

# Surgical treatment for carcinoids-What's New & What's Next?



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**Lymphatic mapping  
helps define resection  
margins for midgut  
carcinoids.**

# Background

- **Midgut Carcinoid:**
  - **Uncommon Disease**
  - **Vague symptoms**
- **Delayed/ Retrograde Diagnosis**
  - **Bowel obstruction**
  - **Flushing & Diarrhea**

# Treatment of Primary Disease

**Surgery, Surgery, Surgery**

**Margins**

**Lymphatic**

**Blood Supply**

# Common Intra-operative Findings

**Partial Bowel Obstruction**

**Massive Mesenteric Lymphadenopathy**

**Mesenteric Vessels Encasement**

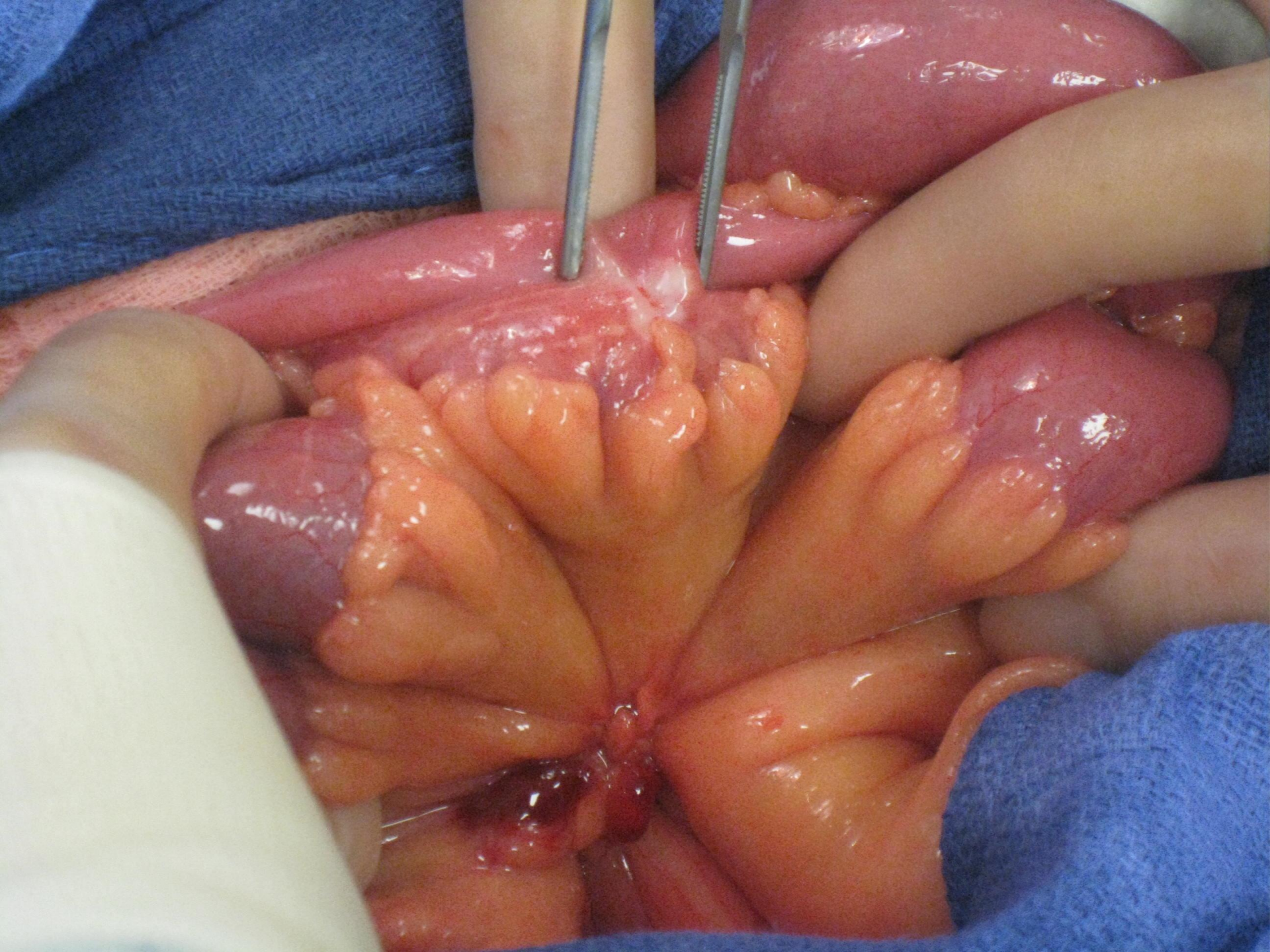
**Intestinal ischemia**

**Multiple “Primary” tumors**

**Liver or other Metastasis**









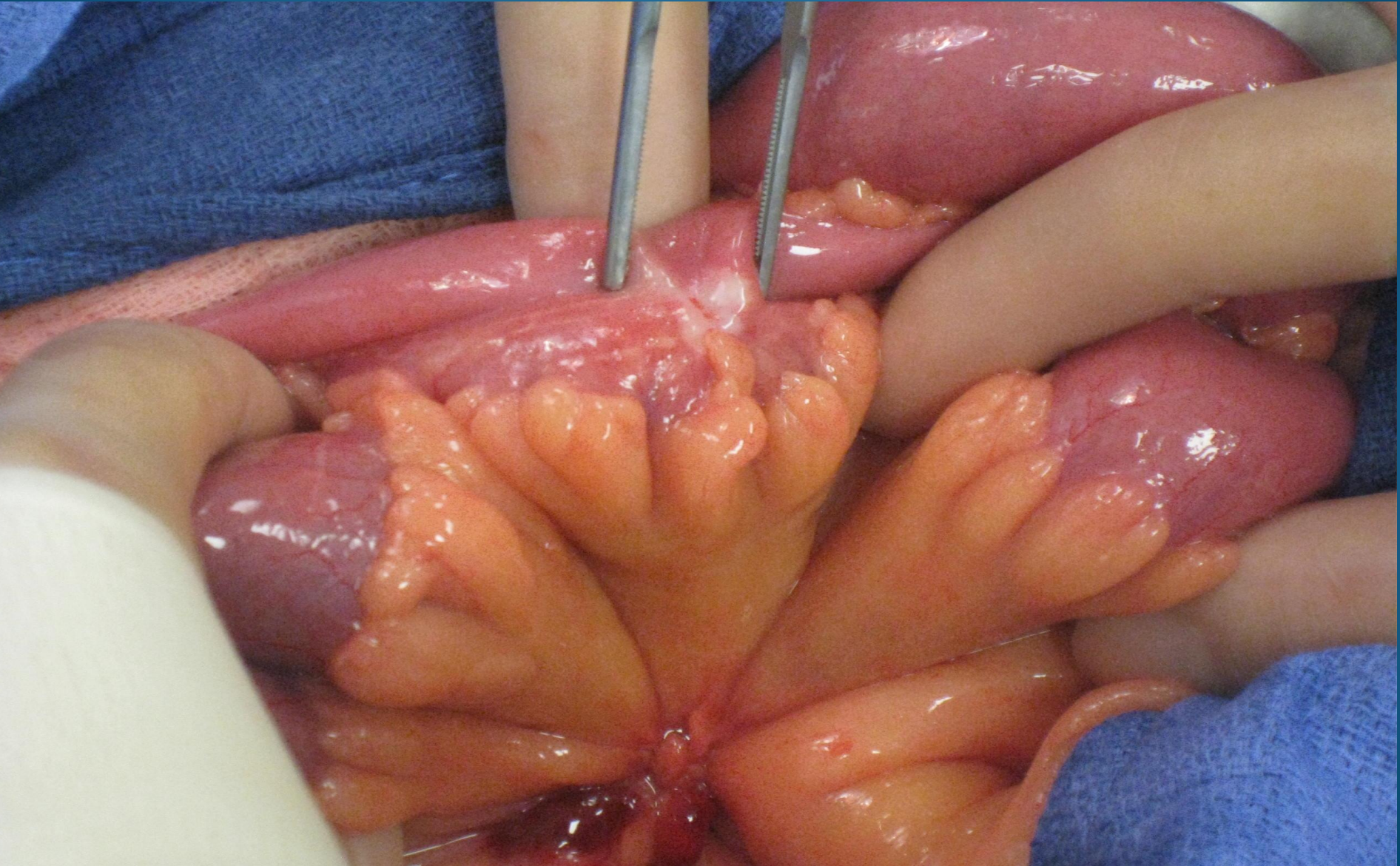
# Traditional Surgical Approach

- Bowel lymph travels bi-directionally along subserosal channels
- Resection margins classically 5 cm to get lymphatics of bowel



William Hunter- 1<sup>st</sup> lymphatic mapping

# How much to resect?

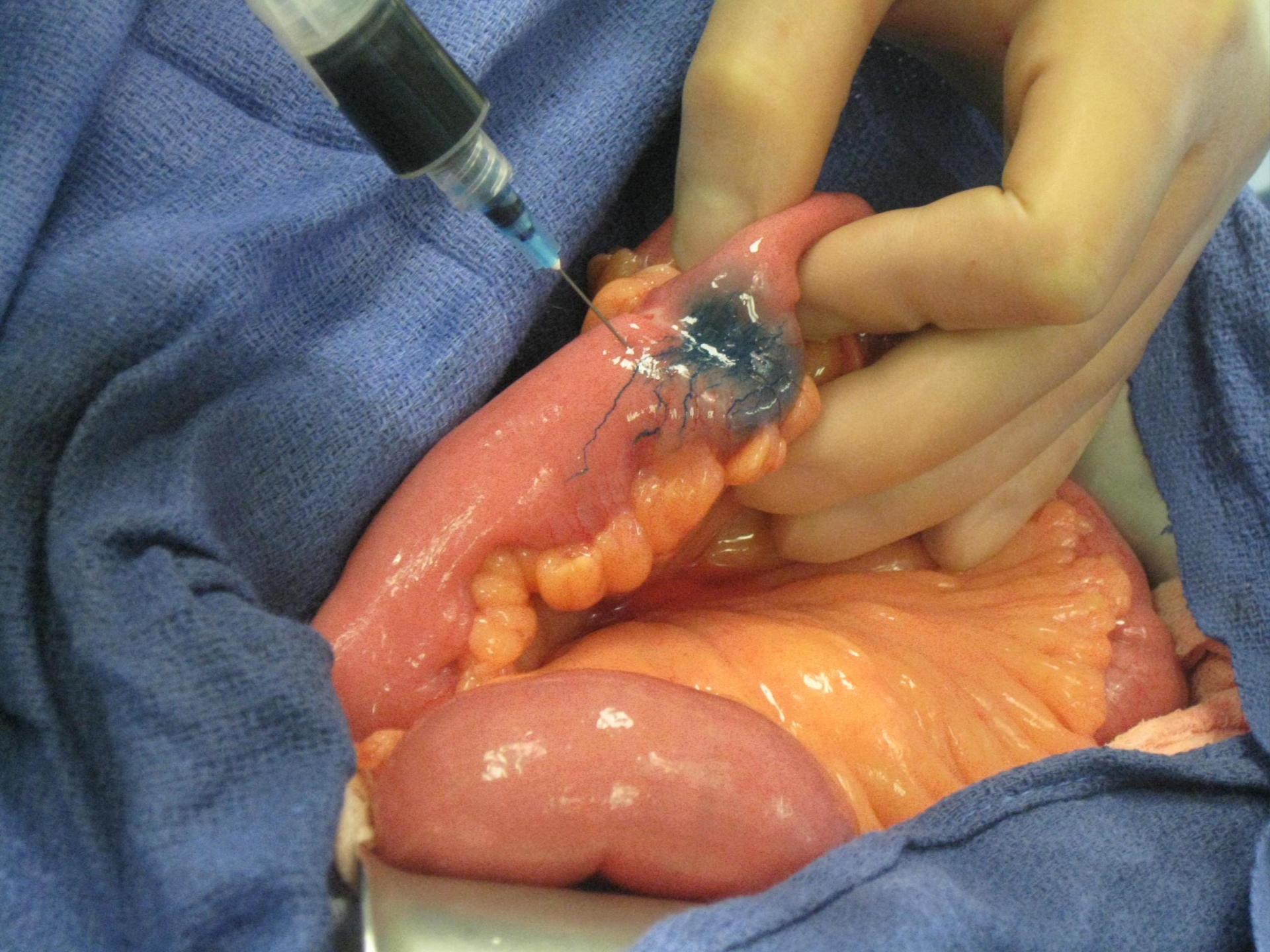


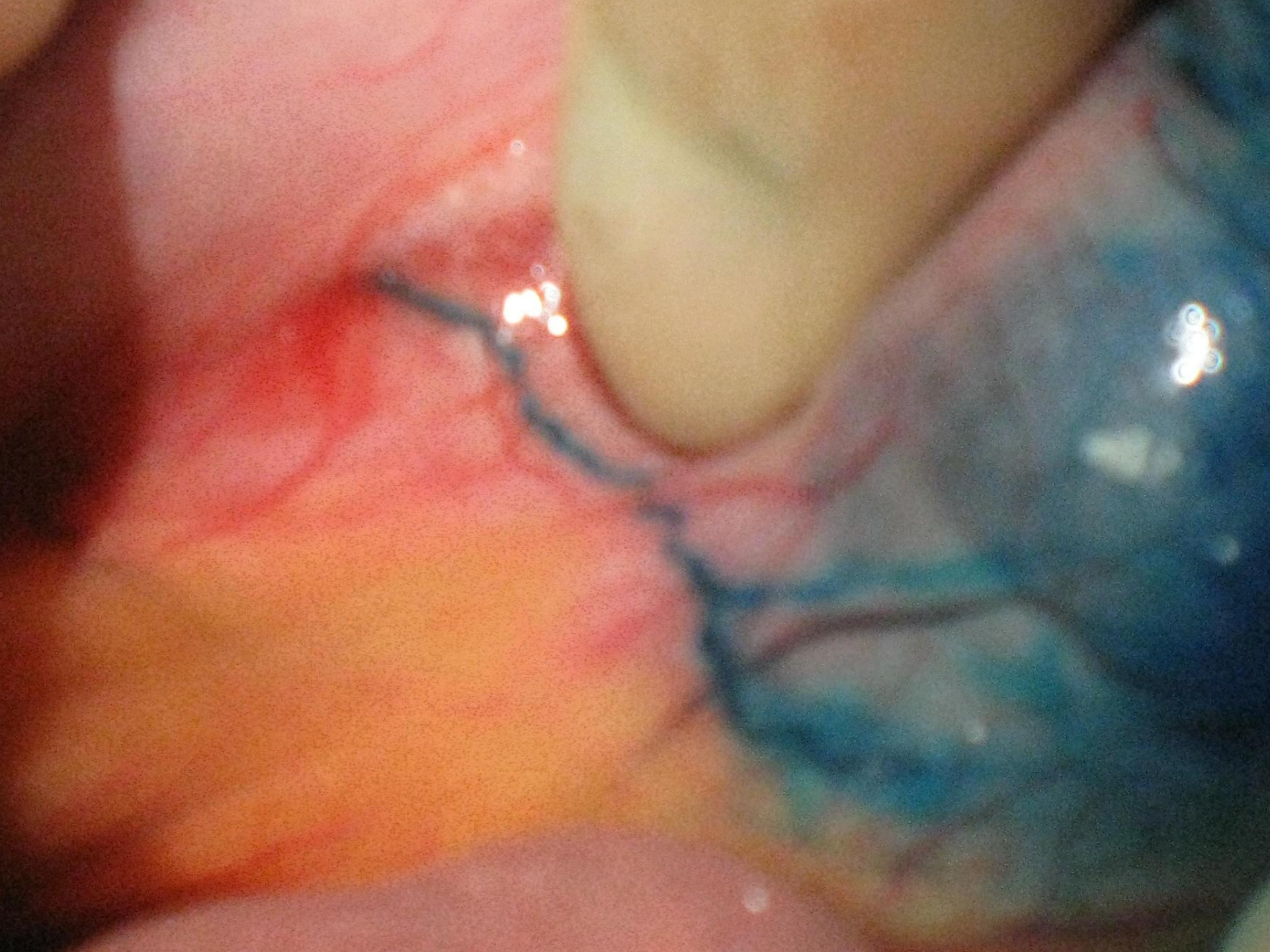
# New concept---Sentinel Lymph Node & Lymphatic Mapping

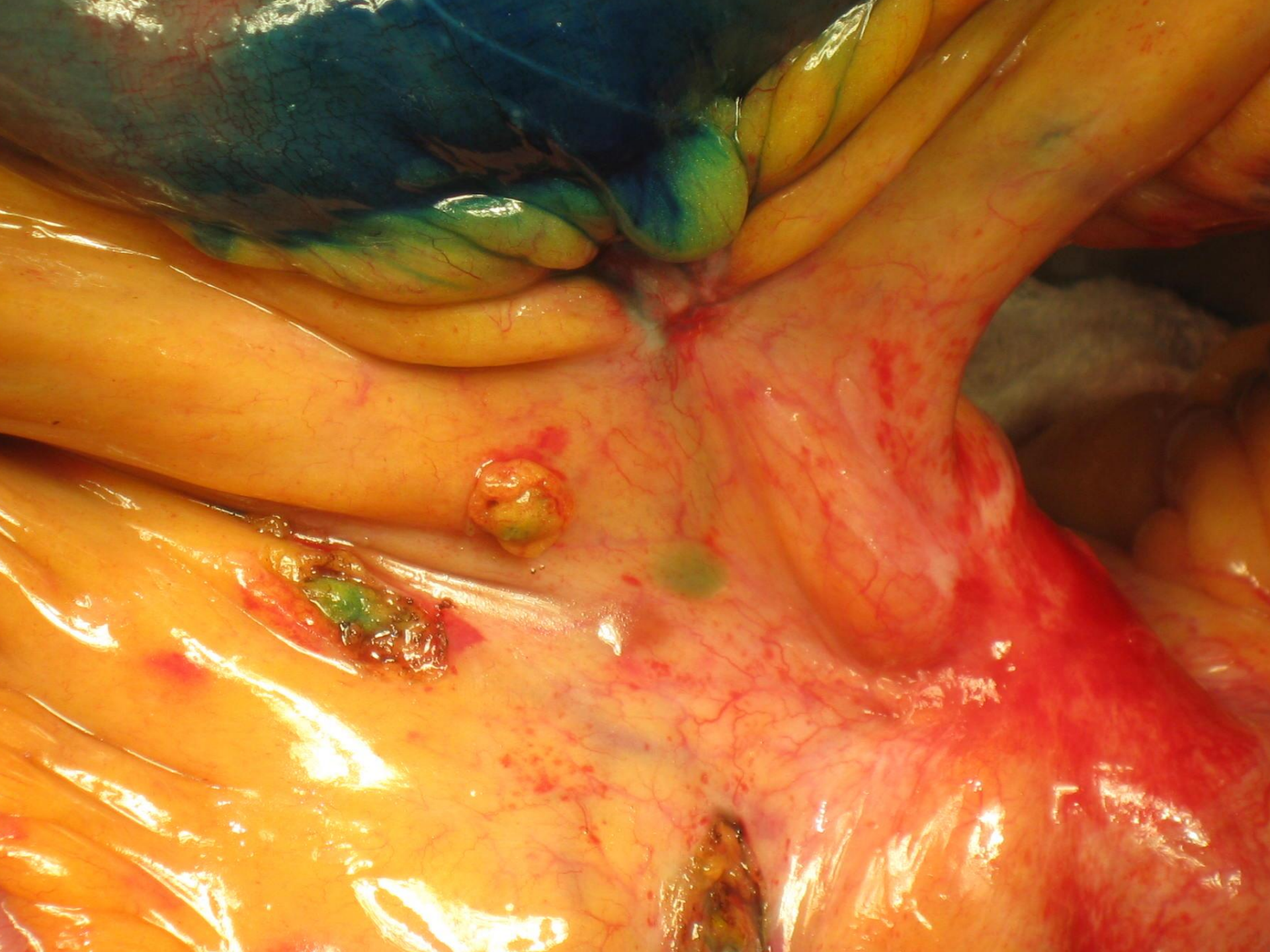
**Breast Cancer**

**Melanoma**

**GI Tract Malignancy?**

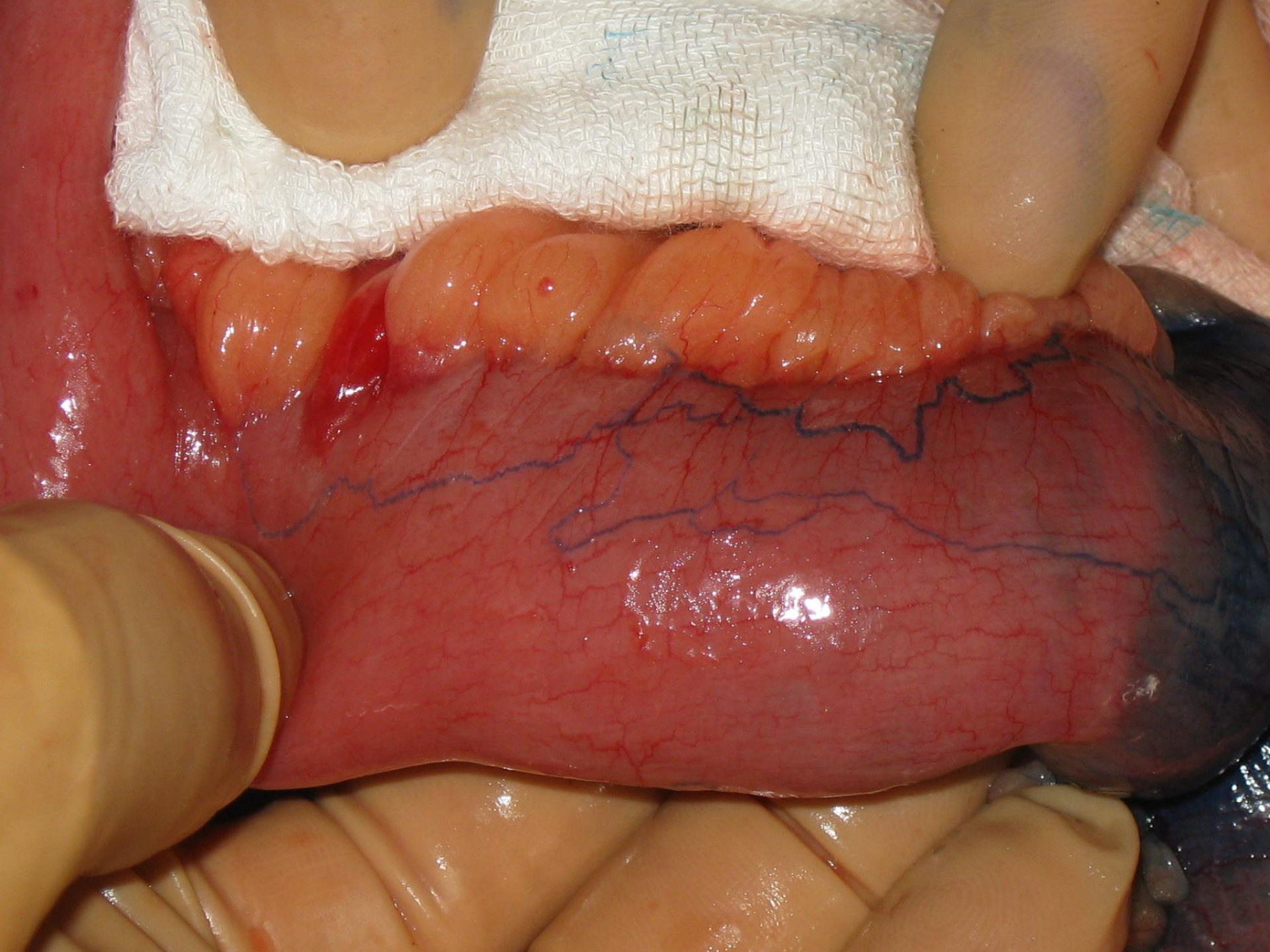




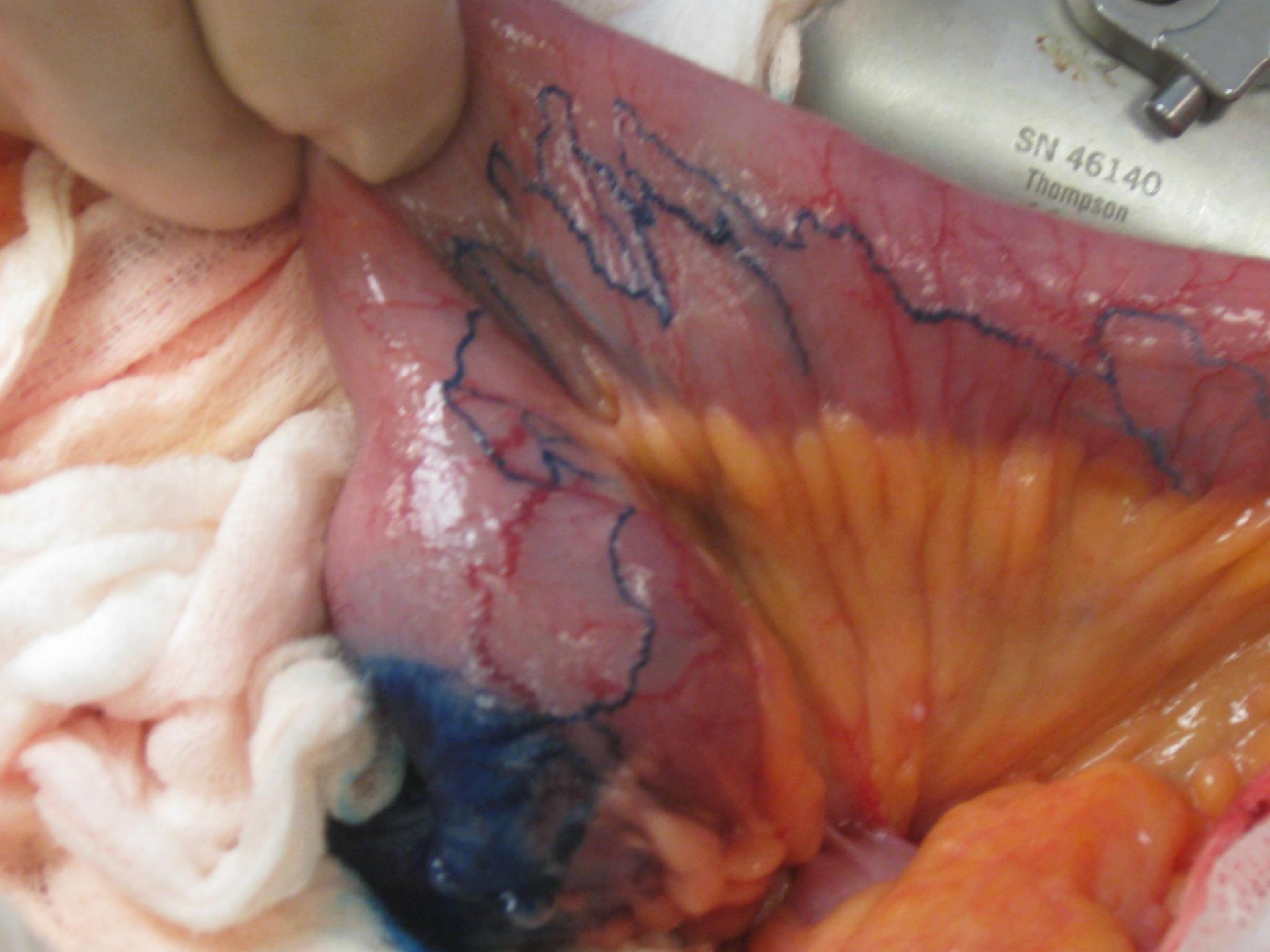


# Unexpected Findings

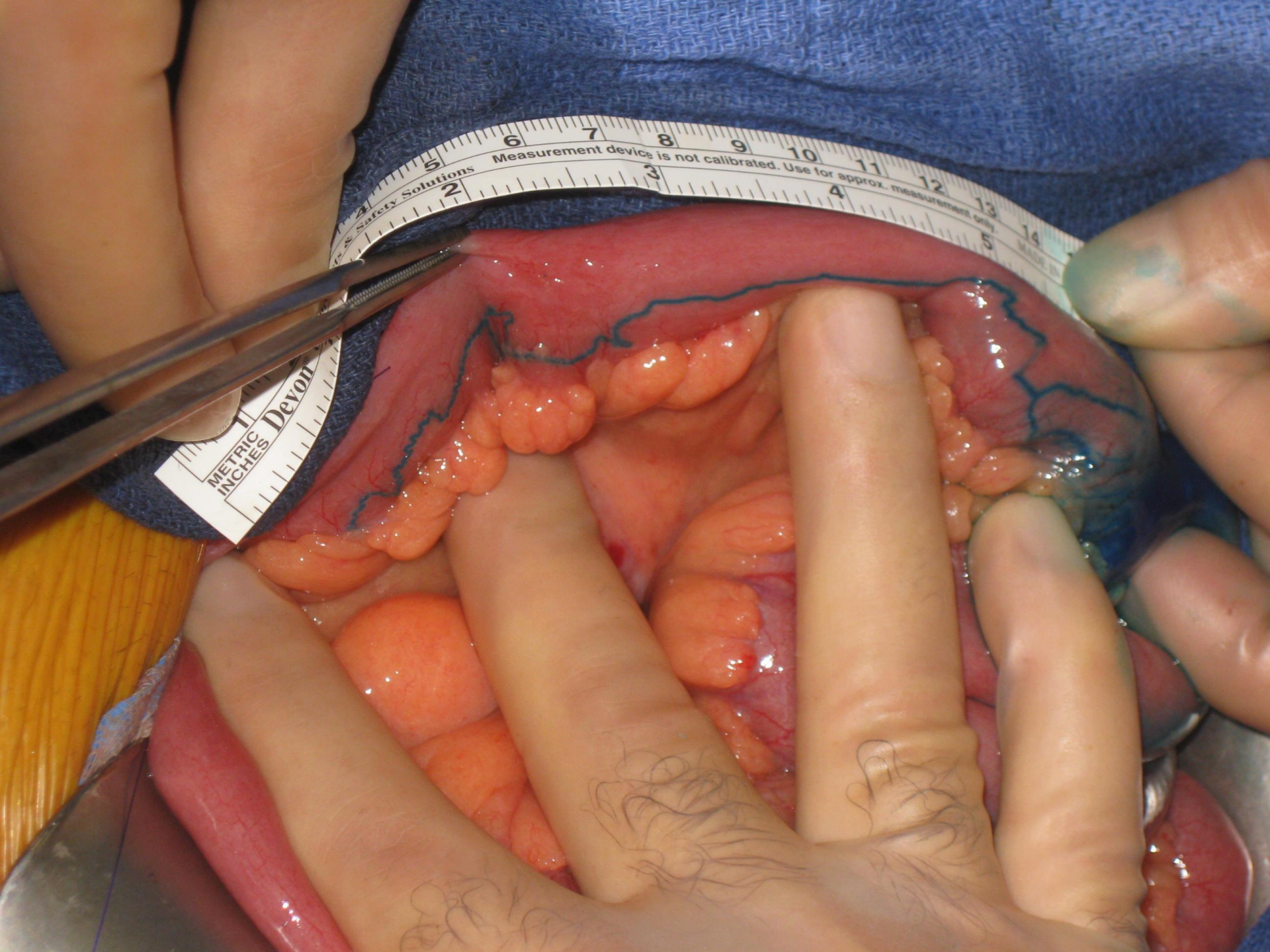
- **Boggy and Massive Lymphadenopathy**
- **Alternative Sub-Serosal Lymphatic Pathways**
- **Multiple “Primary” Tumors**
- **True, True, & True but Unrelated?**
- **Untold Story?**





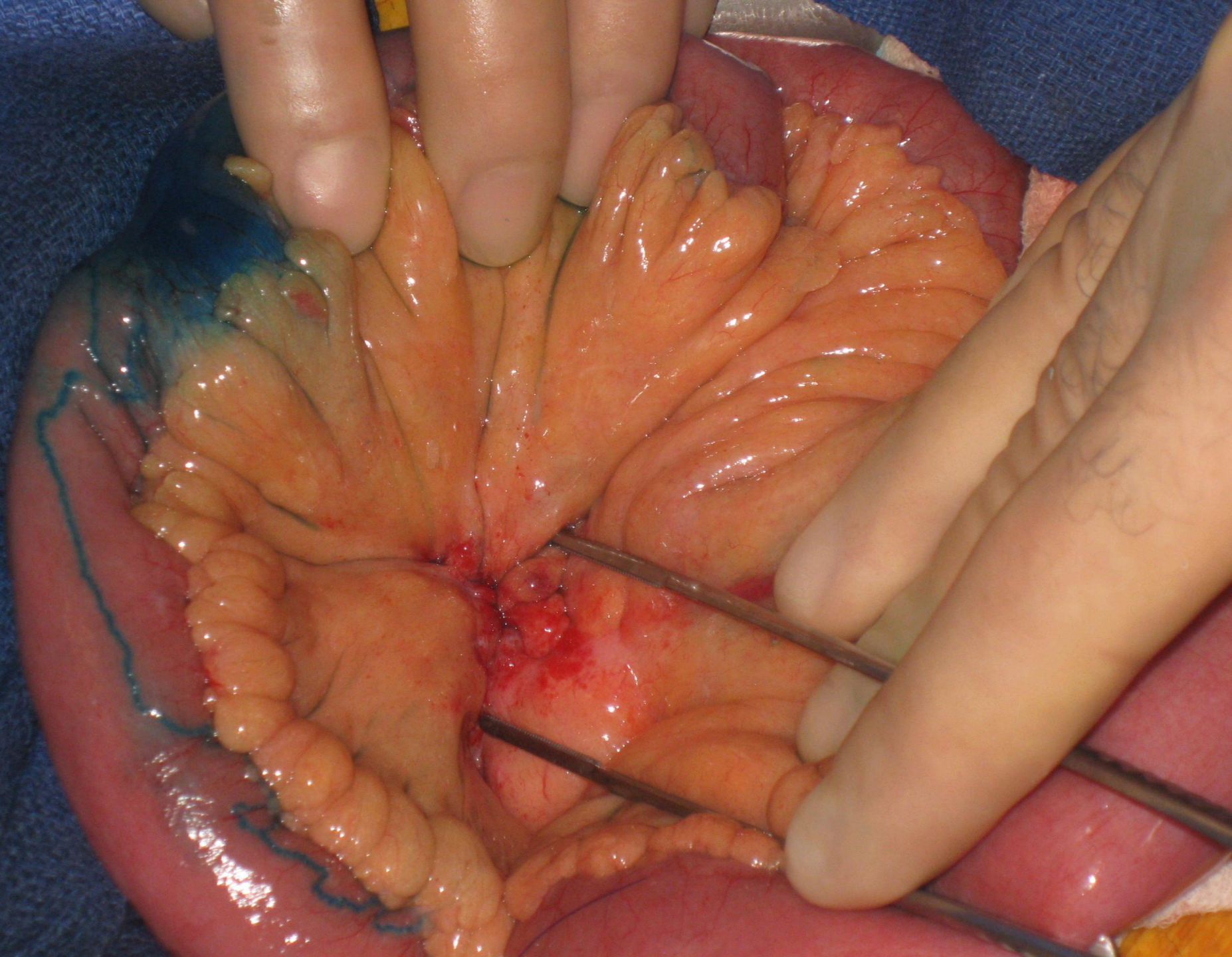


SN 46140  
Thompson



METRIC  
INCHES  
Devon

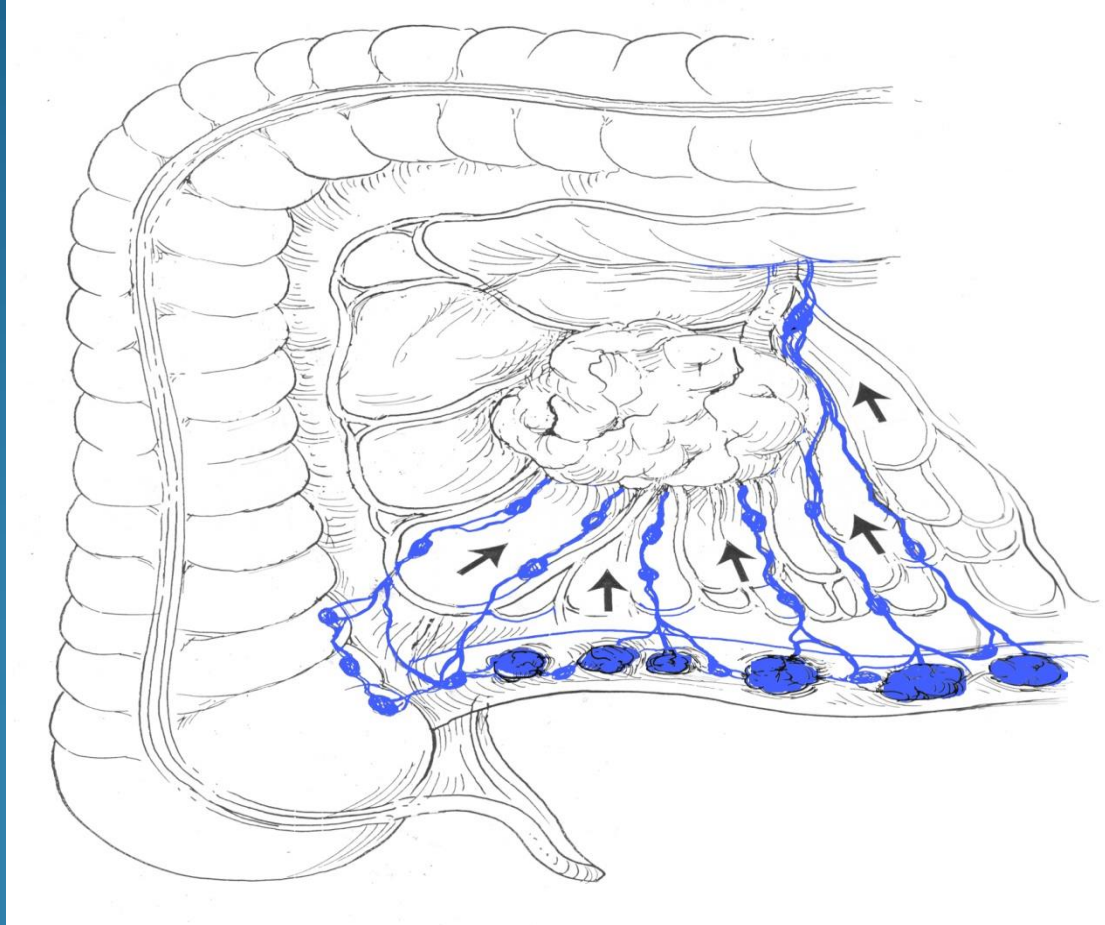
5 6 7 8 9 10 11 12 13 14  
Safety Solutions  
Measurement device is not calibrated. Use for approx. measurement only  
2 3 4 5 6 7 8 9 10 11 12 13 14  
MADE IN



# Hypothesis

- Massive Lymphadenopathy ---- Obstruction of normal “radial” mesenteric lymphatics --- Detour --- “Longitudinal” alternating intra-intestinal sub-serosal pathways --- returns into unobstructed mesenteric lymphatics
- Multiple “Primary”
- Recurrences at or adjacent to resection sites

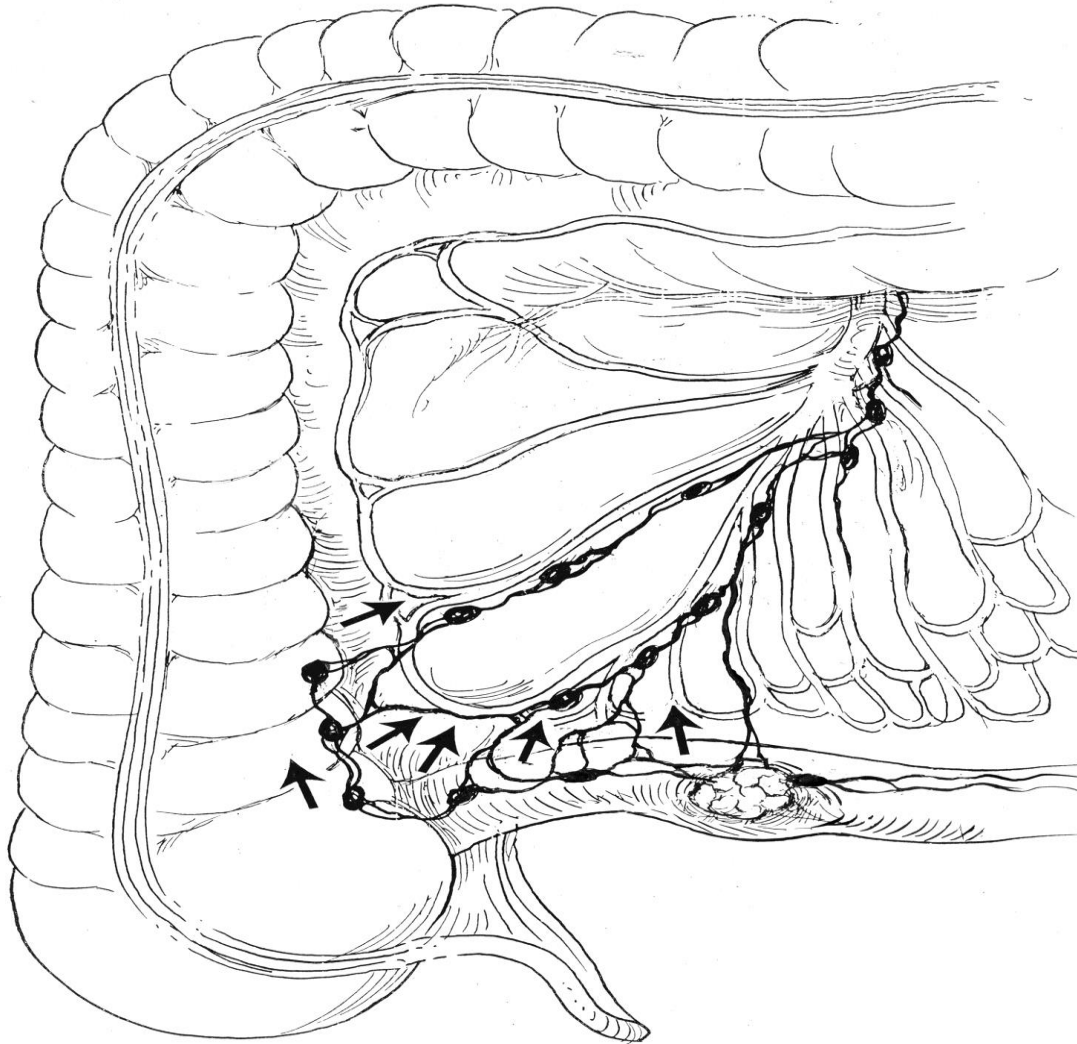
# Drop metastasis developed on route of Lymphatic detour



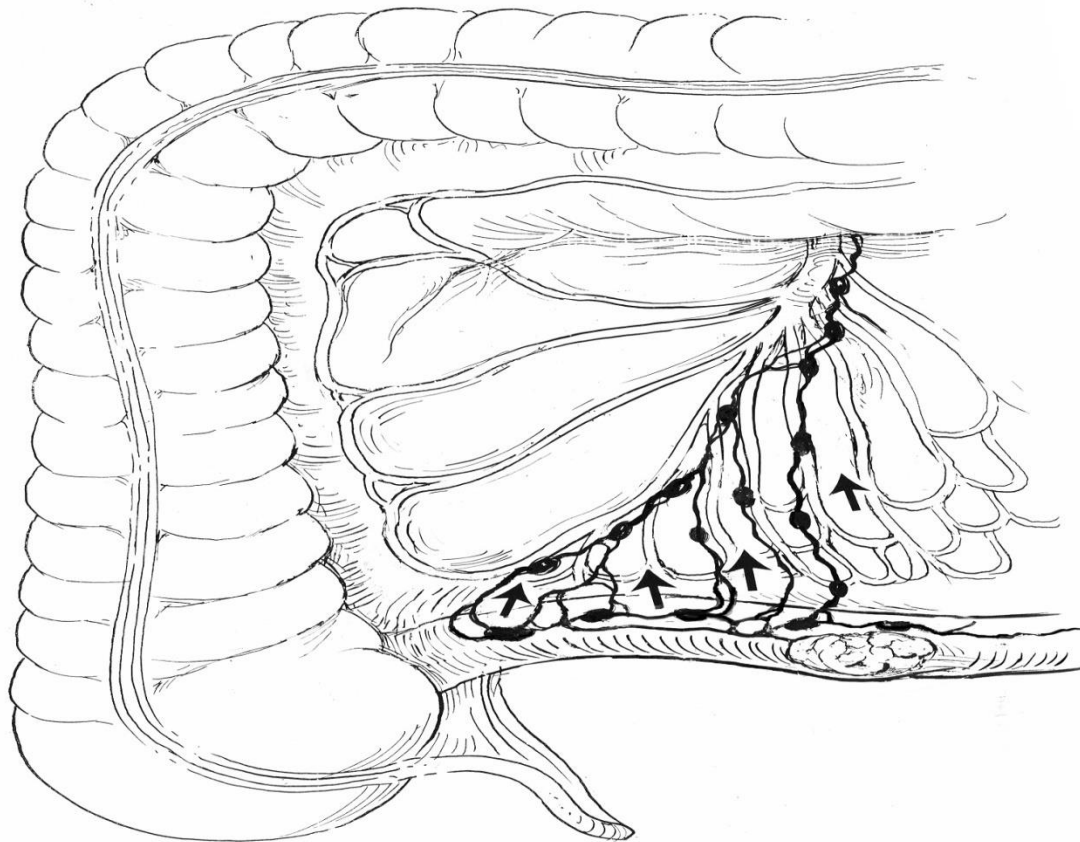
# Method

- Resects Tumor(s) with “Adequate” Margins using Lymphatic Mapping
- Conservation of Bowel Length
- Mesenteric Lymphadenectomy
- Restore Blood Supply
- Spare Ileocecal Valve Whenever Possible based on Mapping

# Lymphatic drain crossing ileo-cecal valve



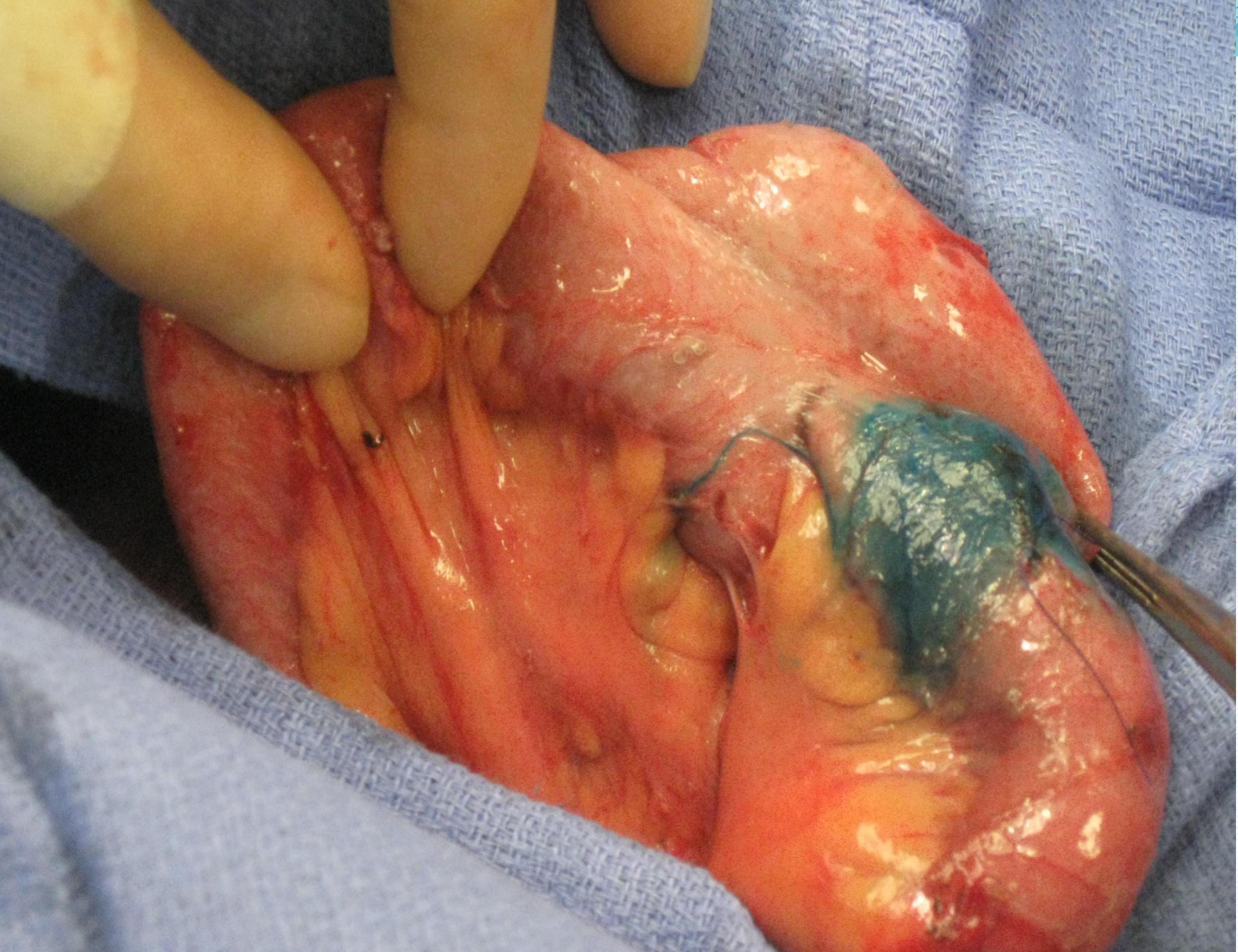
# Lymphatic drain doesn't cross ICV





# Results

- 303 Patients for cyto-reductive operations (11/2006-10/2011)
- 112 patients underwent mapping (35 REDO)
- 98 patients with midgut primary
- 45 patients with tumor near ileo-cecal valve
  
- 92% resection margins modified
- 44% ileo-cecal valve preserved
- 54% Disease found at or near the anastomosis
- 0 % had anaphylactic reaction

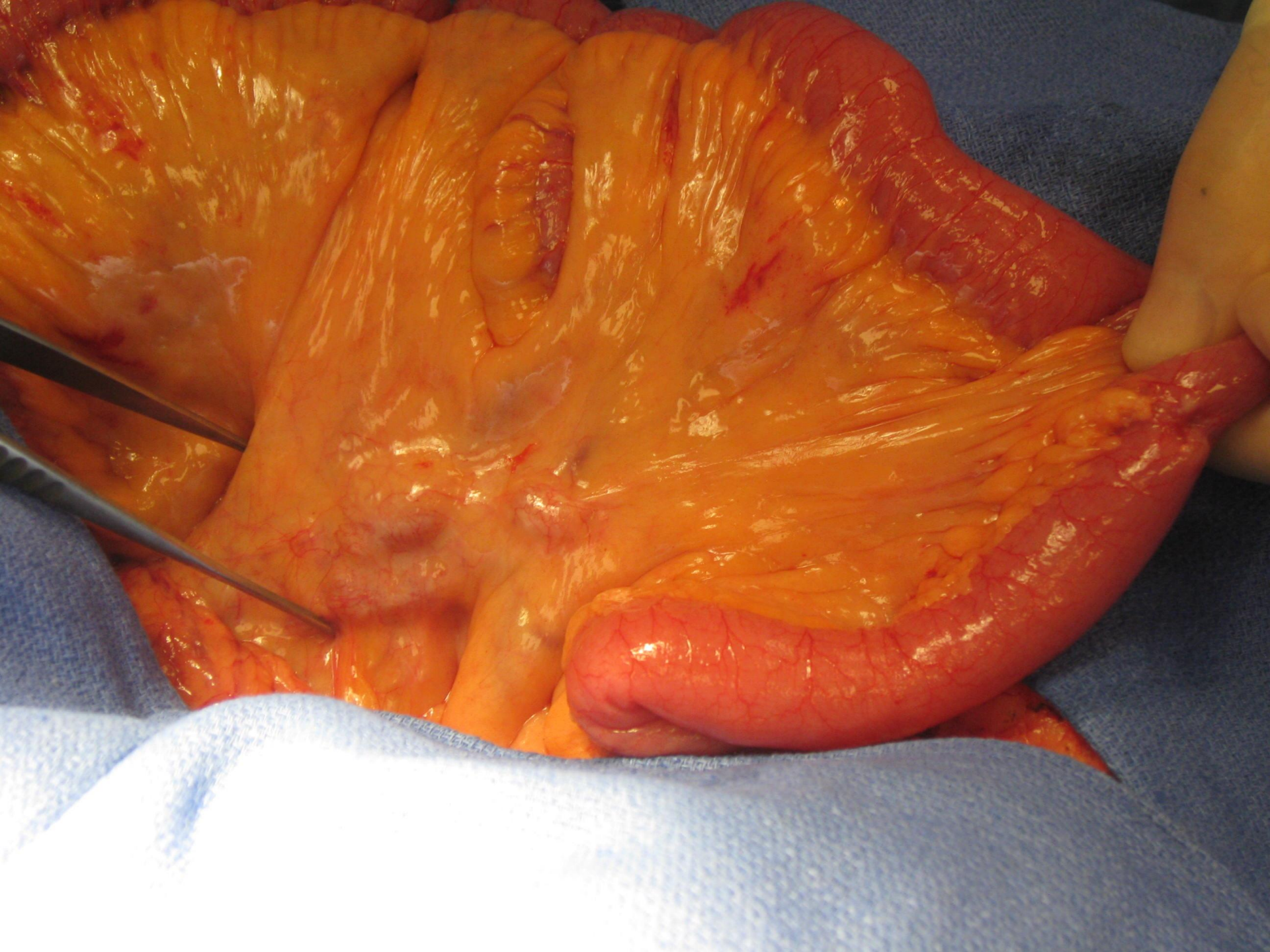


# Conclusion

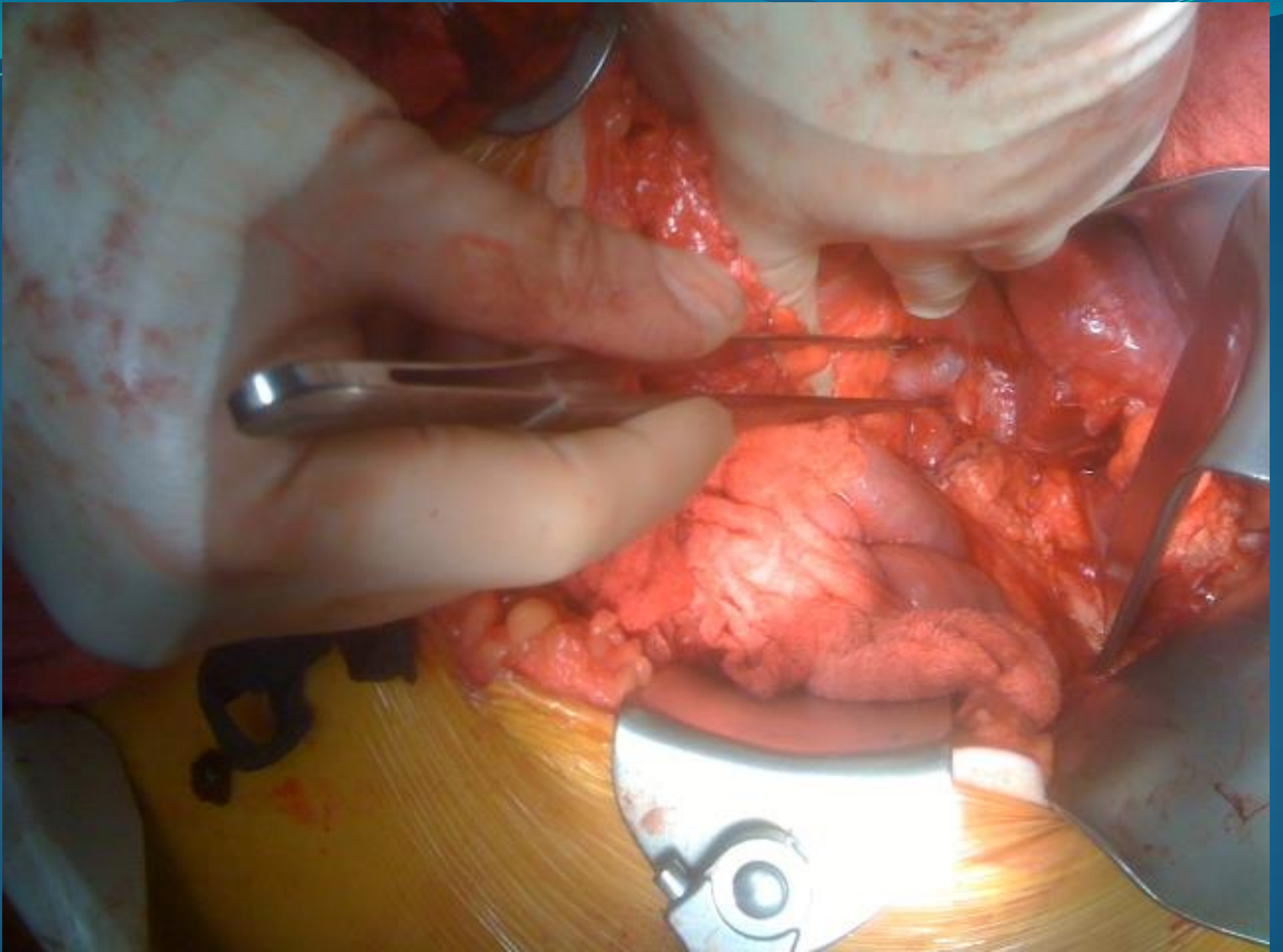
- Time-effective & Safe
- Better cytoreduction
- No “arbitral” margins
- Ileo-cecal valve sparing
  
- Less local recurrence
- Less diarrhea
- Better quality of life
- Improve long term survival

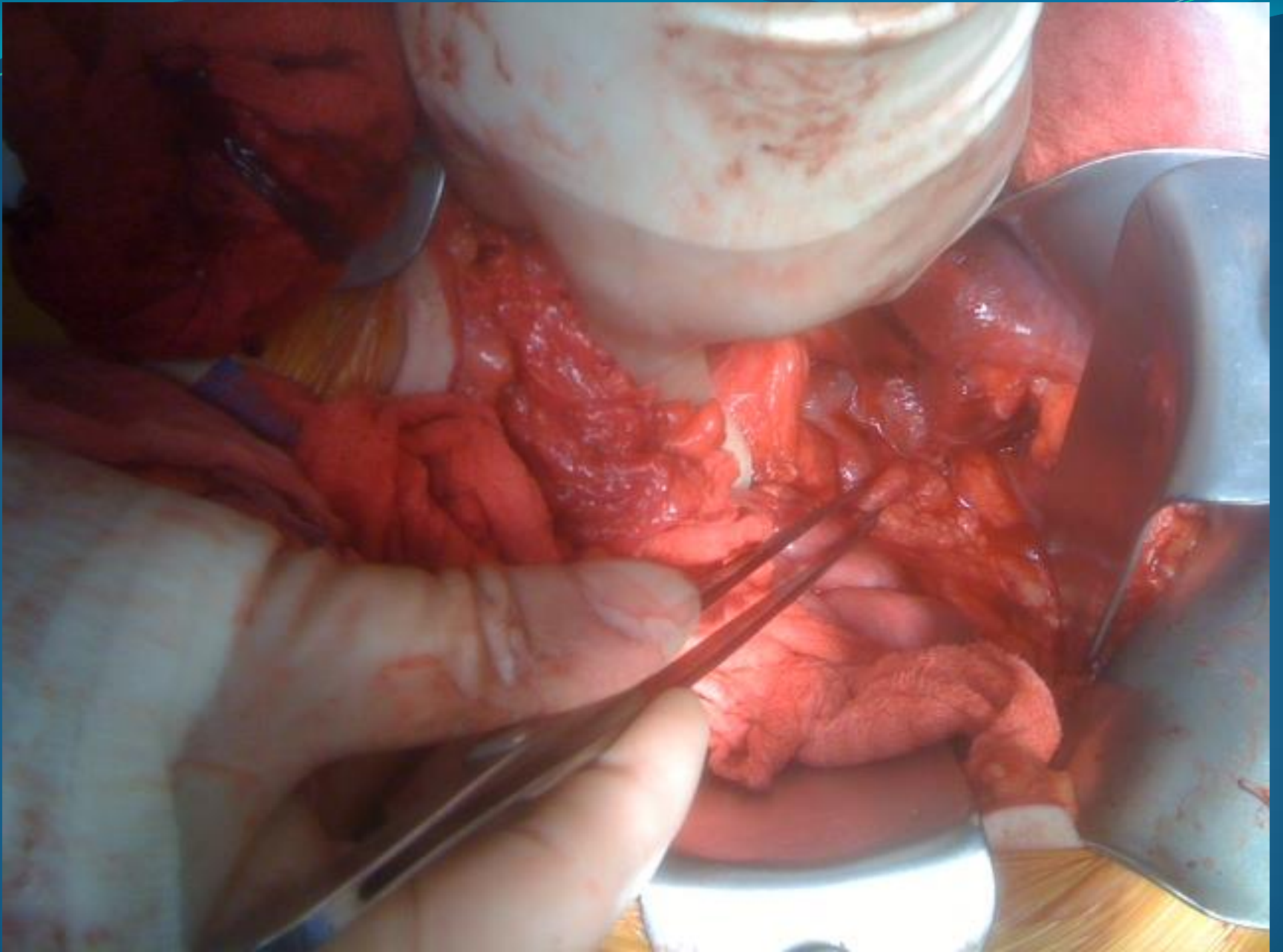
# Mesenteric lymph node dissections

An important step for maximum debulking and restoring blood supply to the ischemic bowel secondary to an extensive mesenteric lymphadenopathy and vascular encasement

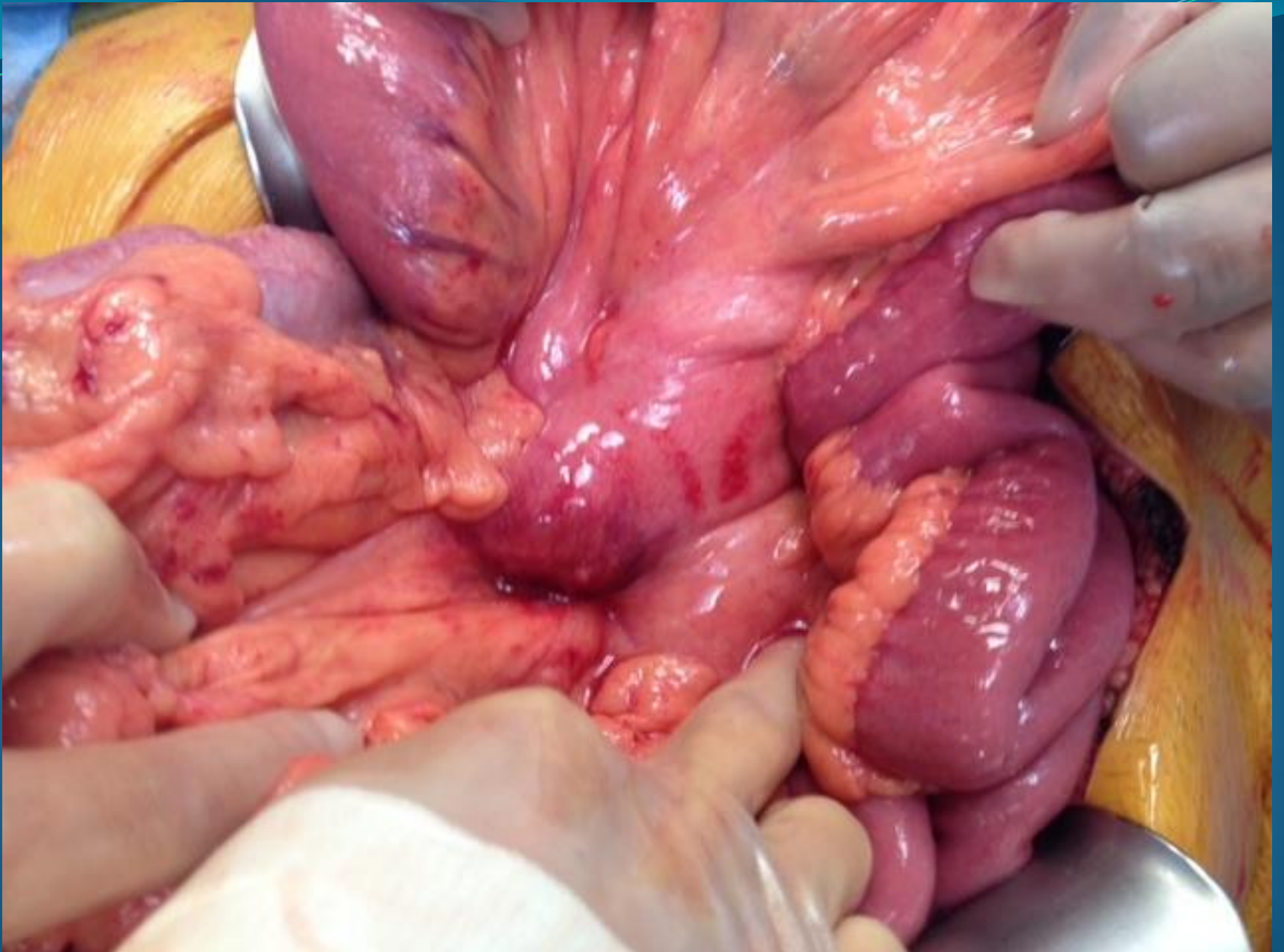


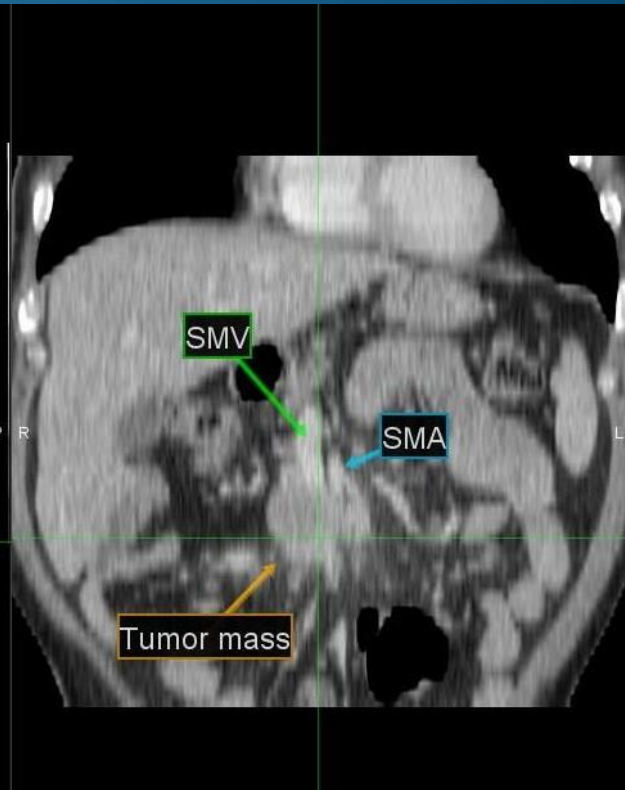
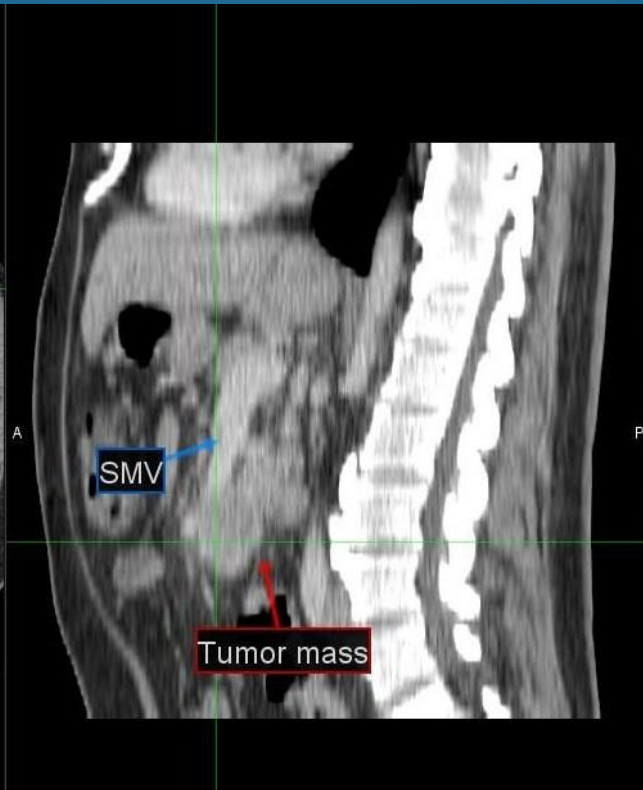
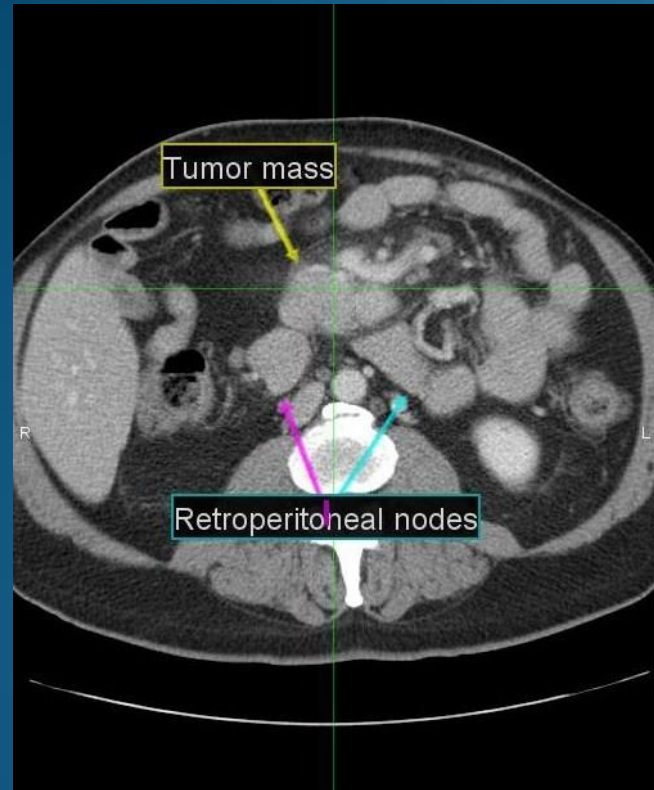


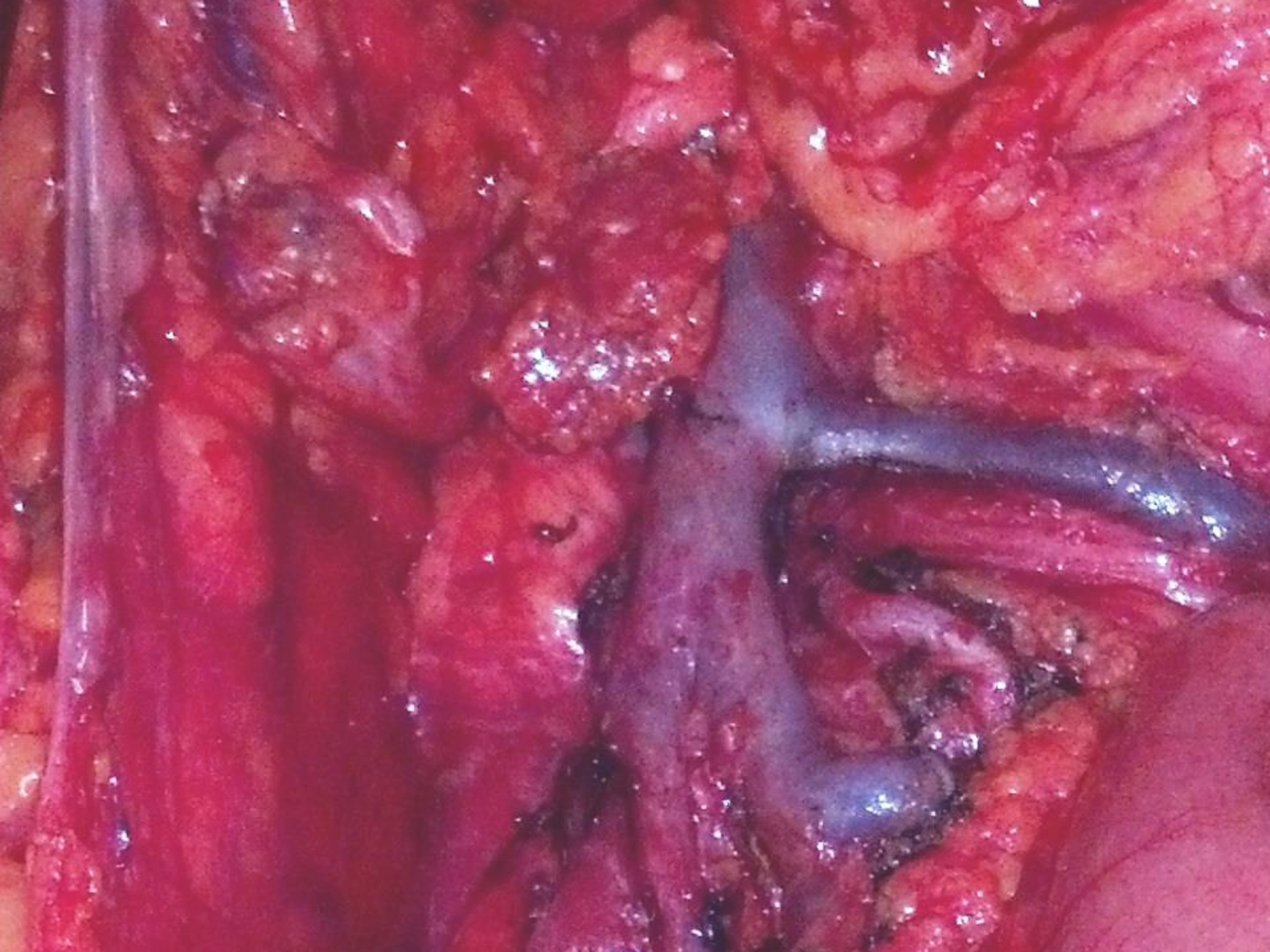


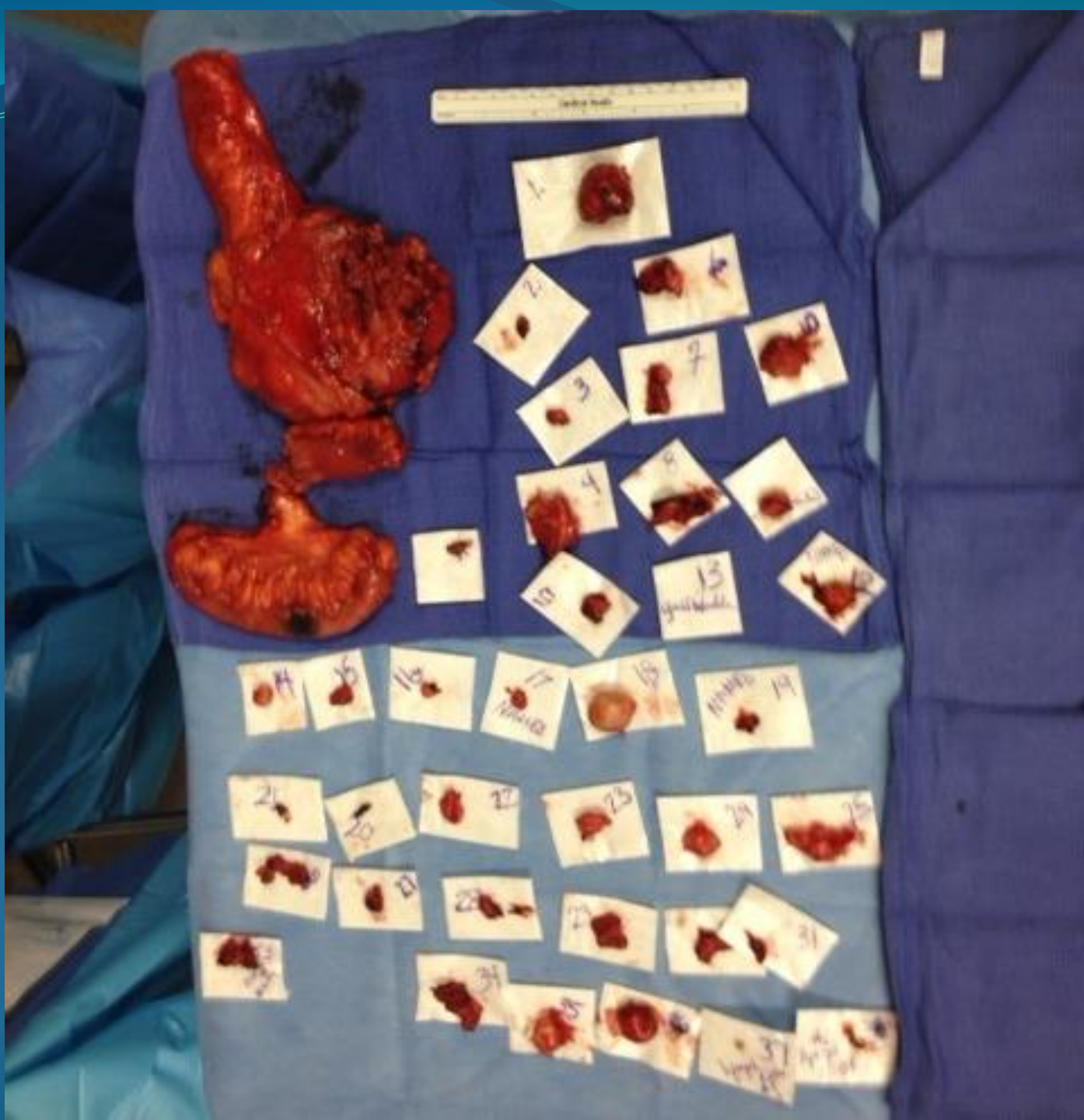


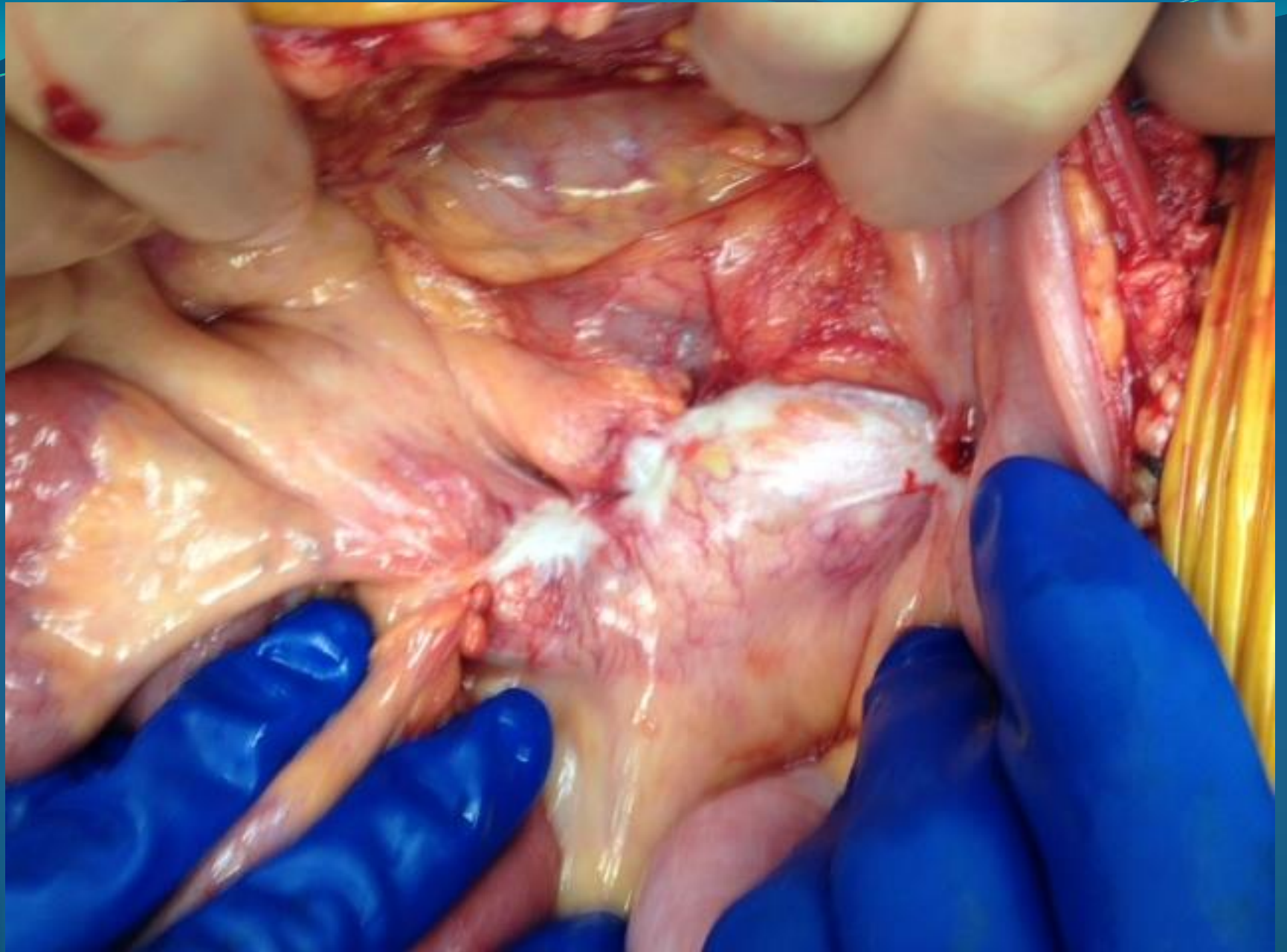










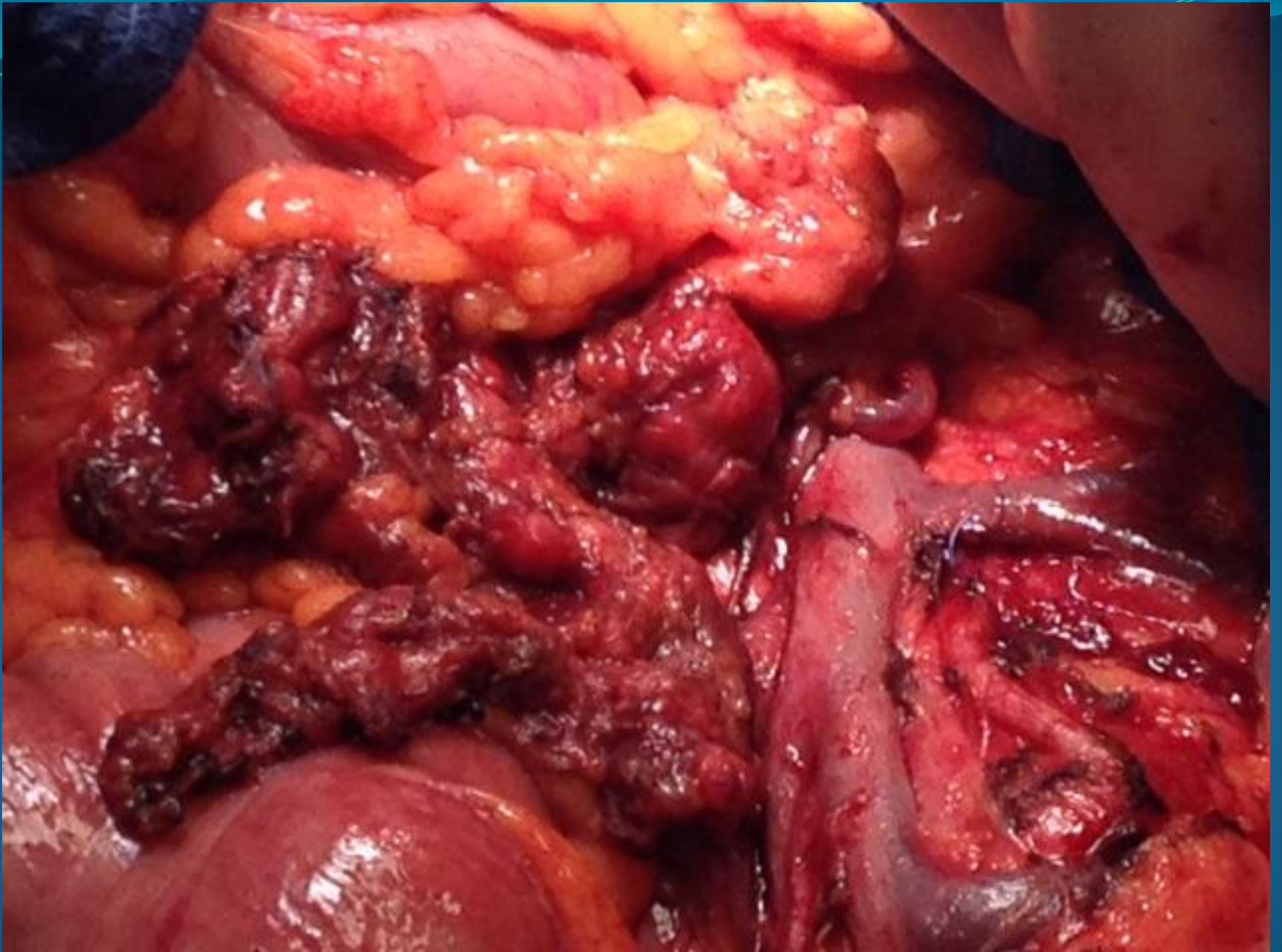


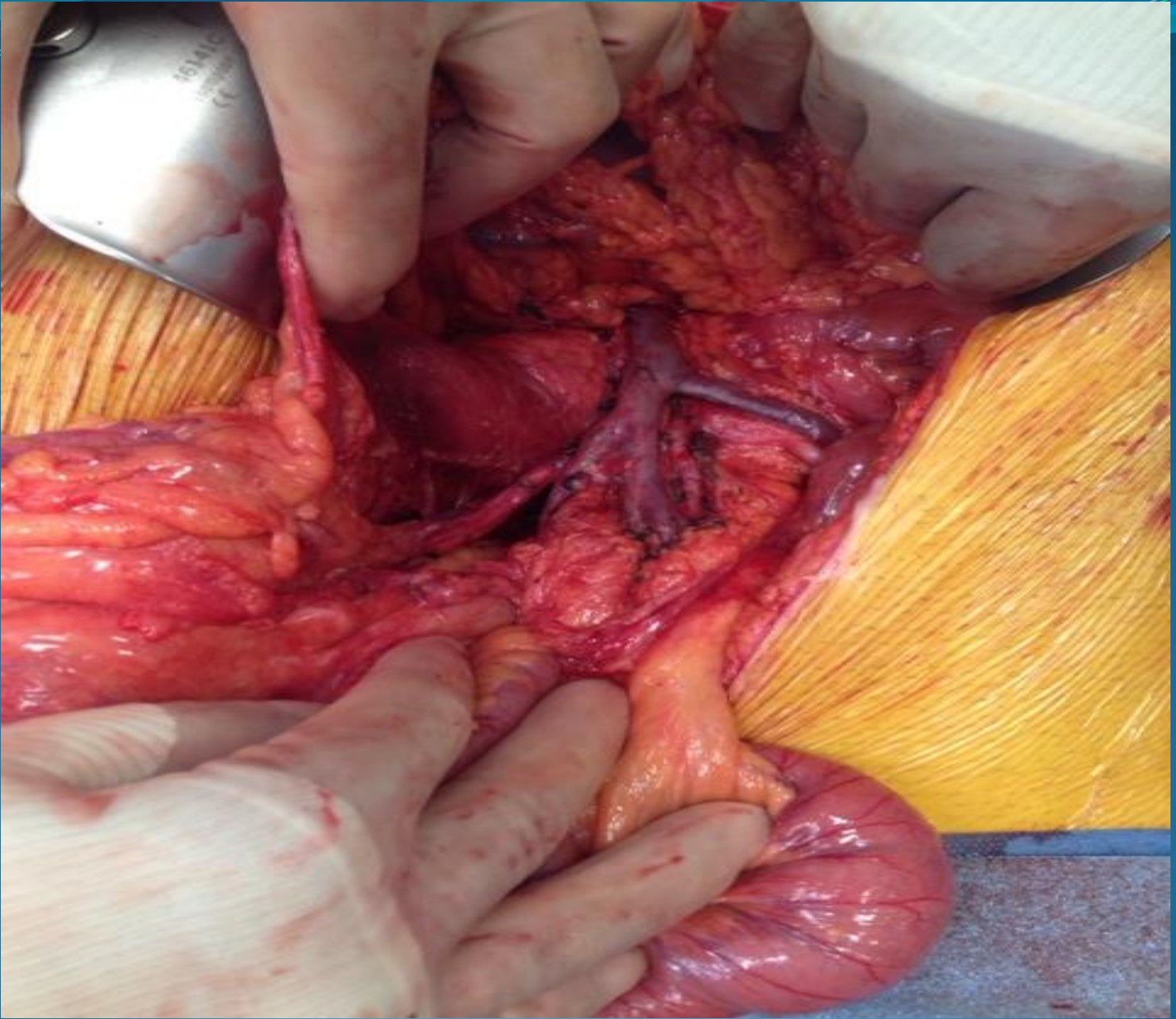


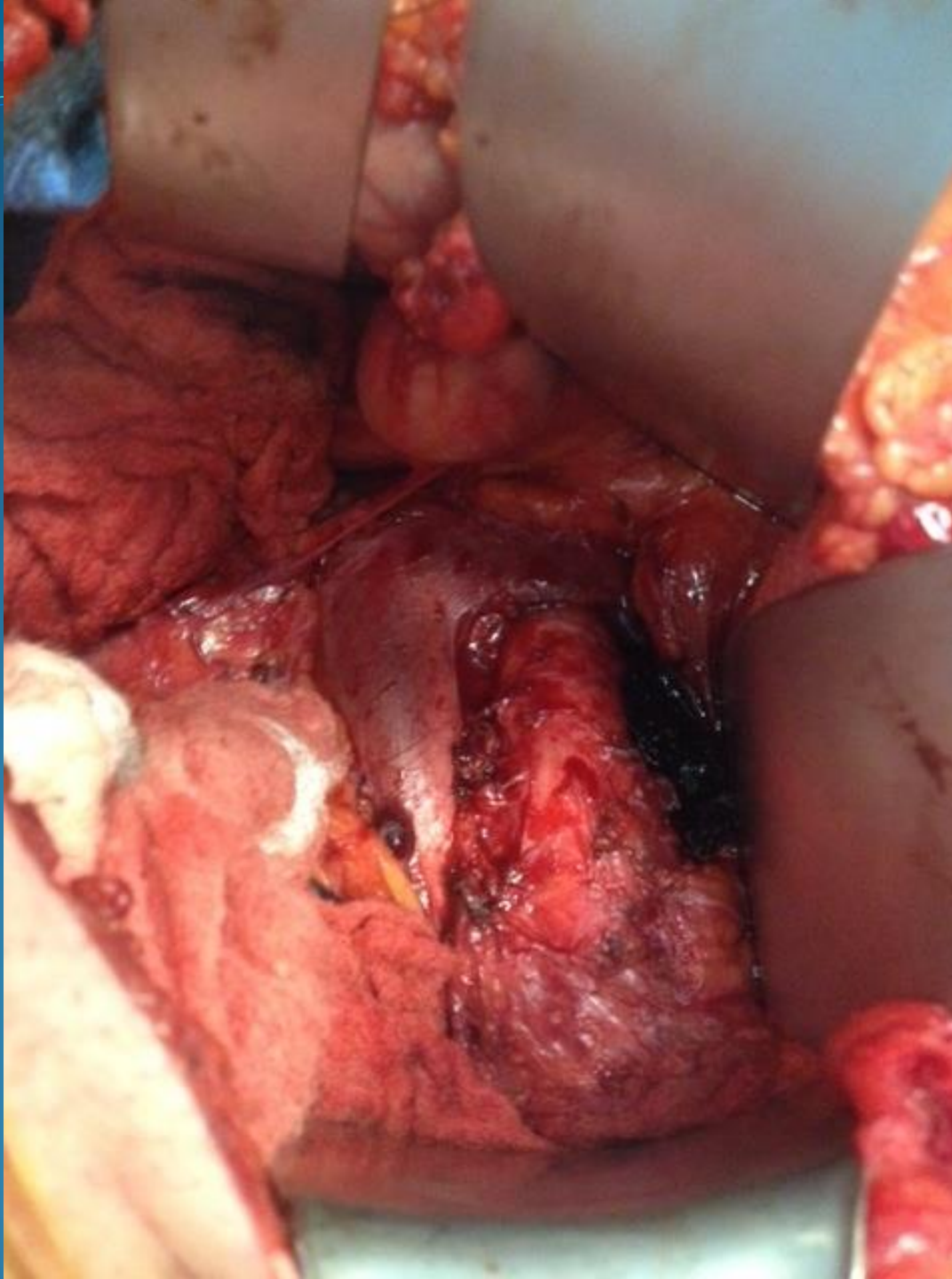












HBA

Splenic

PV  
SAV

IMV

ICA





LightSpeed Pro 32

H

Moffitt Cancer Ctr at Int Plaza

Ex: 2794

ARTERIAL

C: 135CC OF OPTIRAY

Se: 400/9

Im: 53/146

Cor: A52.9

Acc: CT20130020893

2013 Jun 18

Acq Tm: 14:46:19

Mag: 1.1x

512x512

STANDARD

R

L

120.0 kV

634.0 mA

Tilt: 0.0

ET: 0.5 s

GP: 0.5 s

TS: 38.75 mm/s

SPR:

Lin:DCM / Lin:DCM / Id:ID

W:400 L:40

F

DFOV: 38.3 x 38.3cm



LightSpeed Pro 32

H

Moffitt Cancer Ctr at Int Plaza

Ex: 2794

ARTERIAL

C: 135CC OF OPTIRAY

Se: 400/9

Im: 64/146

Cor: A25.4

Acc: CT20130020893

2013 Jun 18

Acq Tm: 14:46:19

Mag: 1.1x

512x512

STANDARD

R

L

120.0 kV

634.0 mA

Tilt: 0.0

ET: 0.5 s

GP: 0.5 s

TS: 38.75 mm/s

SPR:

Lin:DCM / Lin:DCM / Id:ID

W:400 L:40

F

DFOV: 38.3 x 38.3cm



LightSpeed Pro 32

A

Moffitt Cancer Ctr at Int Plaza

Ex: 2794

ARTERIAL/VENOUS

C: 135CC OF OPTIRAY

Acc: CT20130020893

Se: 3/9

2013 Jun 18

Im: 91/268

Acq Tm: 14:46:19

Ax: F53.8

Mag: 1.1x

512x512

STANDARD

R

L

120.0 kV

700.0 mA

2.5 mm Tilt: 0.0

ET: 0.5 s

GP: 0.5 s

TS: 38.75 mm/s

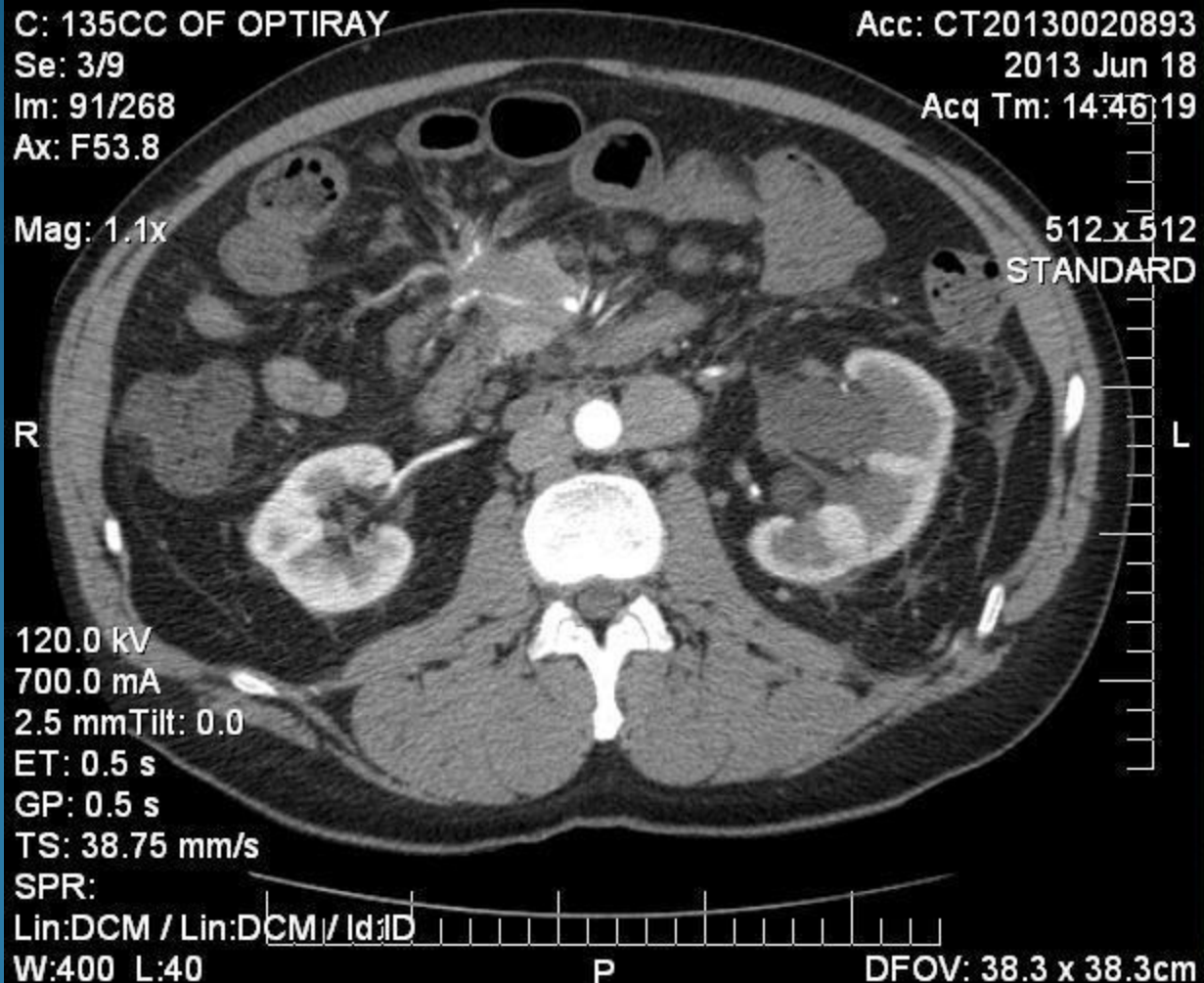
SPR:

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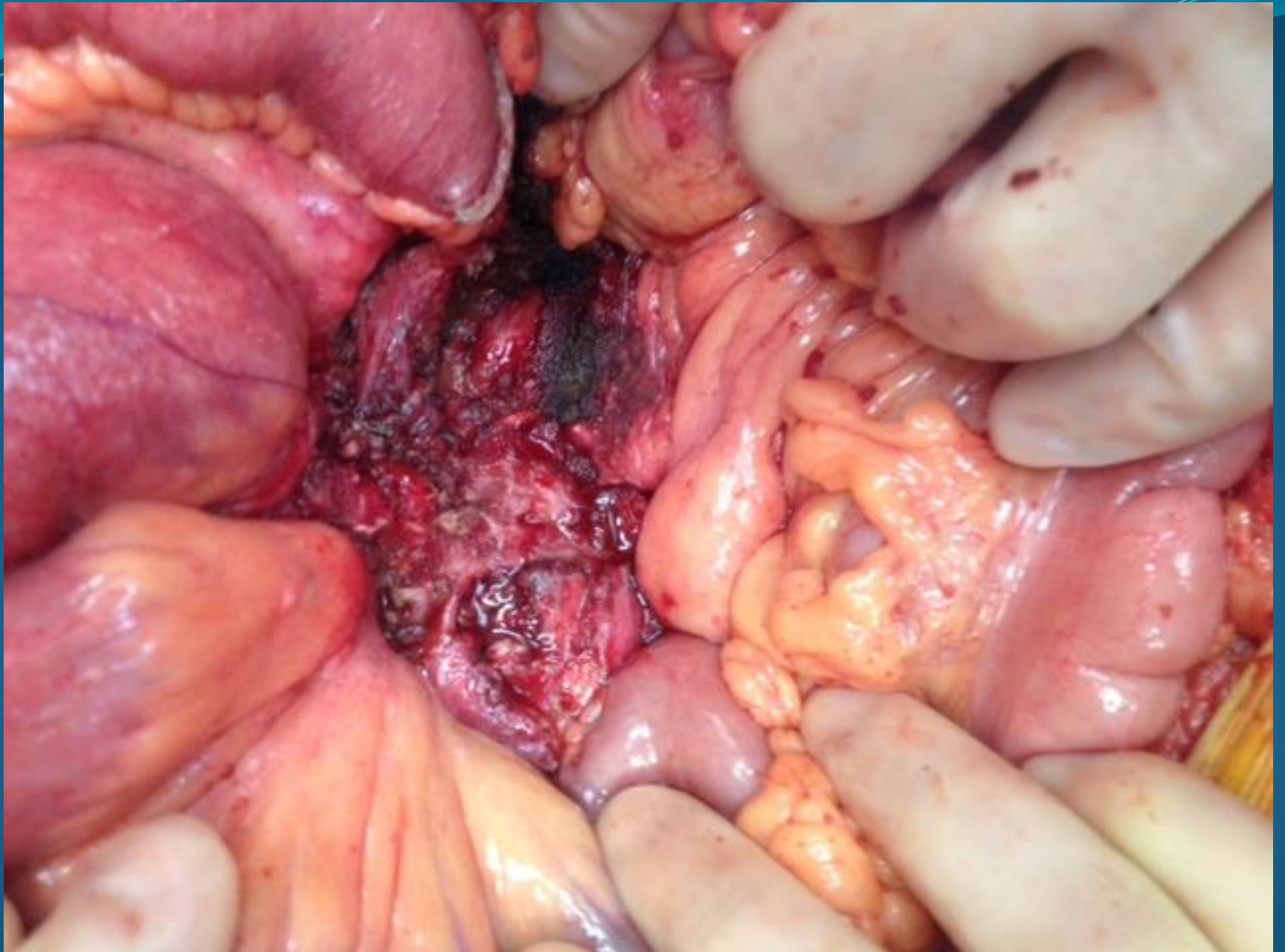
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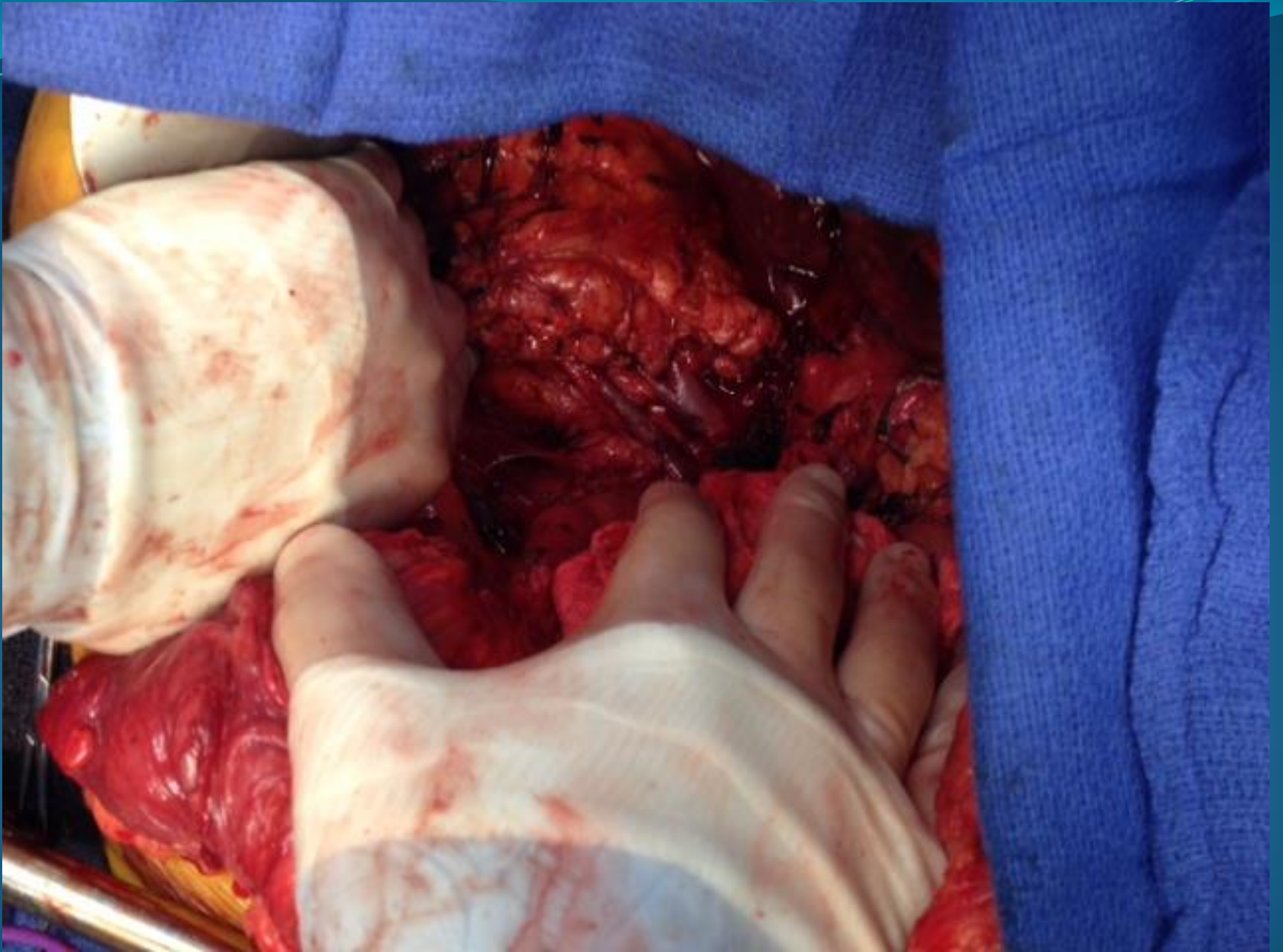
DFOV: 38.3 x 38.3cm





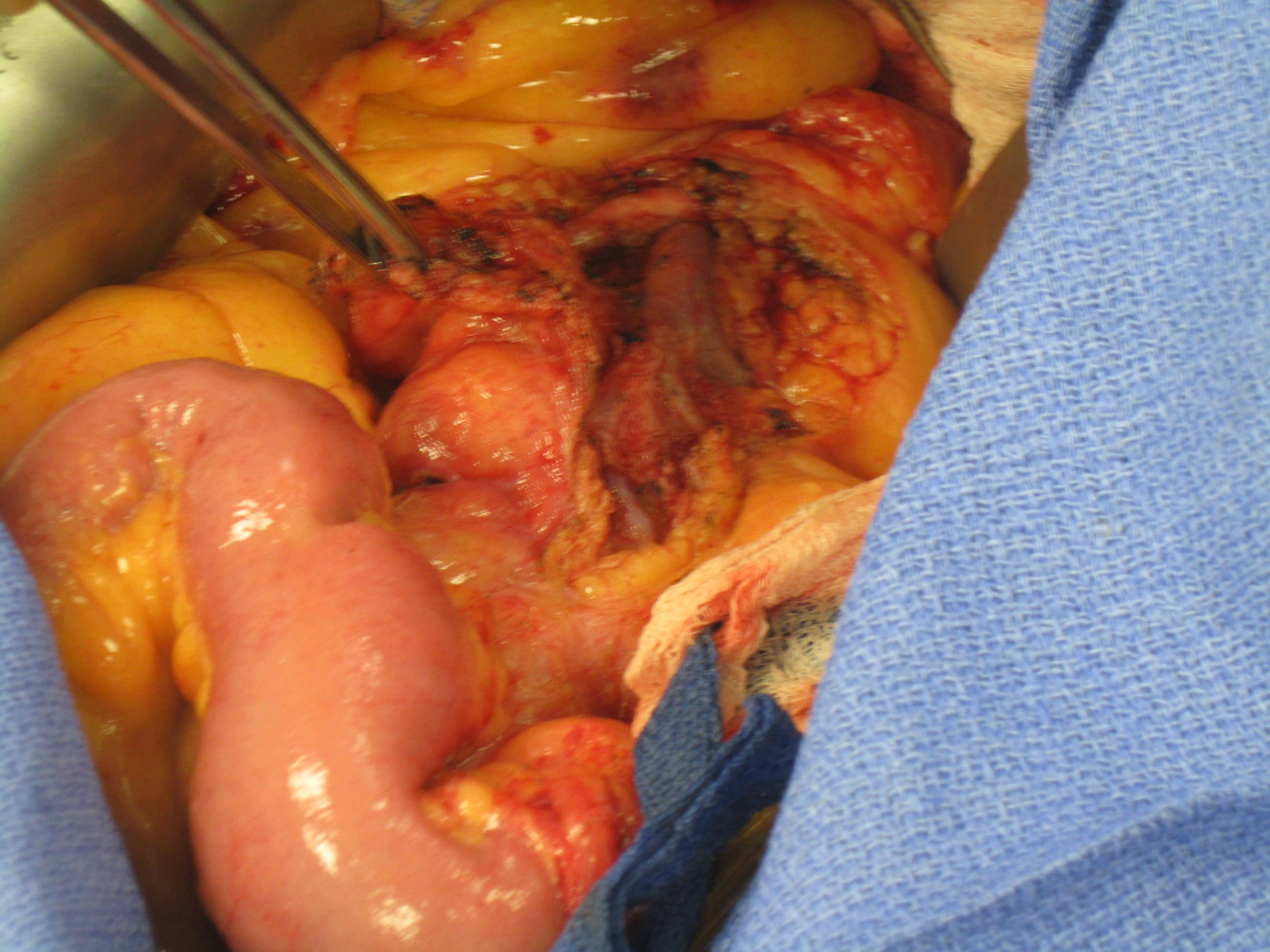




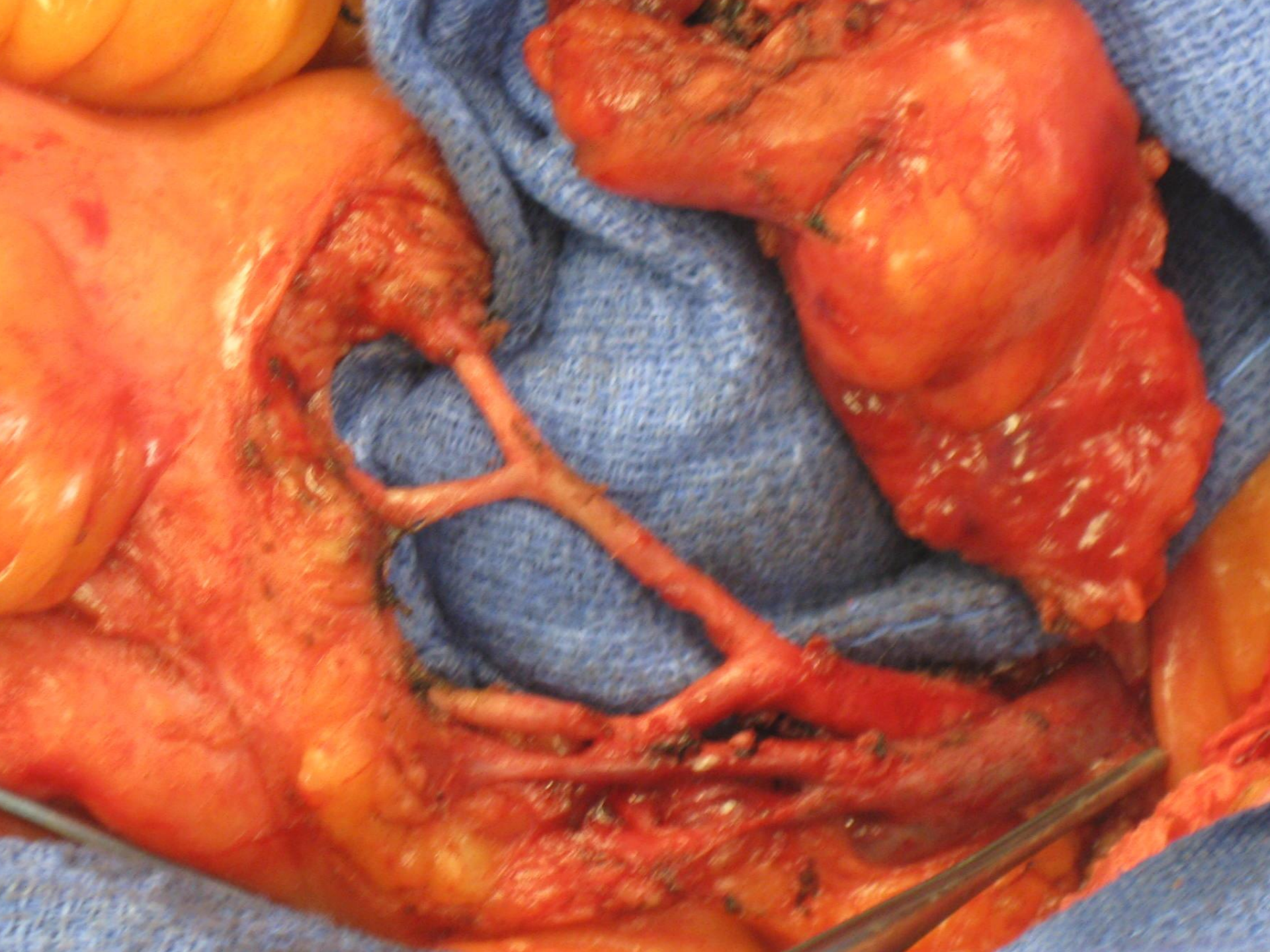














# Intraoperative chemotherapy

Dissolvable foam soaked in  
chemotherapeutic agent

Liver resection cavities

Mesentery defects after dissection

Pelvis

Diaphragm

SPECIMEN SITE: **omentum**

TESTING LABORATORY: **PTI-Southside**

TUMOR TYPE: **Gastrointestinal: Small Intestine** LAB ADDRESS: **2516 Jane Street, Pittsburgh, PA 15203**

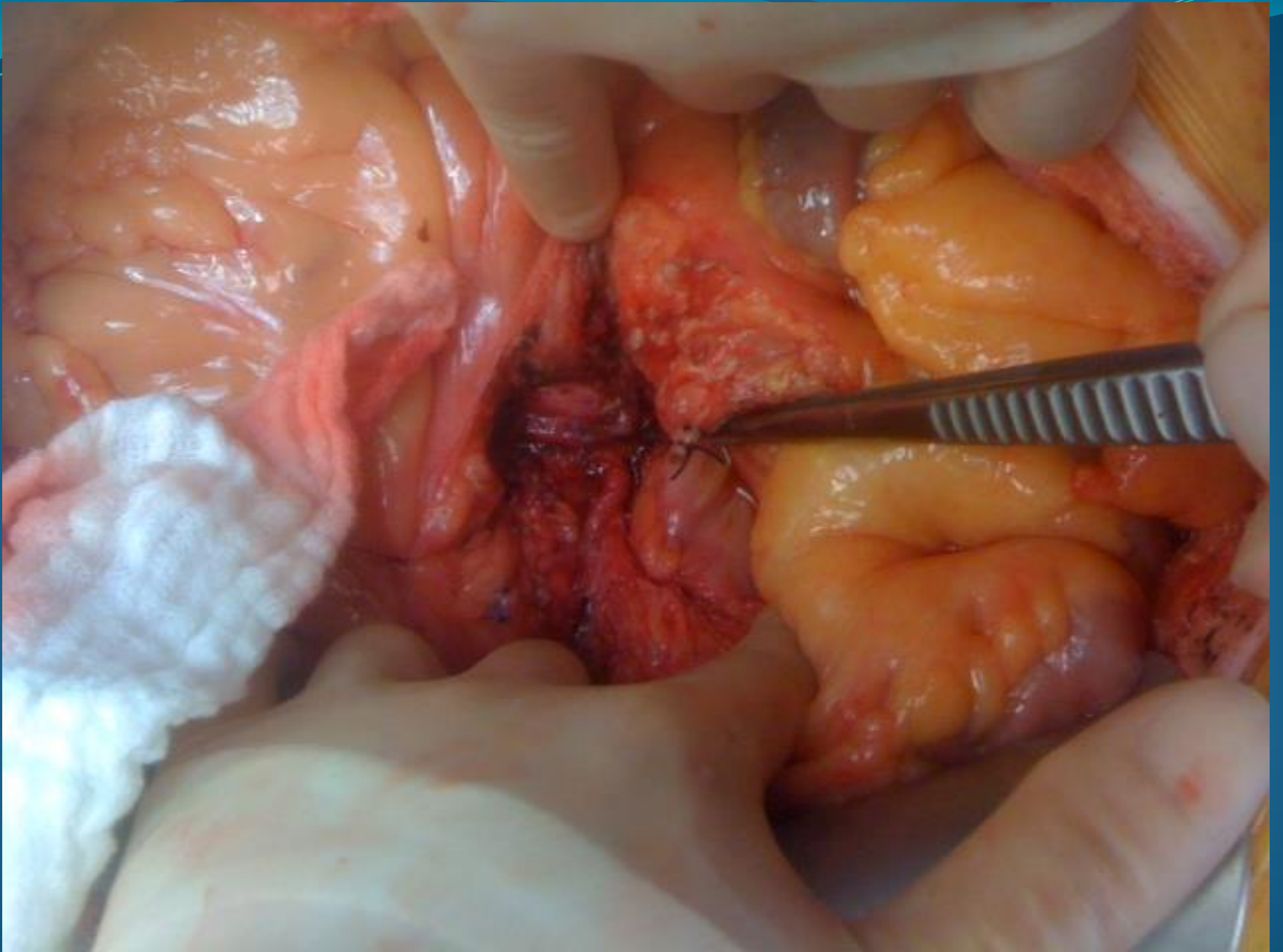
## TESTING INFORMATION

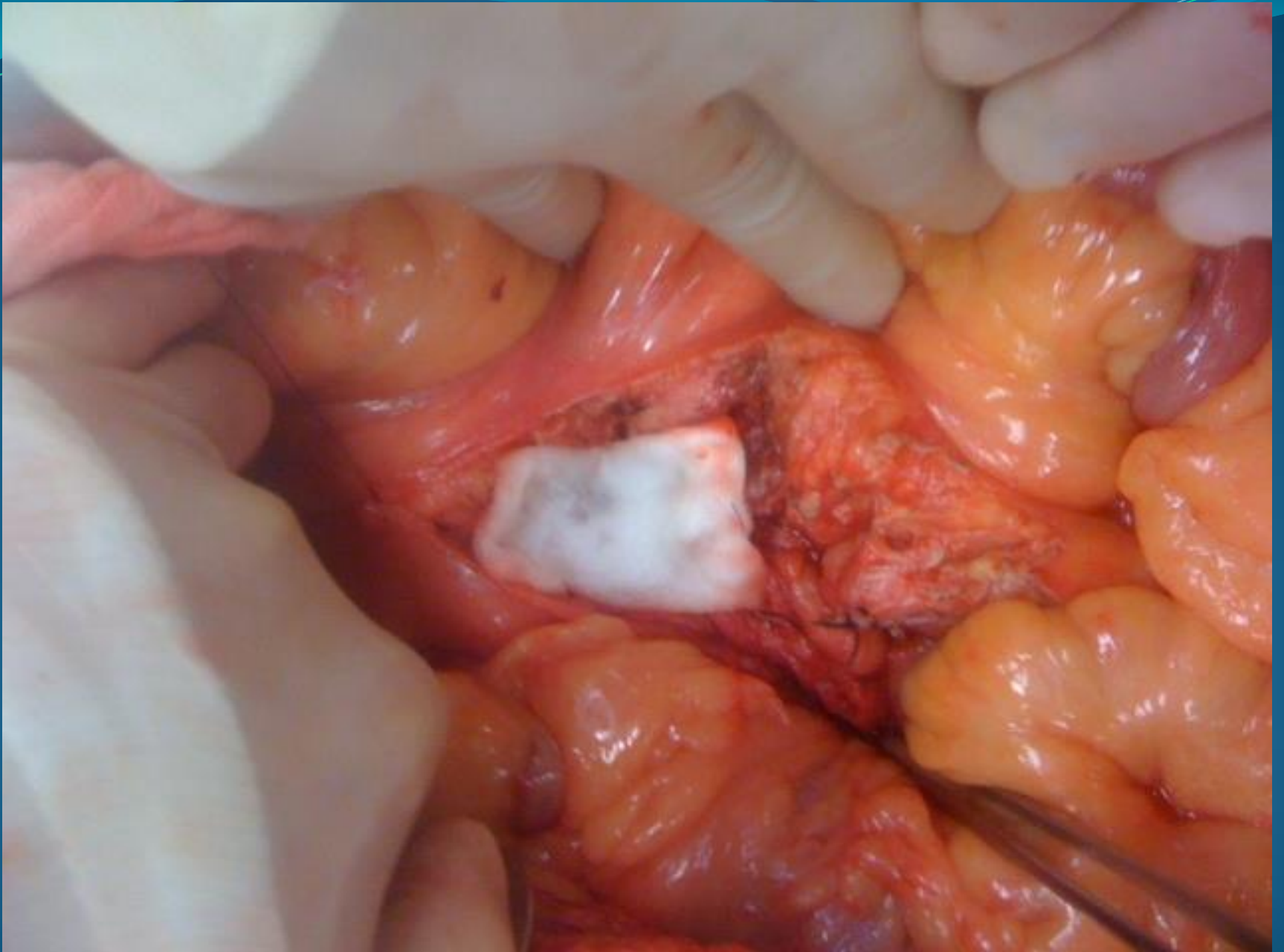
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SINGLE AGENTS: **7**

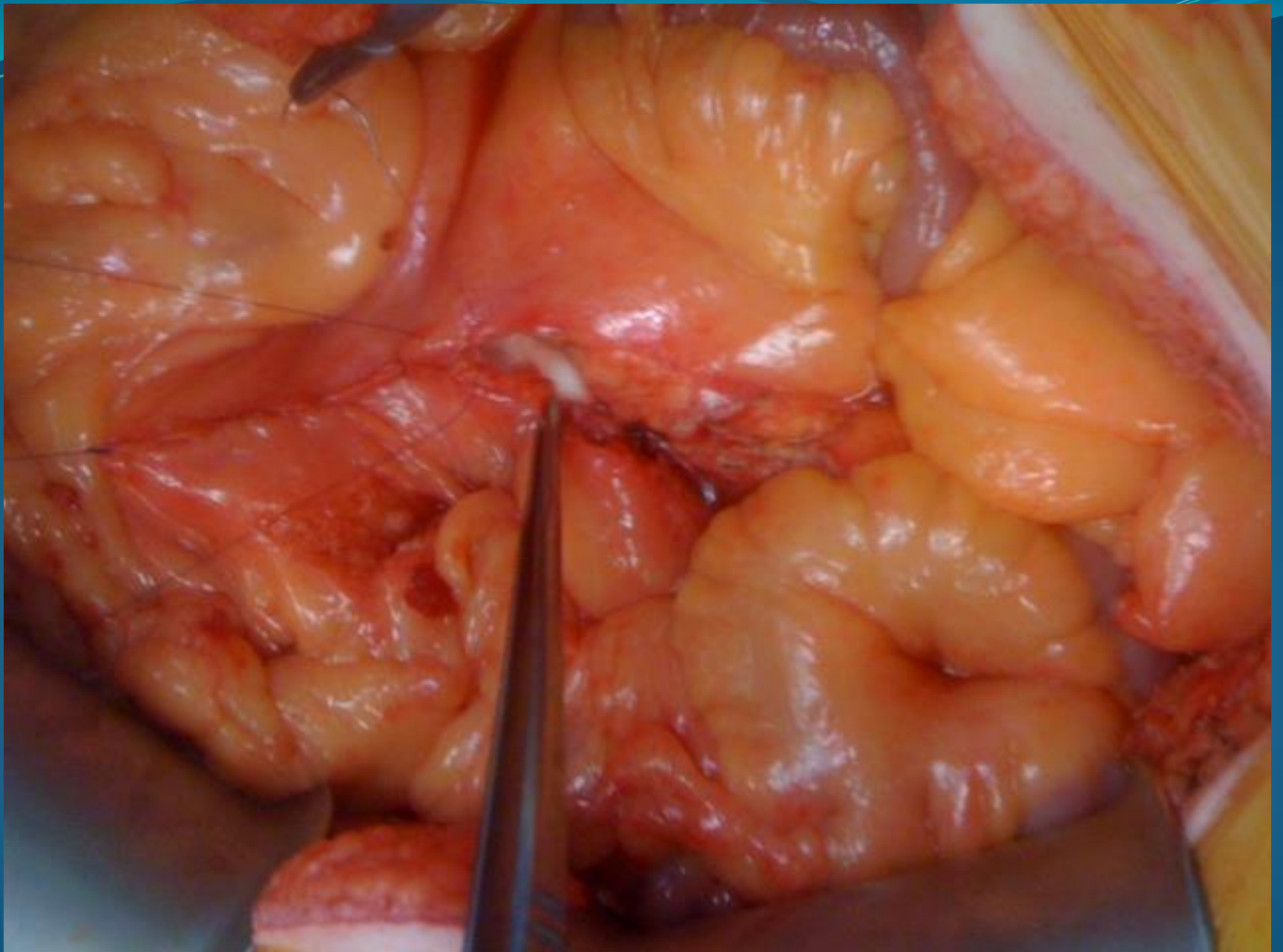
COMBINATION AGENTS: **3**

IN VITRO RESPONSE SUMMARY		
Responsive	Intermediate Response	Non-Responsive
<b>DOXORUBICIN/ FLUOROURACIL ETOPOSIDE</b>	<b>SUNITINIB PACLITAXEL CISPLATIN DOXORUBICIN</b>	<b>FLUOROURACIL/ TEMOZOLOMIDE FLUOROURACIL CISPLATIN/ ETOPOSIDE TEMOZOLOMIDE</b>









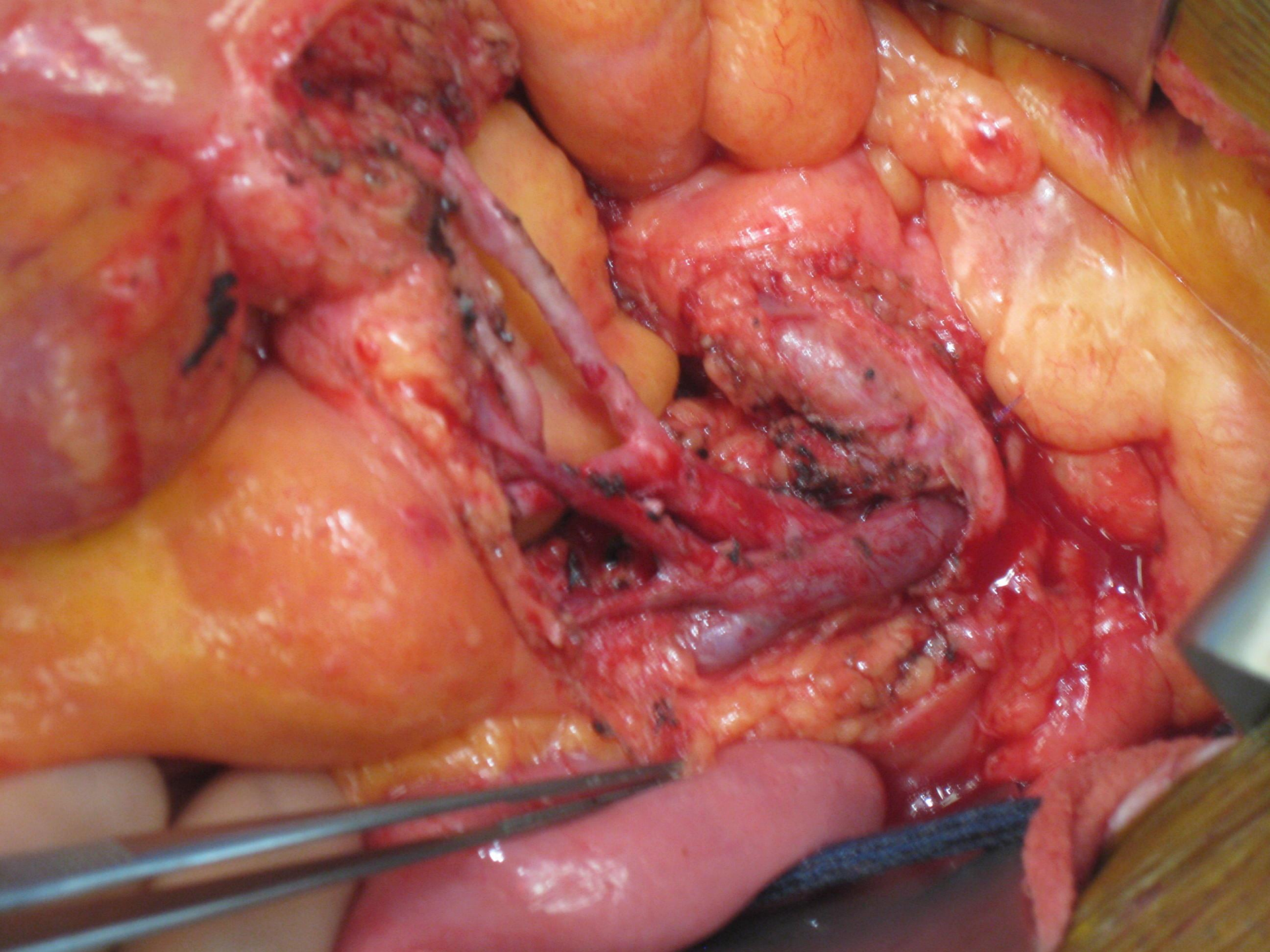
# Results

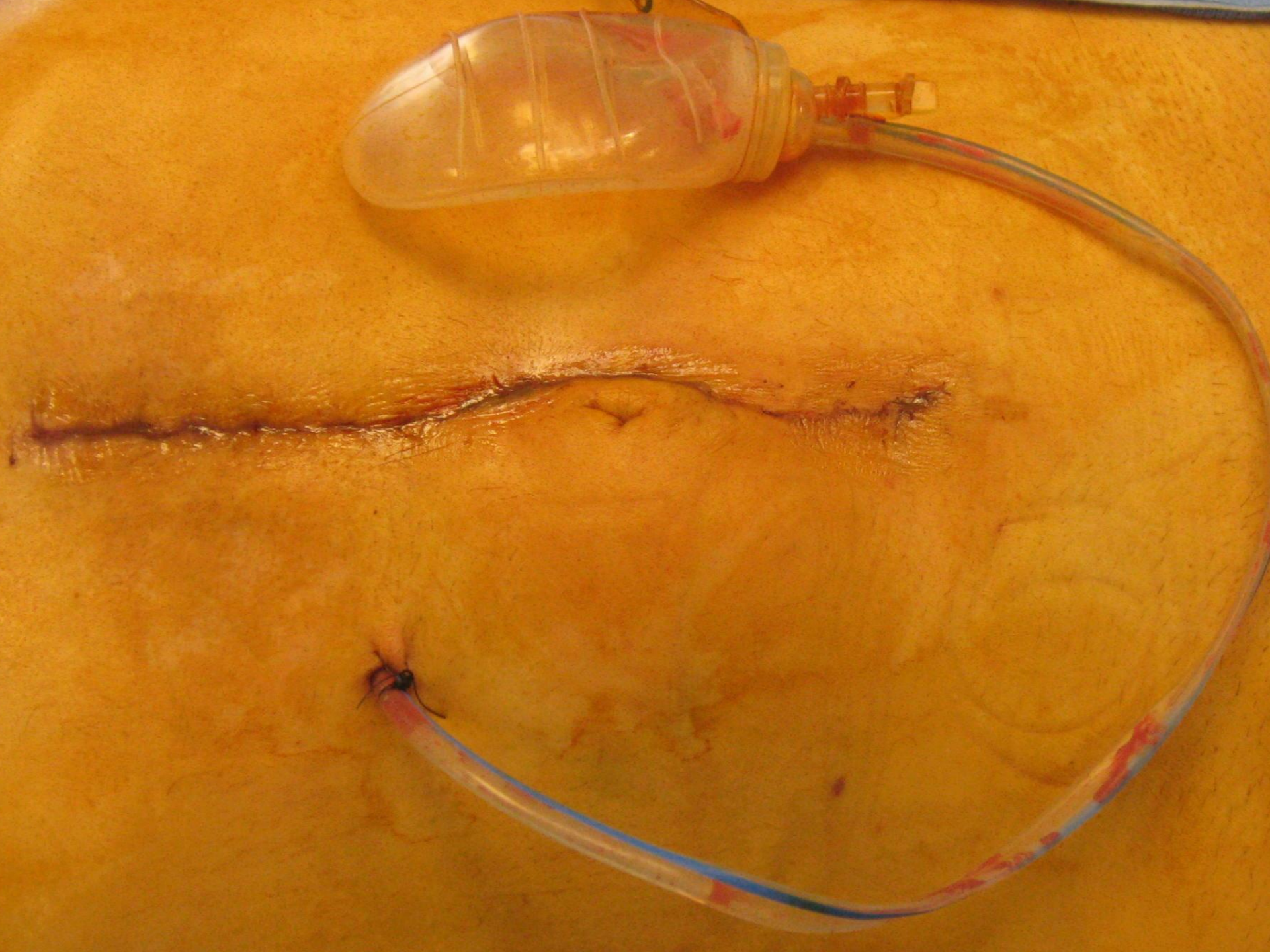
- 62 consecutive Mid gut carcinoid Patients for cyto-reductive operations (1/2007-12/2009)
- 32 patients underwent intra-op chemo
- 30 patients without tx as control
  
- 5 year survival rates are the same so far
  
- 18.8% (6/32) vs 53.3% (16/30) need re-exploration
- 56.3% (9/16) vs 33.3% (2/6) had local recurrence
- 6.25% (2/32) vs 30% (9/30) had local recurrence

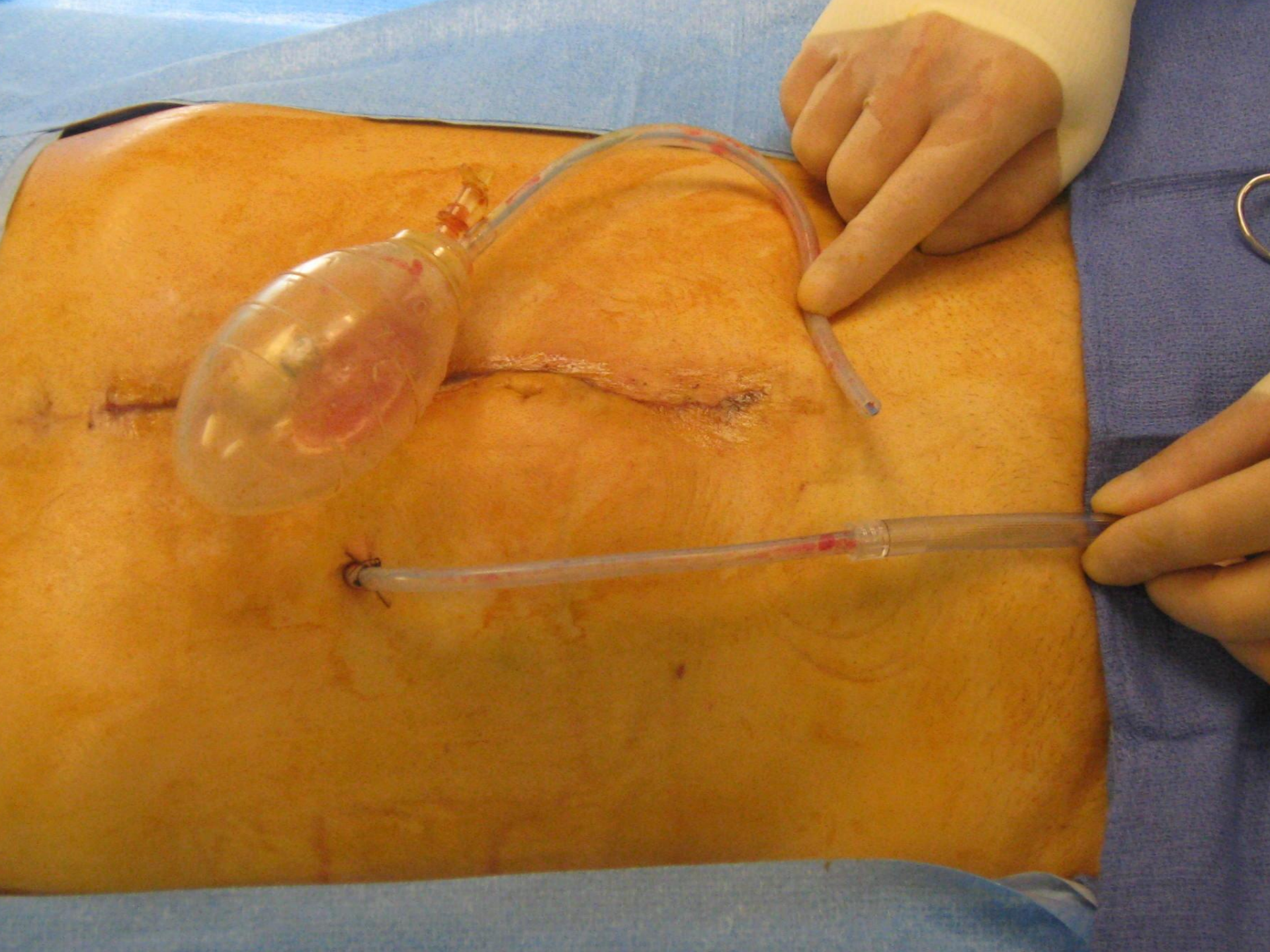
# **Staged second-look laparoscopy:**

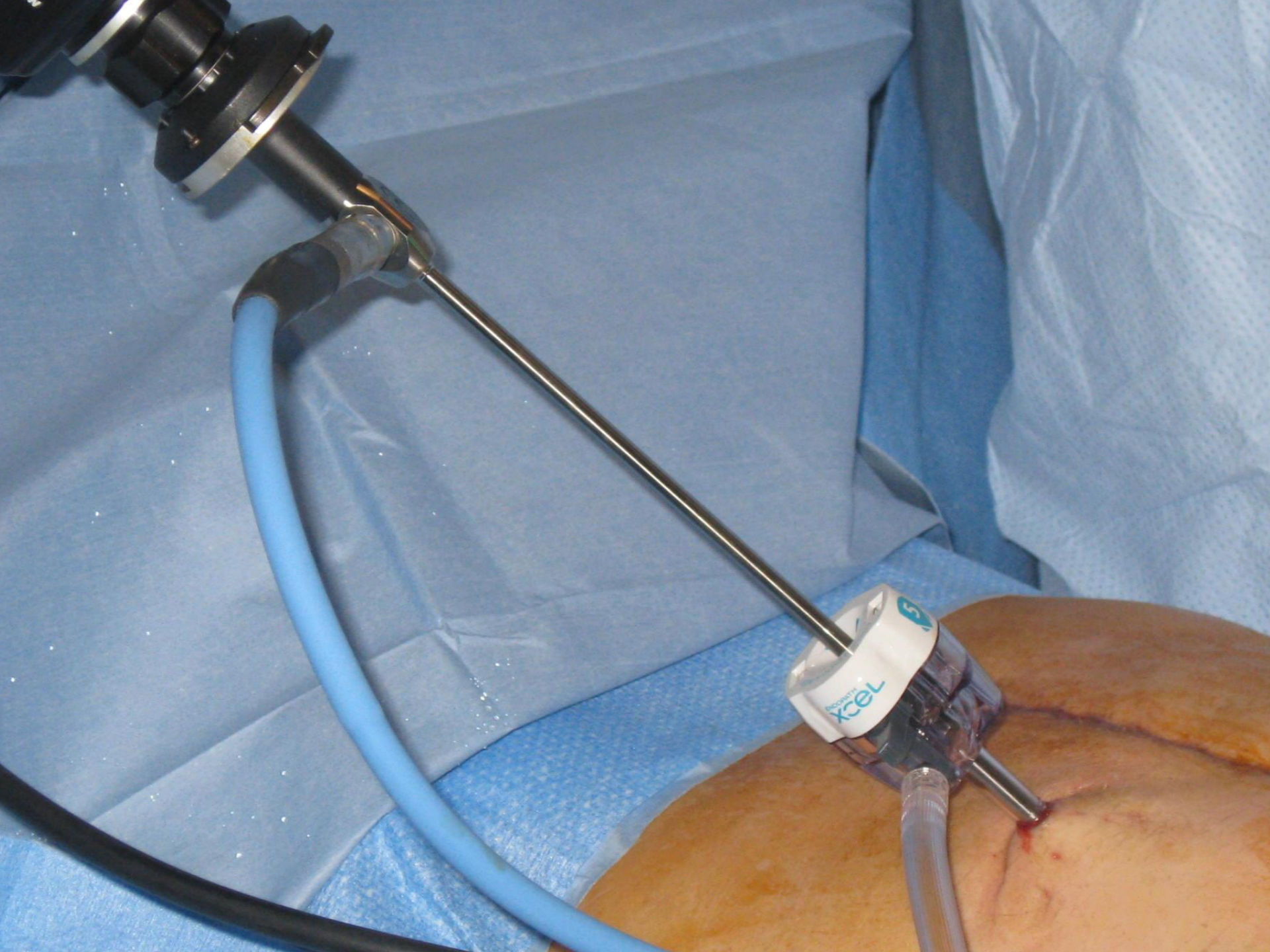
**A new approach for evaluating ischemic bowel following extensive mesenteric lymphadenectomy for midgut carcinoid**











Diagnostic Lap.



# Results

Between 6/2006 and 10/2010, a total of 12 patients underwent staged 2<sup>nd</sup> look laparoscopies; six were conducted to evaluate the integrity of anastomoses between ischemic looking bowel segments following extensive mesenteric lymph node dissection.

All initially ischemic looking bowel segments restored normal perfusion and all anastomoses remained intact. All staged 2<sup>nd</sup> look laparoscopies were concluded in 5-10 minutes without any complications or prolonged hospital stays.

**Radio-guided  
exploration facilitates  
surgical cytoreduction of  
Neurendocrine tumors.**

# Common Pre-operative Imaging Studies

Octreoscan : 90% positive

MIBG Scan : 70% positive

CT Scan

MRI

PET



# Radio-guided Surgery

- Sentinel lymph node biopsy
  - Breast Cancer
  - Melanoma
  - Lung Cancer
- Tumor marker-guided 2<sup>nd</sup> look
- Minimally invasive Parathyroidectomy
- Neuroendocrine Tumors

# Adaptation of gamma probe use intraoperatively

- Target-directed dissection
  - Time saving, less tissue damage and blood loss
- Most minimally invasive procedure possible
  - Small incision, minimal dissection, rapid recovery
- Real time differentiation
  - Scar, desmoplastic tissue, viable vs nonviable tumor
- Enhance the degree of debulking
  - Identify and locate tumor burden missed by surgeon
- Confirmation of target removal
  - *Ex vivo* count of specimen, *in vivo* count of field

# Results

46 patients had gamma probe guided explorations

3 patients injected with  $^{99m}\text{Tc}$ ,

3 patients injected with  $^{123}\text{I}$  MIBG (3)

40 patients injected with  $^{111}\text{In}$  pentetretotide.

37 out of 40 (93%) of the  $^{111}\text{In}$ -pentetretotide guided explorations the gamma probe was deemed helpful

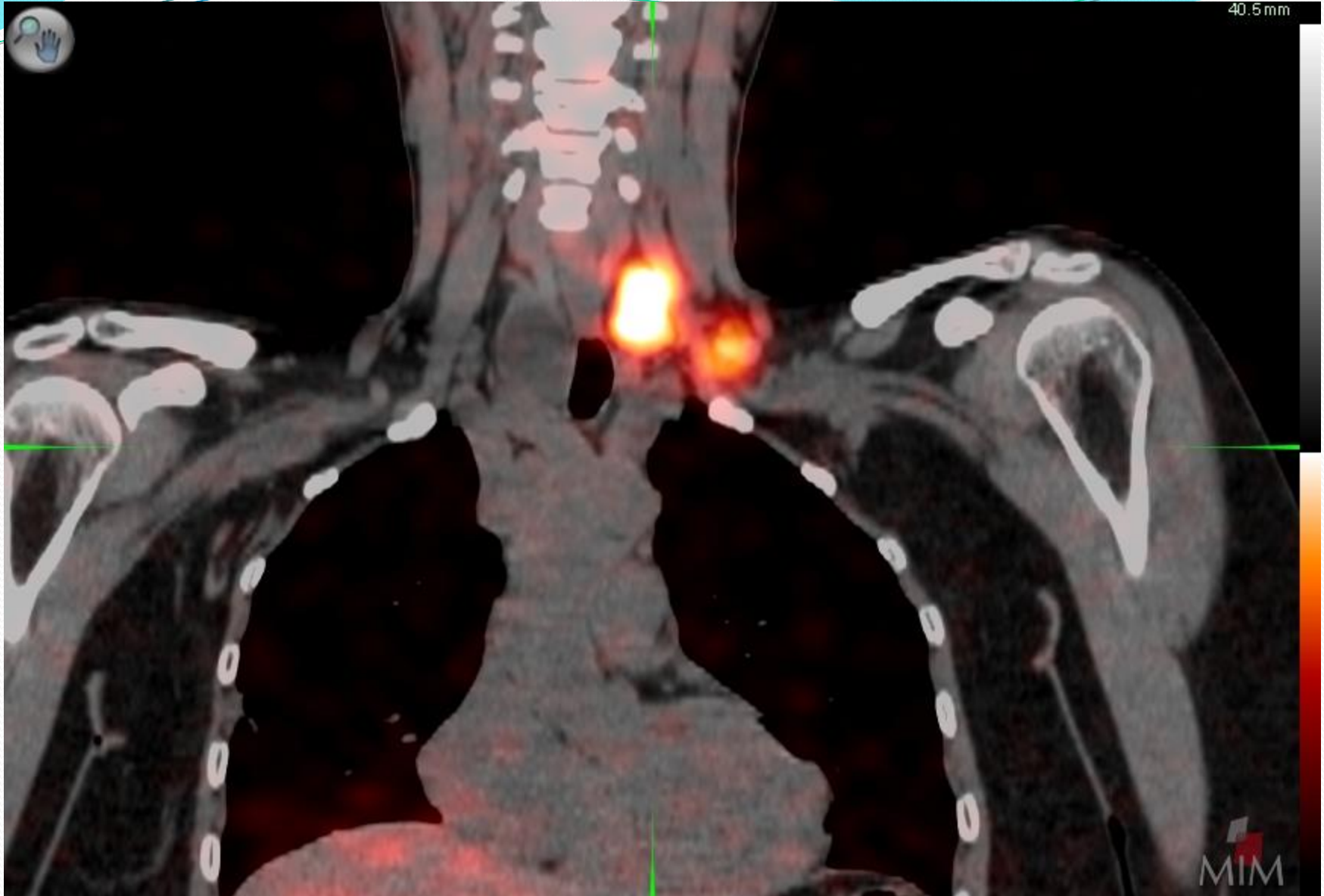
5 out of 6 neck and mediastinum explorations the gamma probe was essential

$^{123}\text{I}$  MIBG was not useful in all three patients

The optimal doses and interval between injection and exploration of  $^{111}\text{In}$  pentetretotide is 6 mCi injected 6-7 days prior to surgery.

# Discussion

- Useful and powerful adjunct, especially for re-exploration and unusual anatomic locations
- Essential for neck and mediastinal lymph node metastasis
- Great potential for rectal carcinoid: defining lymphatic drainage and proximal margins
- Isotope selection, injection dose and timing of exploration are the keys for a successful outcome







44



2



In

Count



Background Count



Mute



Volume



Binary Pitch

Dynamic Pitch

Count Range

100

1,000

10,000

50,000

Ochsner Medical Center Westbank



820-00466

BIOMED#  
436-15894

OCF ELECTRICAL ENGINEERING

SAFETY INSPECTION BY *AG*

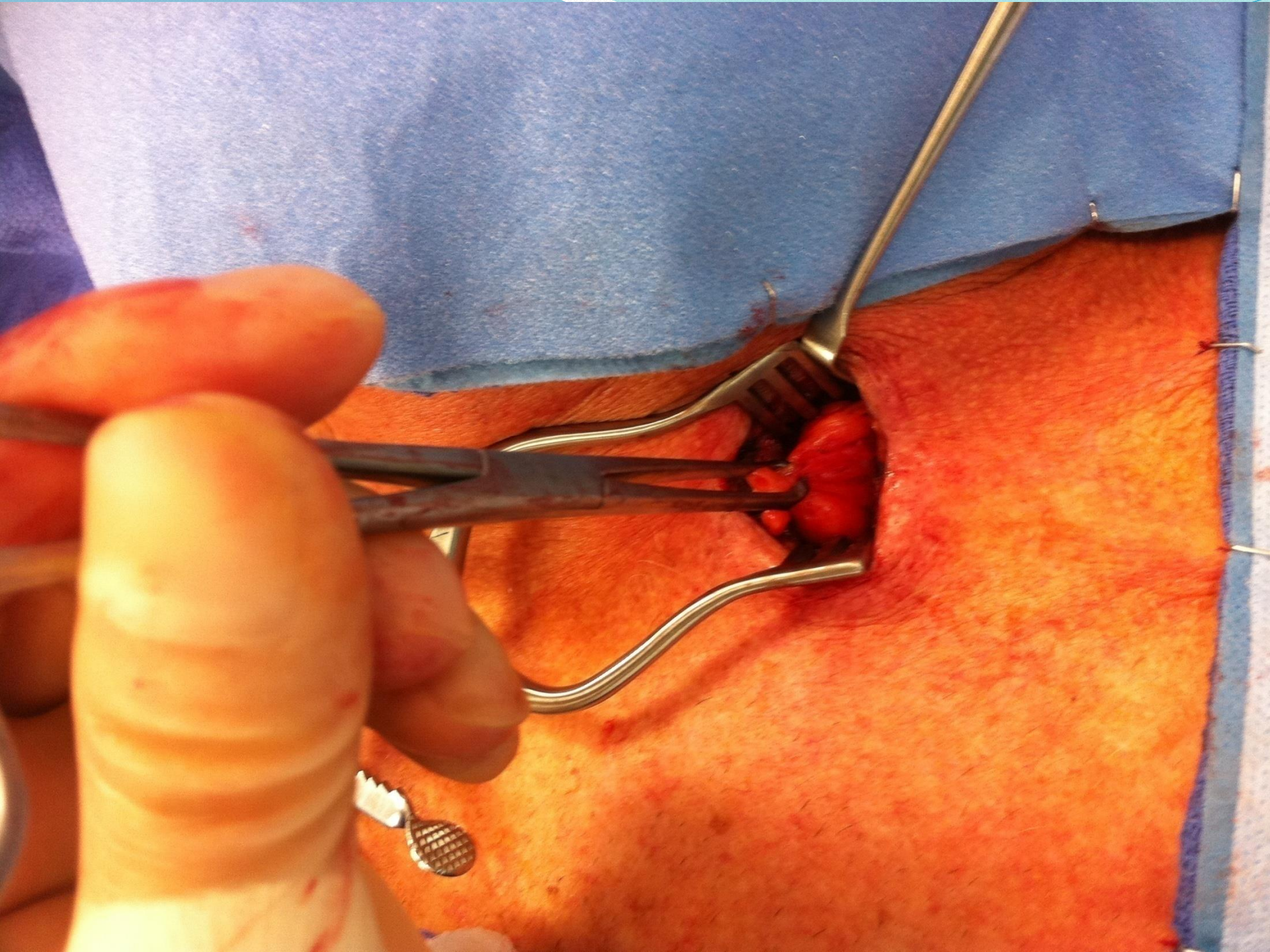
AVN *436-15894*

NEXT DUE *09/09*

NEO2000®

Gamma Detection System









Power



8 8 8

39



8 8 8

8 8 8 8 2



111  
In

Binary Pitch

Dynamic Pitch

Count Range

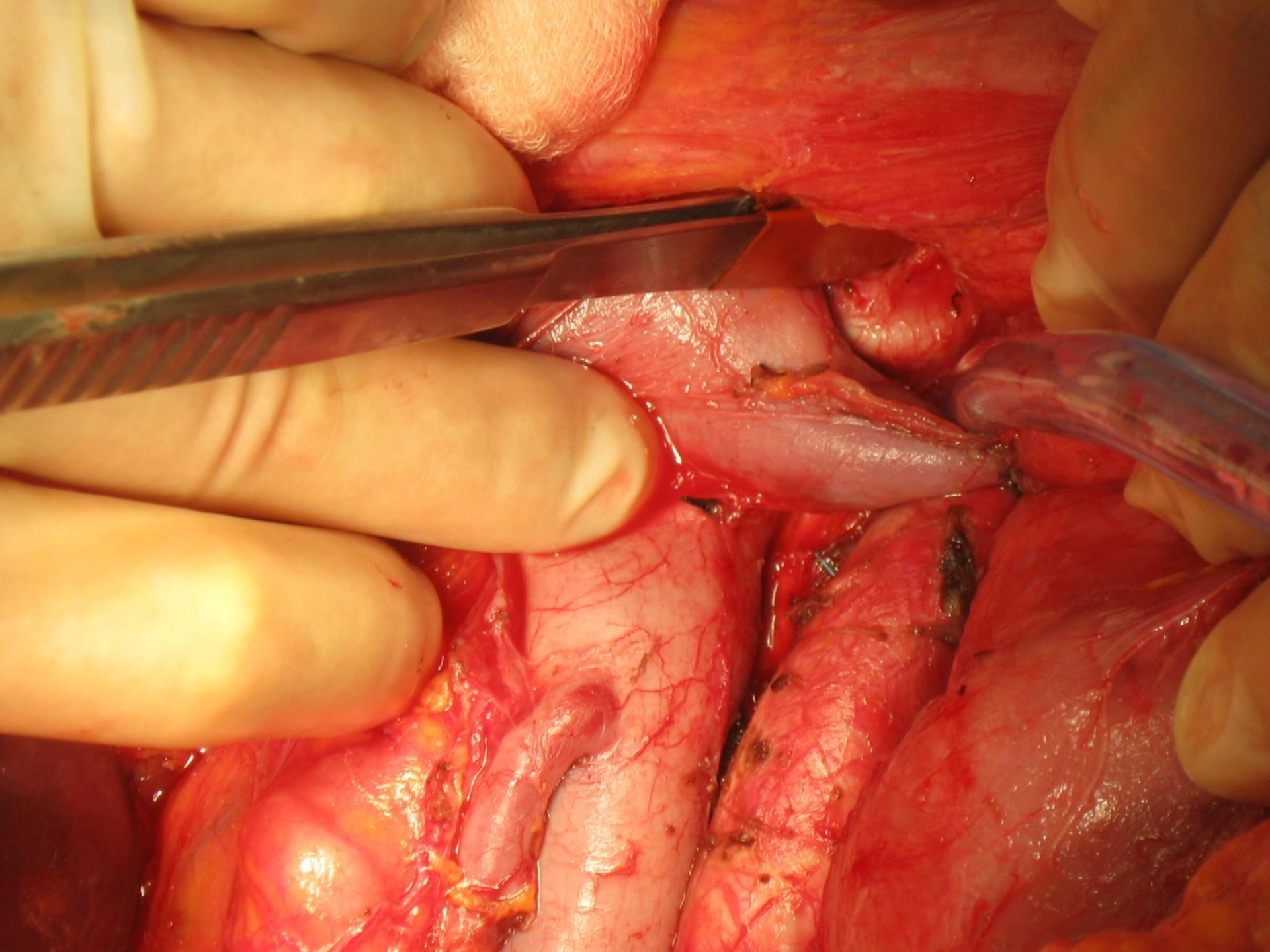
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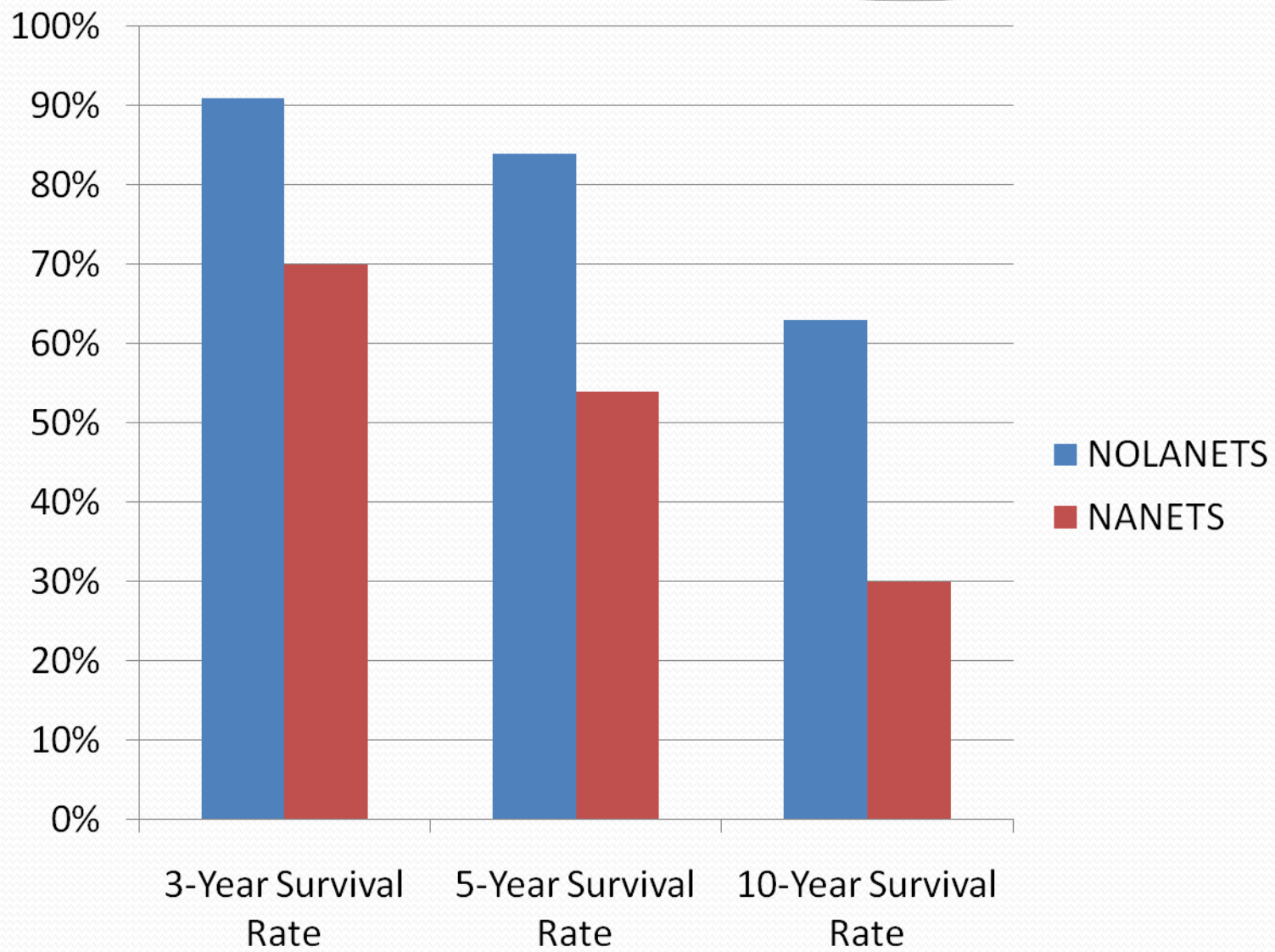












Comparison of patients with metastatic small bowel neuroendocrine tumors (distant disease) between the NOLANETS clinic and the SEER national database

	<b>N=</b>	<b>Median Survival (months)</b>	<b>3-Year Survival</b>	<b>5-Year Survival</b>	<b>10-Year Survival</b>
<b>NOLANETS</b>	319	141	91%	85%	64%
<b>SEER</b>	116	60	67%	48%	34%

# New technology: Irreversible Electroporation (IRE)

High voltage electrical pulses

Low energy direct current

Permanent cell membrane disruption

Without heat

# Potential New Approaches

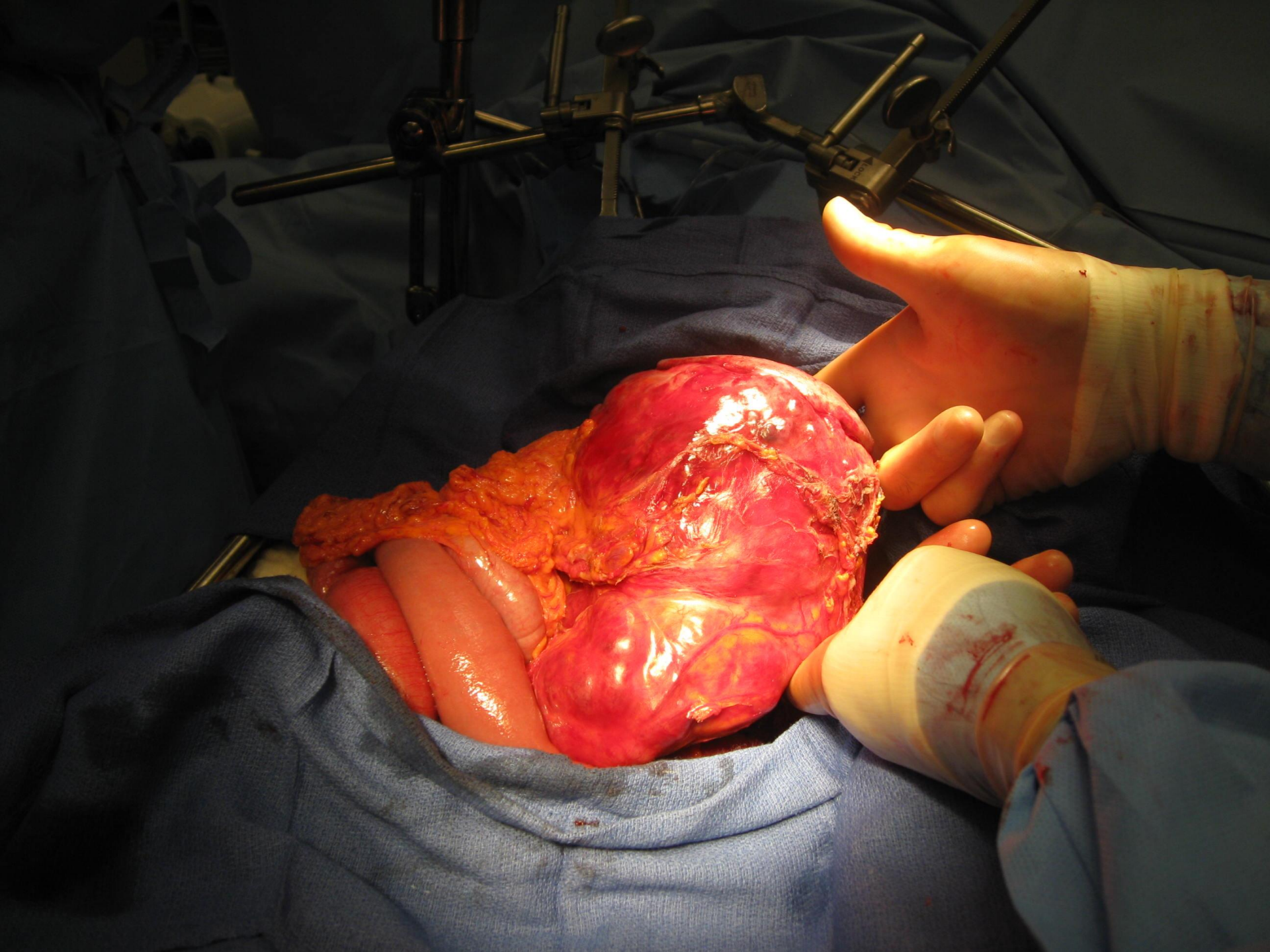
For extremely advanced diseases or carcinomatosis :  
Biopsy of primary, lymph node and liver metastasis

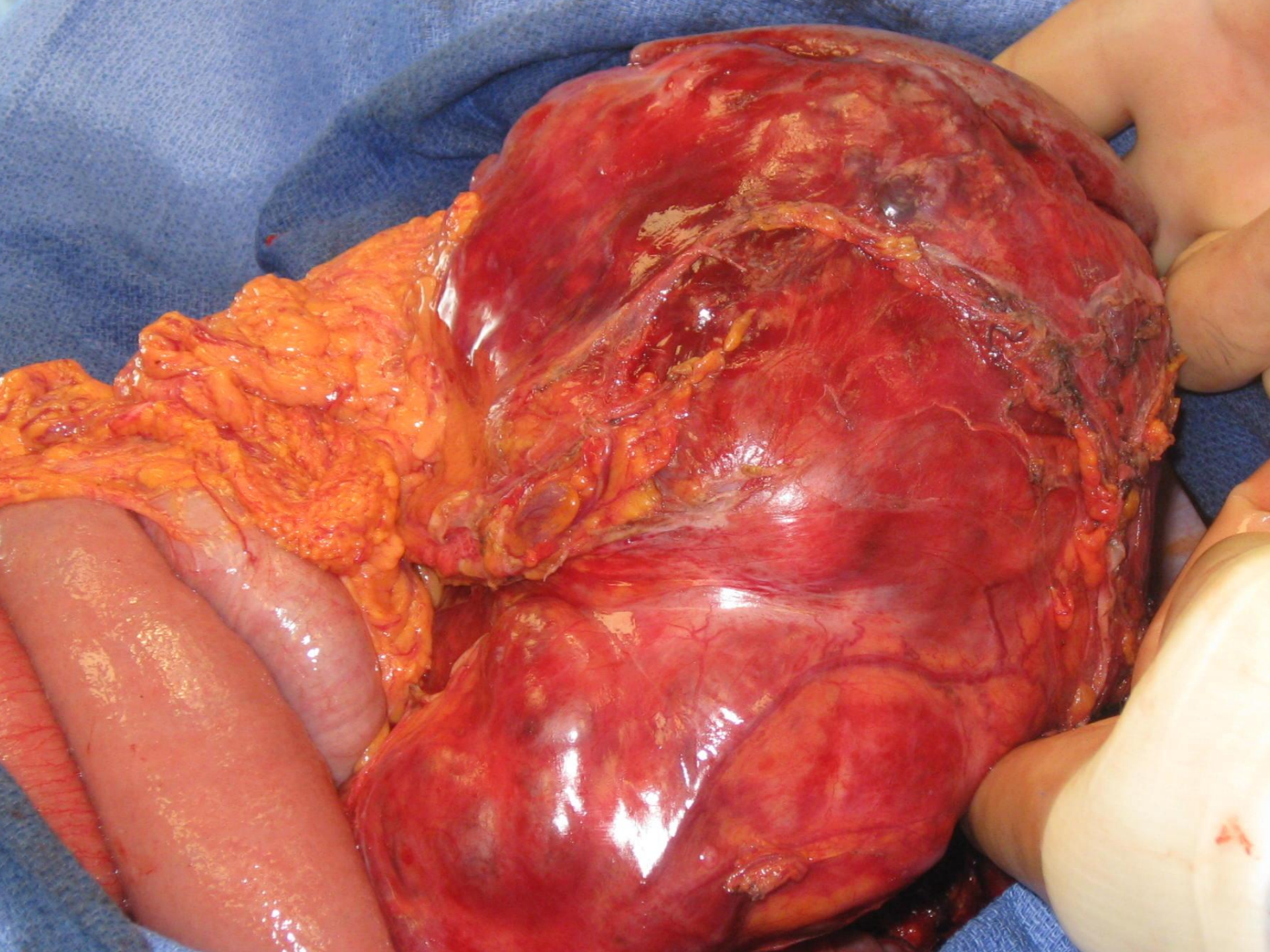
Biological / chemo-sensitivity tests &/or  
Immunological prep: Anti-CEA/SM Designer T-cells

Neo-adjuvant biological or immuno or chemo therapy

Post- treatment Surgical exploration: cytoreduction;  
Electrooperations with intralesional-chemotherapy;  
Intra /prei tumor injection of Anti-SM Designer T cells;  
Intra-operative chemo-infusion: divers' approach

- Functioning vs Nonfunctioning tumors
- Local/ regional vs Distant diseases
- Surgical vs Non-surgical treatment
- Combine surgical non surgical txs and the sequences
- Surgical procedures for pancreatic primaries
  - A). Enucleation
  - B). Beger's procedure
  - C). Whipple
  - D). Central pancreatectomy
  - E). Distal pancreatectomy with or without en bloc resection of adjacent organs
  - F). Total pancreatectomy for MEN I patients
  - G). Ablations



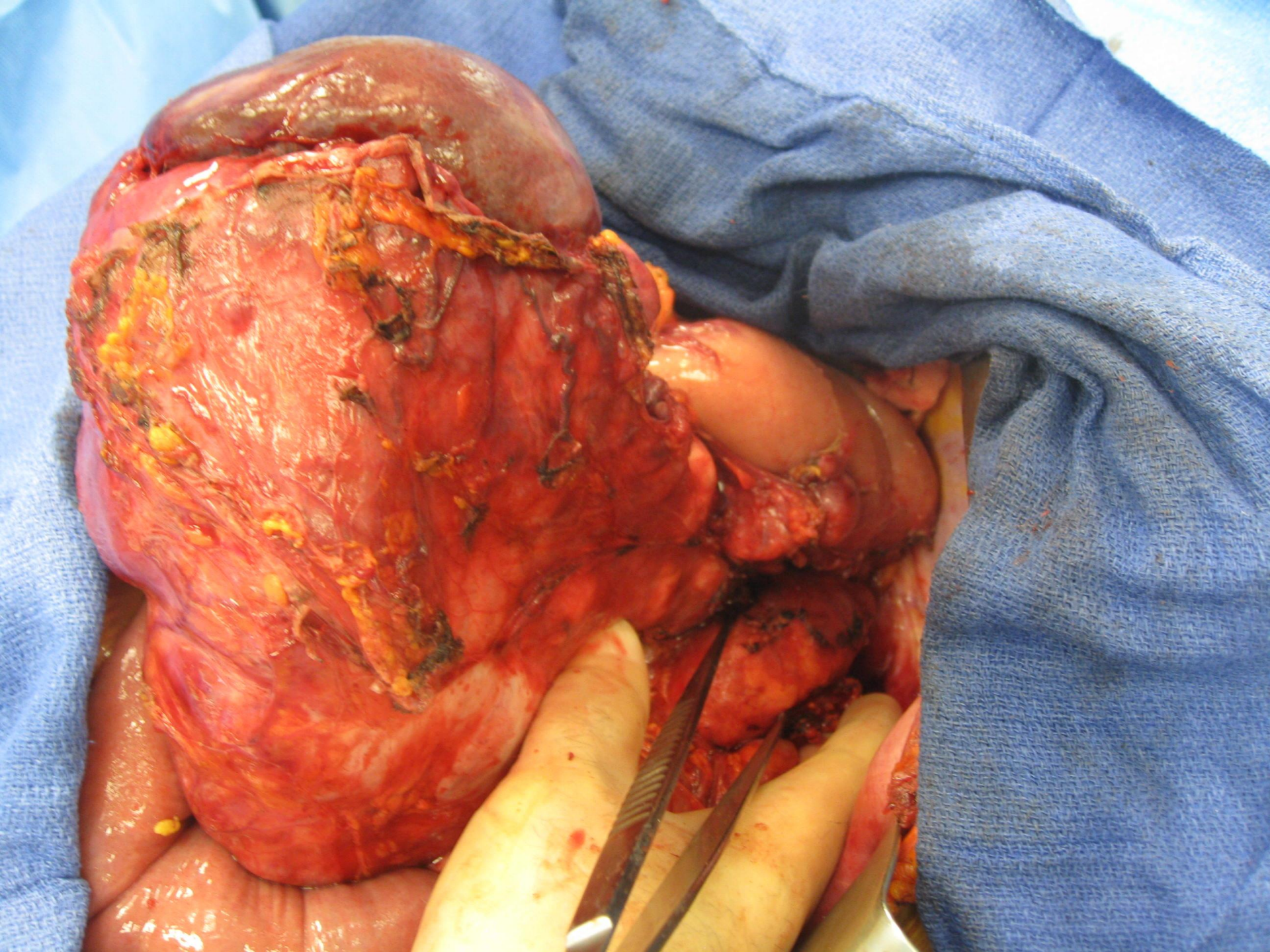


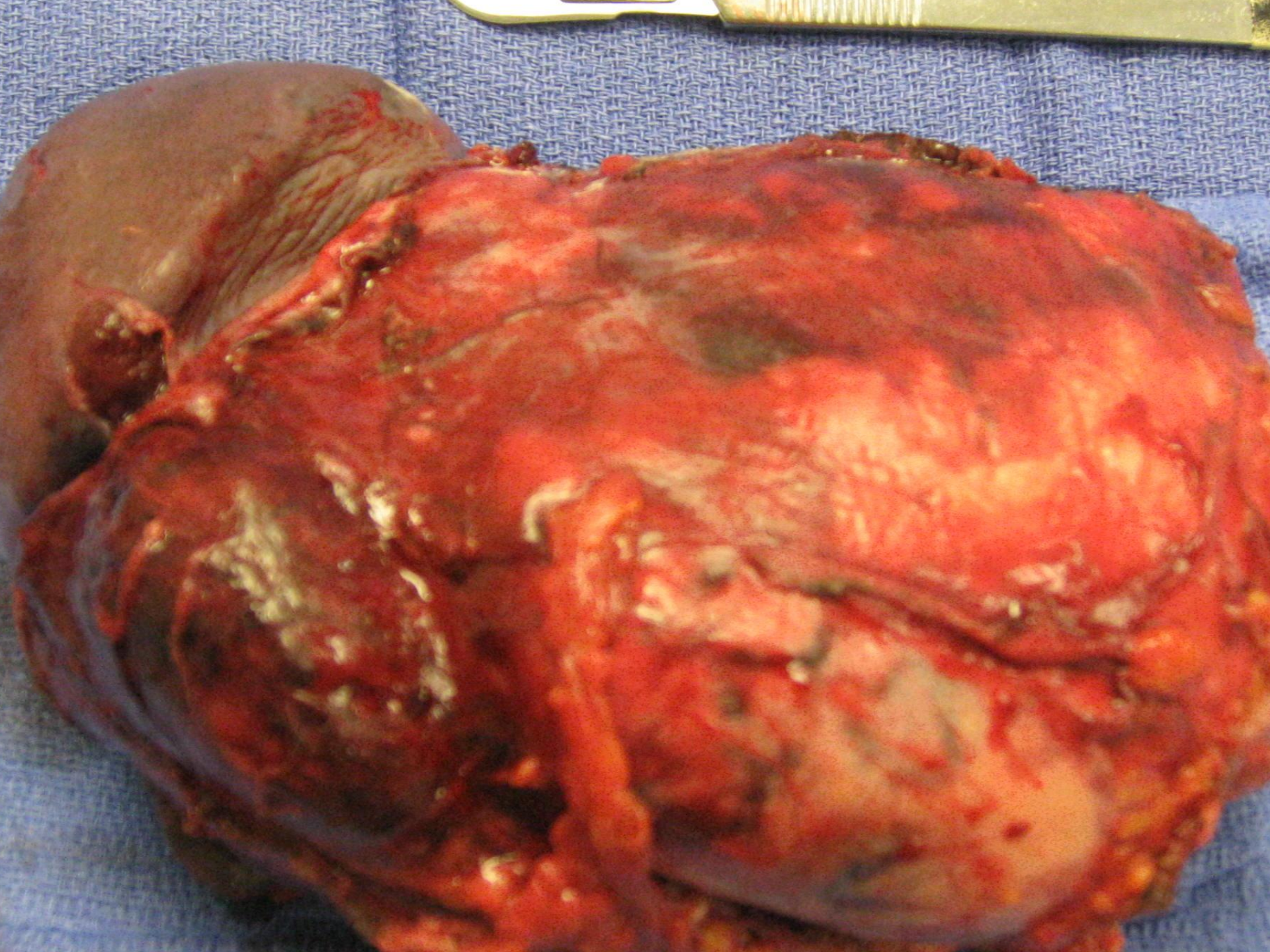




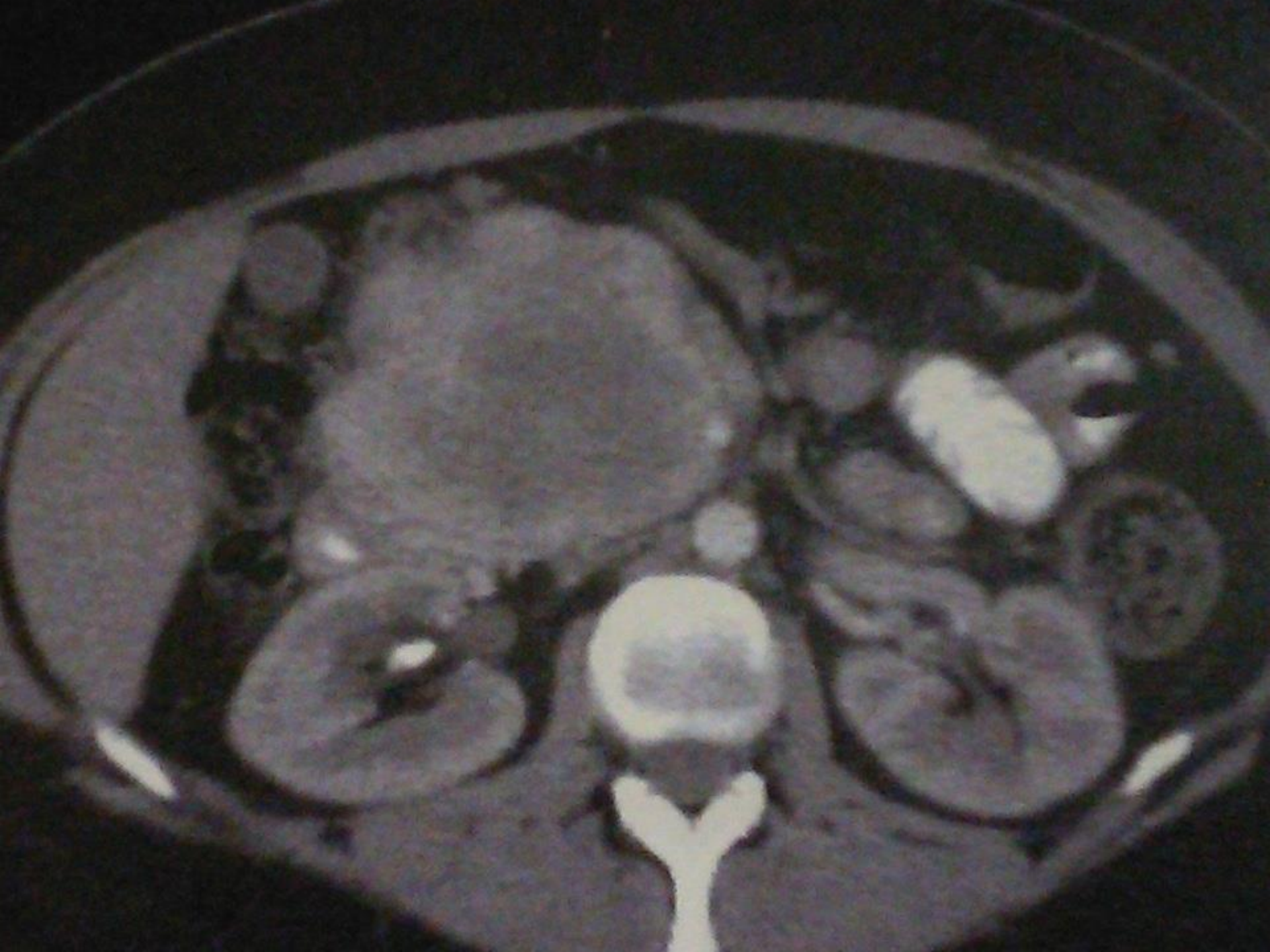


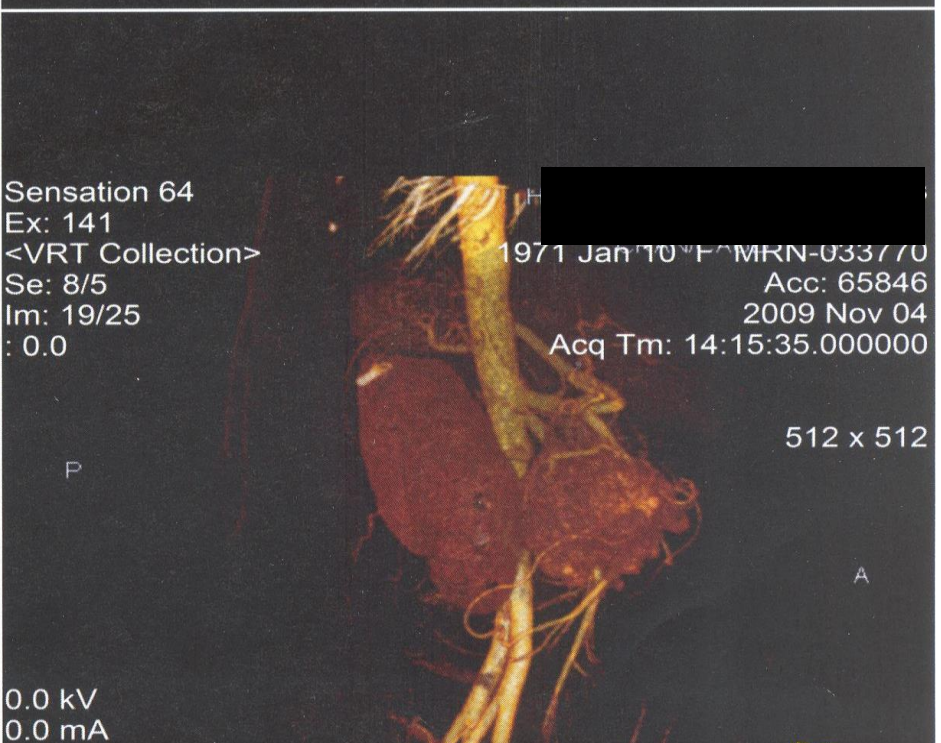
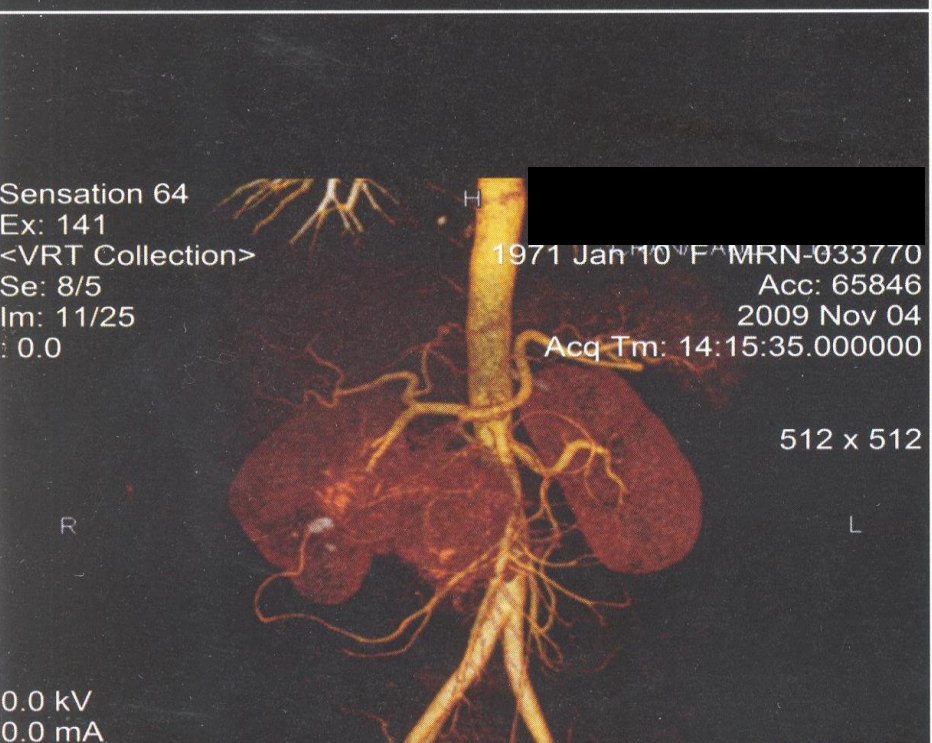
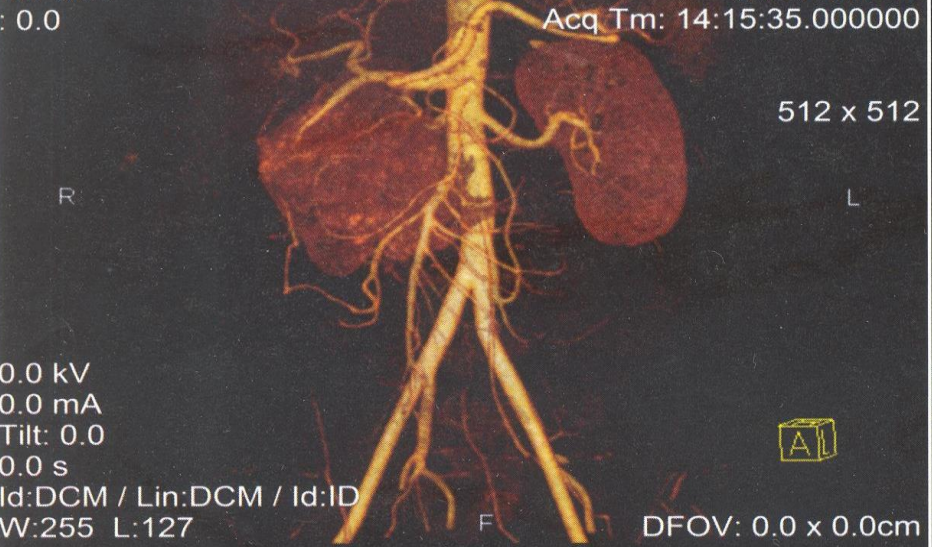
METRIC INCHES  
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15  
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15  
Devon® OR Products & Safety Solutions  
Measurement device is not calibrated. Use for approx. measurement only.  
MADE IN U.S.A.

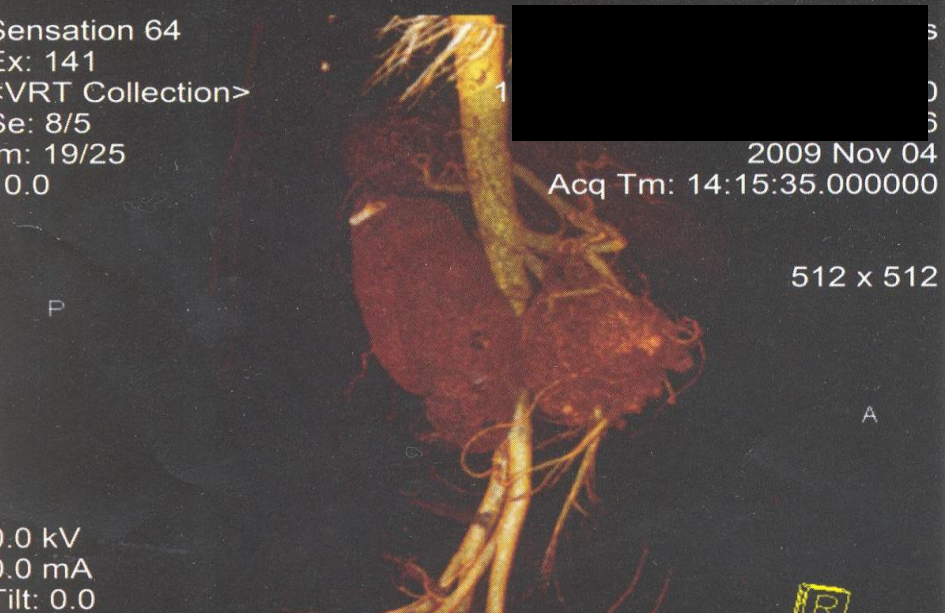
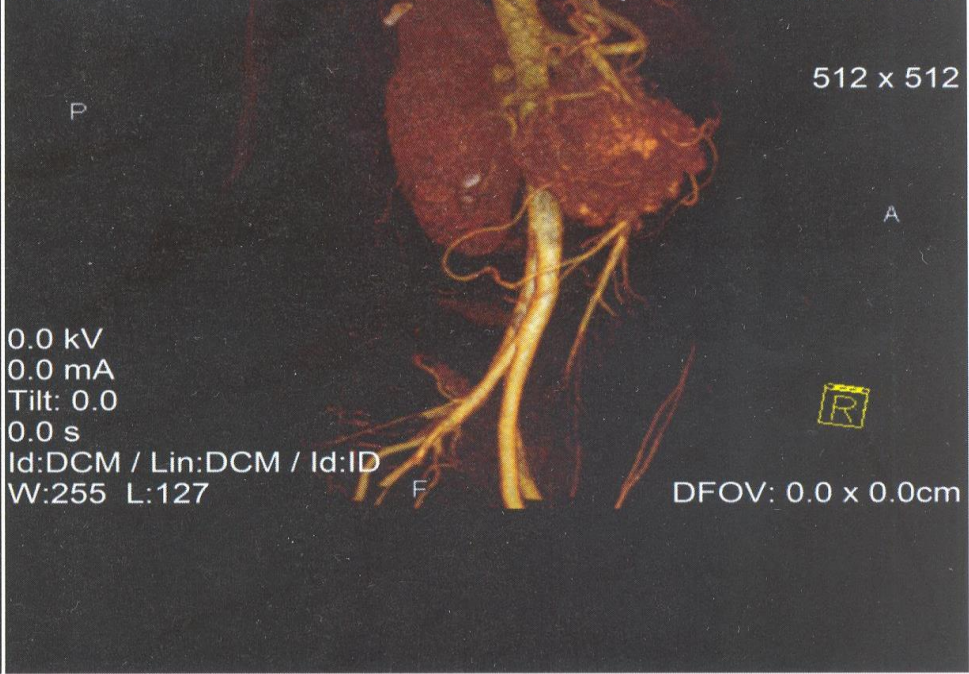
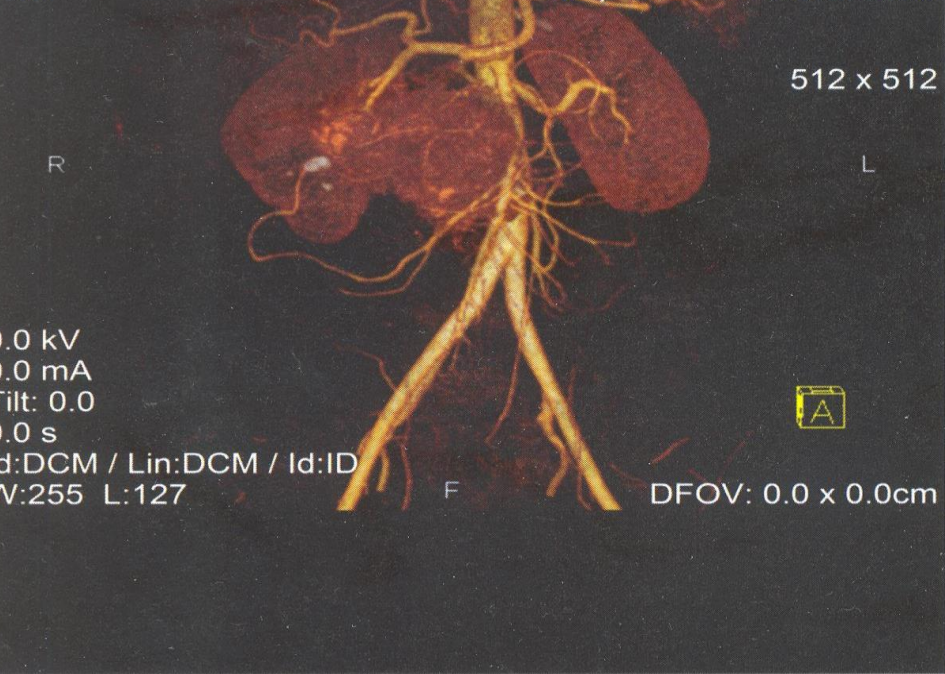
















“Start by doing what is necessary, then what is possible, and suddenly you are doing the impossible.”

— St. Francis of Assisi

**Thank You!!**

Questions?

