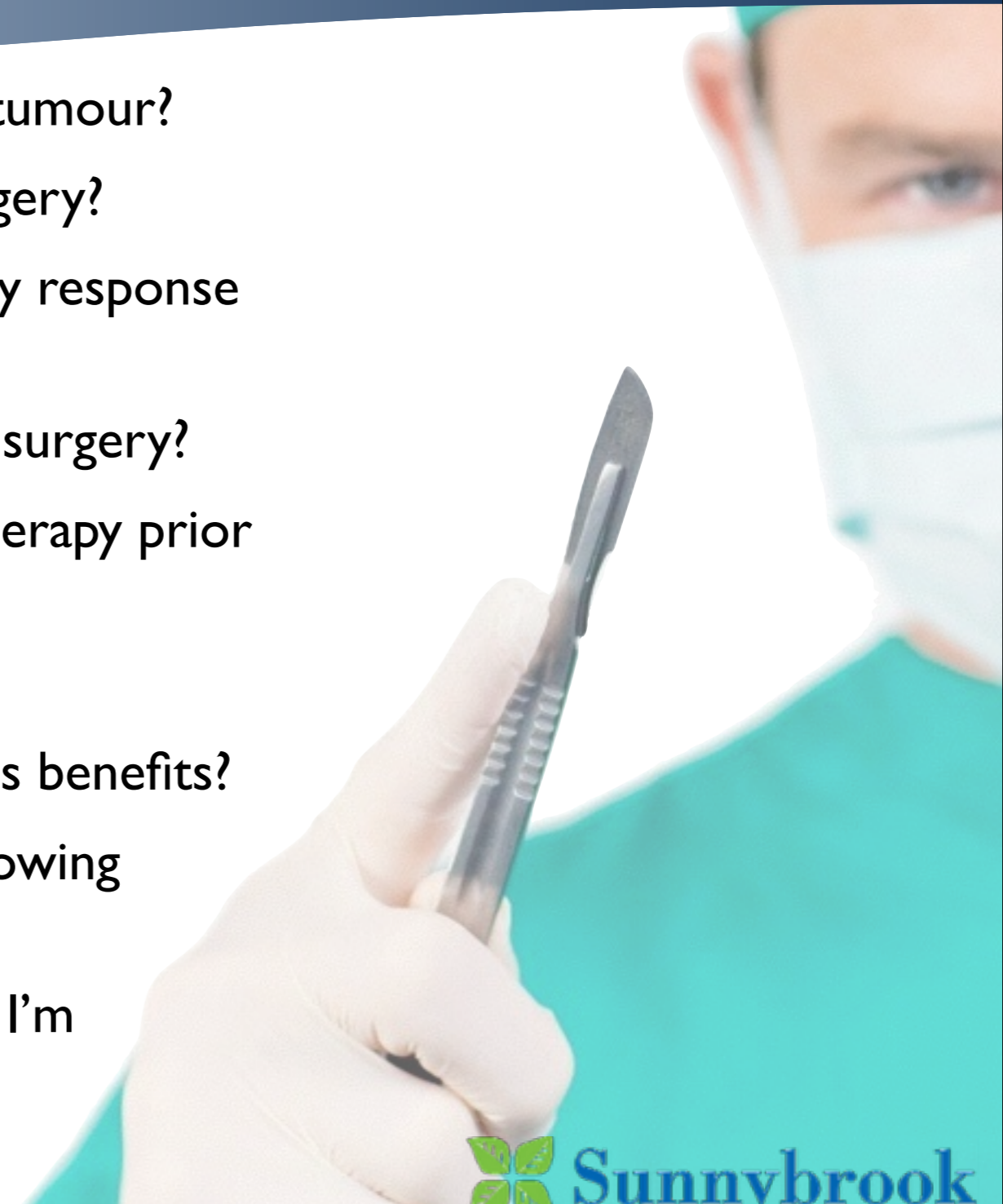
Communication is key





10 Questions to ask before?

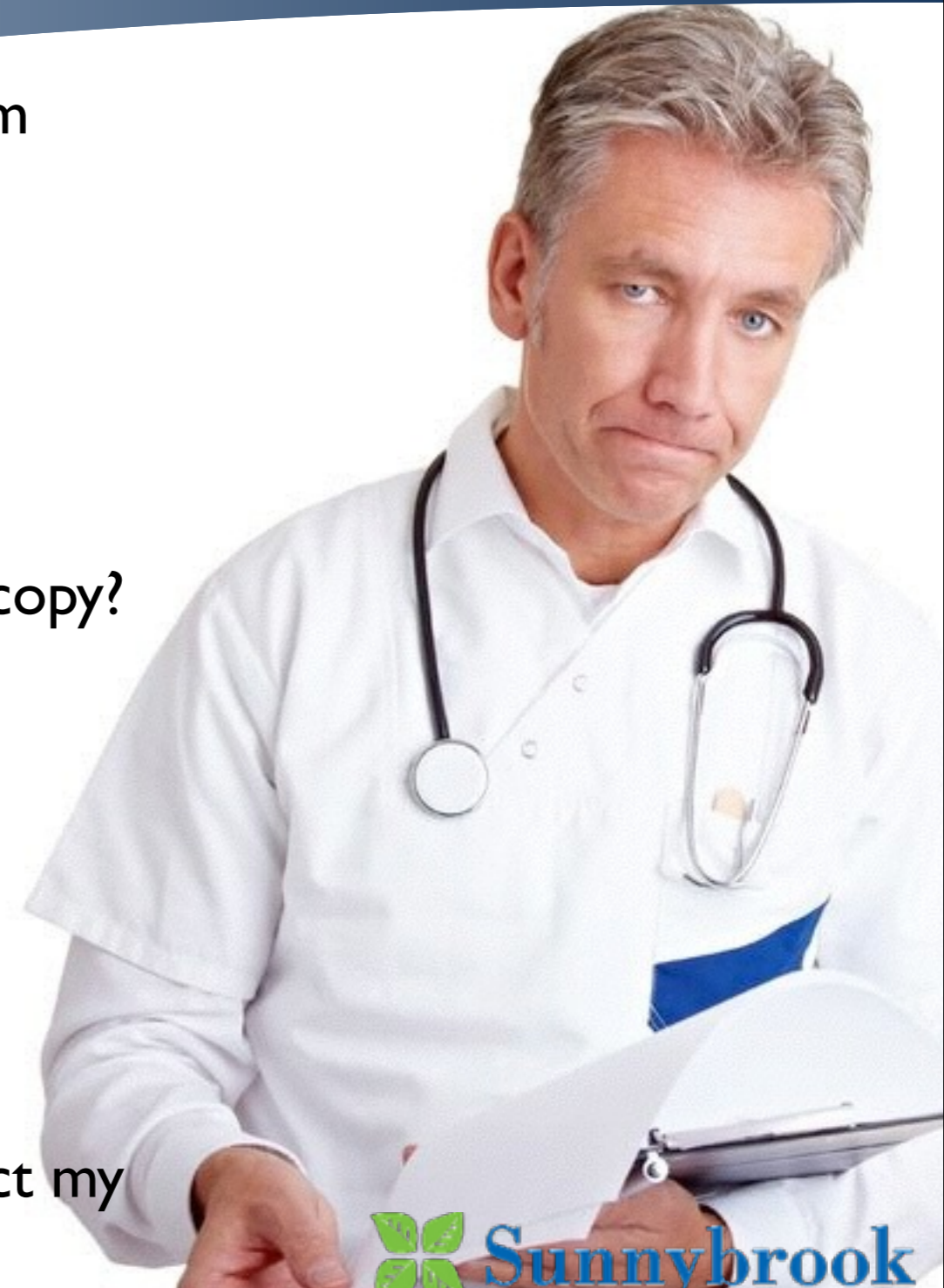
1. How do you know that I have a neuroendocrine tumour?
2. Do I or do I NOT need a biopsy prior to the surgery?
3. What biomarkers will you be using to measure my response to therapy?
4. How will you optimize my health before going to surgery?
5. Is there any need for medications or hormonal therapy prior to the surgery?
6. What are my non-surgical options?
7. What are my surgical options and their risk versus benefits?
8. What should I expect during my hospital stay following surgery?
9. What are short term effects of the surgery while I'm recovering at home?
10. What are the long term effects of the surgery?





10 Questions to ask after?

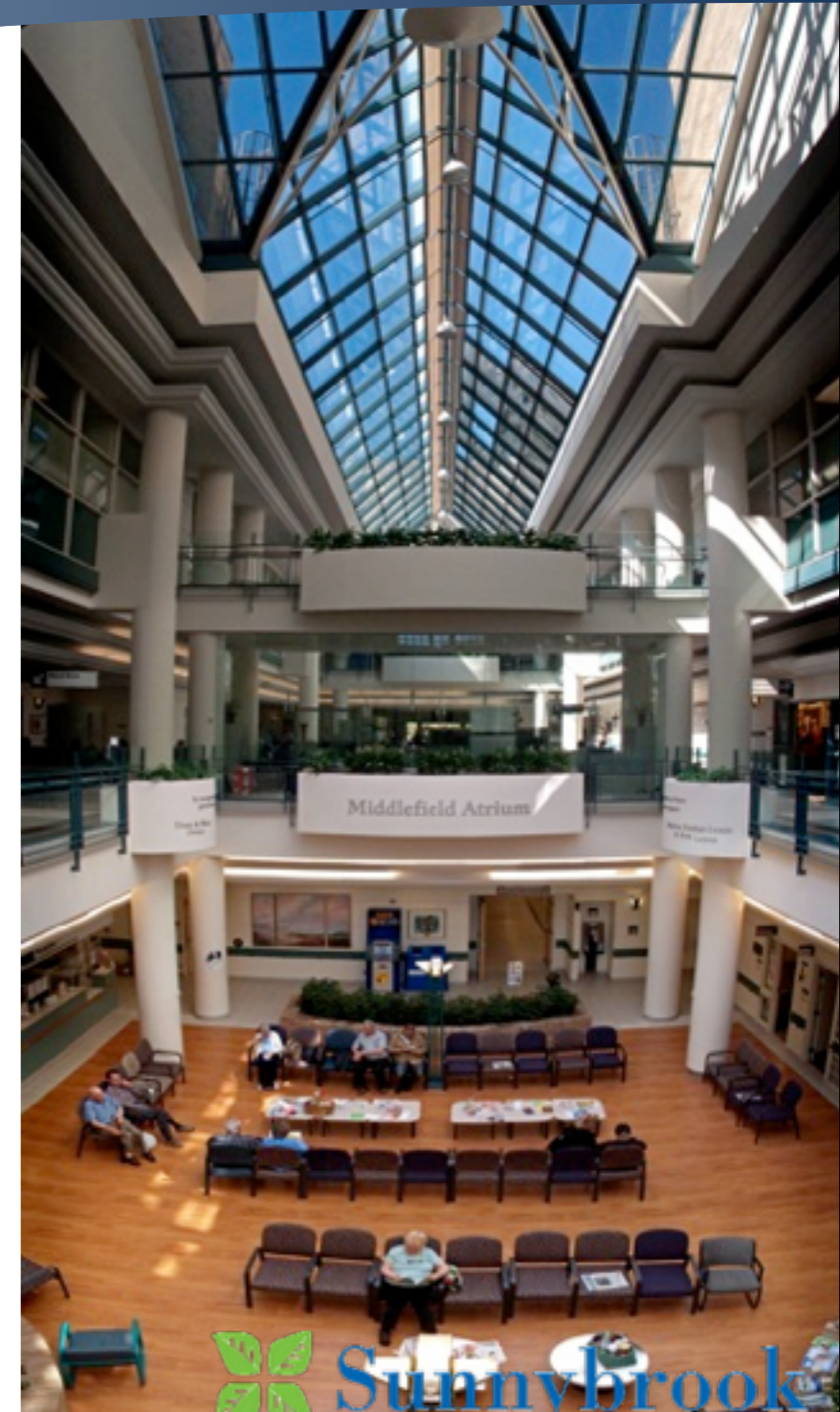
1. What are short term effects of the surgery while I'm recovering at home?
2. What are the long term effects of the surgery?
3. How will my follow-up be setup?
4. Should I receive testing for any other cancers?
5. When should I get my next colonoscopy / gastroscopy?
6. What dietary restrictions or modifications should I consider?
7. When can I return to exercise?
8. What exercises can I participate in?
9. What does the pathology show?
10. Please explain what markers on the pathology affect my future management and prognosis.





Surgery for NETs is special

- Surgery for NETs **MUST** be personalized in so many ways
 - from type of NETs factors
 - from type of patient factors
 - from types of other treatments factors
 - from timelines for treatment factors



Remember these things...

- **Thoughtfulness and patience are needed**
 - *(not saying it's easy!!!!)*
- **You need a team - and the team needs you**
- **The team 'fights' each other - for you!**
- **We are making progress - steadily - and we are so grateful to have a chance to help you.**

