F. COLLAMATI – 04.07.17
INCONTRO CON I REFEREE INFN – CHIR2

FIRST EX-VIVO VALIDATION OF β- RGS IN CLINICAL USE CASES

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TECHNIQUE VALIDATION BY MEANS OF EX–VIVO TESTS

▸ While waiting for probe **certification**, only ex-vivo tests available

▸ Yet a **very important benchmark**! Allows to **check**:

  ✓ Feasibility of the whole **procedure**

    ▸ Injection - time lapse - surgery - probe

  ✓ PET with ^{68}Ga-DOTATOC as a predictor of ^{90}Y-DOTATOC **uptake**

    ▸ to estimate the activity we expect in the surgery from pre-operative standard imaging

  ✓ Our ability to project the **performances** of the probe in the real application case

    ▸ starting from lab measurements + MC simulations

 ✓ **Radioprotection** issues

FIRST APPLICATION CASE: BRAIN TUMORS

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Vol=12ml
SUV=3.1g/ml
TNR=62

▸ **Glioma**:

  ▸ Is a very aggressive, malignant, recurrent and infiltrative tumor that would profit greatly of β⁻-RGS

  ▸ "Application case" in brain tumors

▸ **Meningioma**:

  ▸ Is a (mostly) benign tumor, (mostly) easy to identify and remove completely, low recurrence rate

  ▸ Would not profit much of β⁻-RGS, but it is a very good "use-case" to assess the technique's applicability in brain tumors:

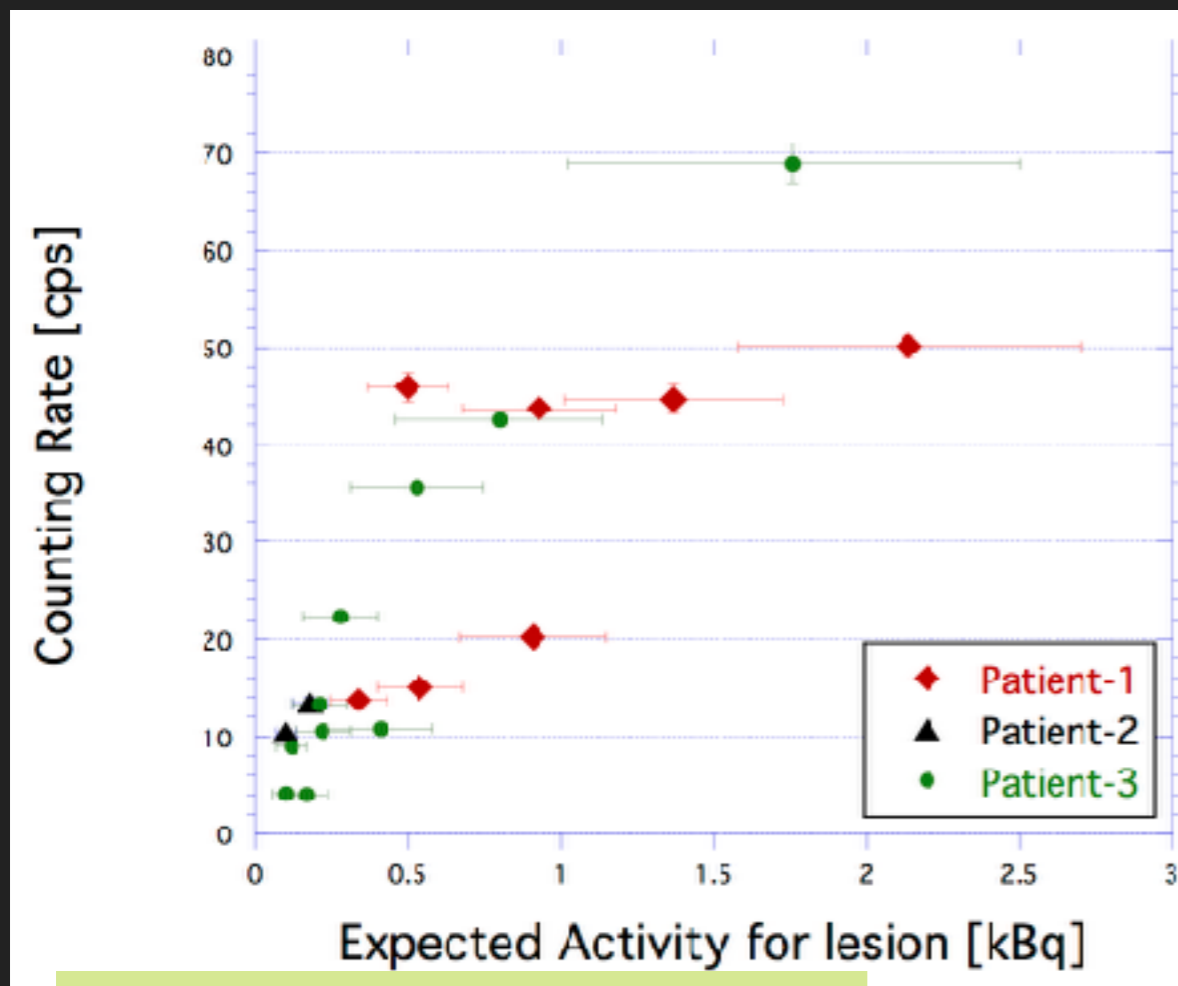   ▸ It shows documented high uptake for DOTATOC, the radio tracer we would like to use!
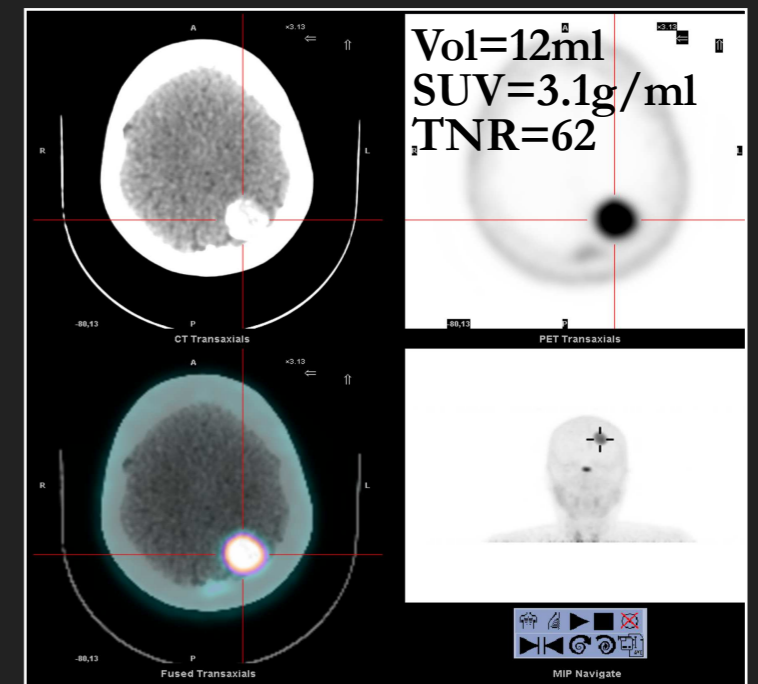
EX–VIVO TESTS ON MENINGIOMA SAMPLES

▸ Collaboration protocol with IEO and Besta Institute (Milano)

    ▸ We enrolled **4 patients** affected by meningioma with demonstrated uptake for DOTATOC (pre-op PET)

    ▸ Patients were **injected** ~24h before surgery with a PET-like dose of DOTATOC

    ▸ **Surgery** was performed **normally**, and we had the opportunity to test with the probe the counts on excised samples (tumor, healthy tissue nearby…)

    ▸ Our findings were compared with the ones from anatomo-pathologists
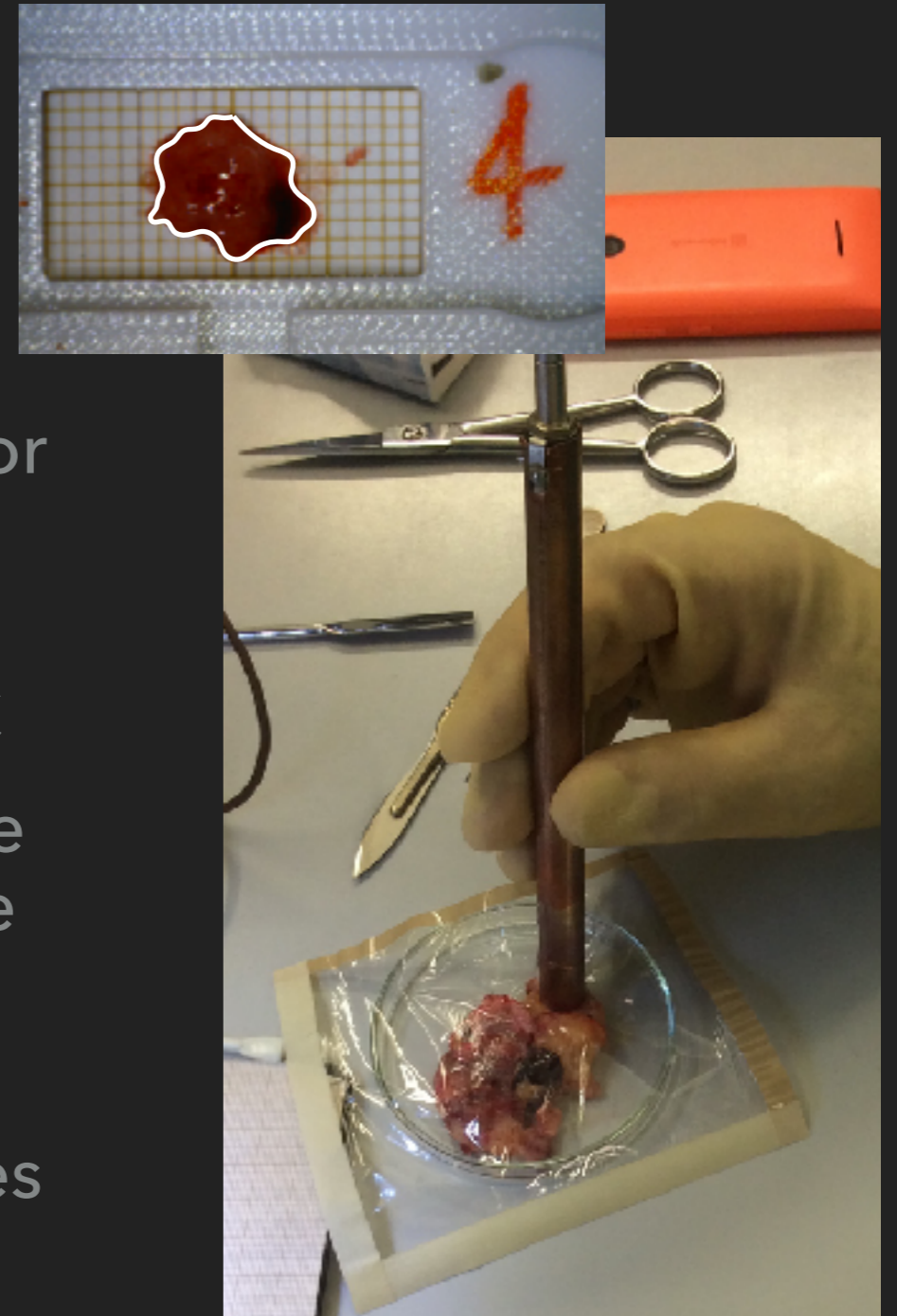
EX–VIVO TESTS ON MENINGIOMA SAMPLES

▸ Starting from pre-operative PET imaging, we are able to foresee the activity in the tumor at the time of surgery and to correlate it with probe counts:

E. Solfaroli, R. Faccini et al, Physica Medica 32 (2016)

A. Russomando, M. Schiariti et al, submitted to J Nucl Med (2017)

Patient	V_T [ml]	$\overline{SUV}$ [g/ml]	SD(SUV) [g/ml]	TNR	A_{adm} [MBq]	W [kg]	A_{est} [kBq/ml]
1	18.3	4.3	1.1	26	167	104	5.4
2	11.9	3.1	0.9	62	111	77	3.4
3	21.5	2.8	1.2	92	93	65	3.0

➡ **All tumor samples were recognised as malignant**

➡ Correlation factor > 80%

   ➡ Ability to evaluate the minimal activity to be injected to reveal a residual within 1s

      ➡ **Room to lower the dose**

➡ Radiation exposure:

   ➡ **Personnel**: almost negligible

   ➡ **Patient**: ~22mSv (almost 2x standard PET)

SECOND APPLICATION CASE: NEURO-ENDOCRINE TUMORS (NET)

SECOND APPLICATION CASE: NEURO–ENDOCRINE TUMORS

▸ Neuro-endocrine tumors:

   ▸ Are **rare**:
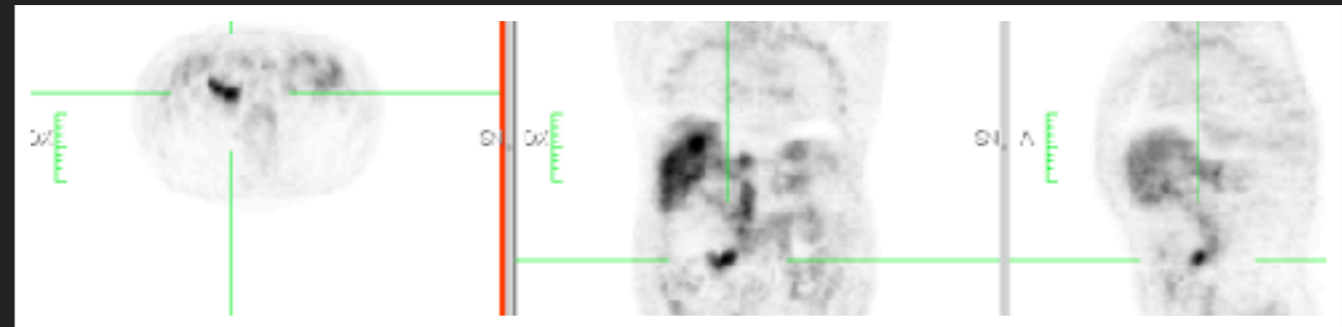
      ▸ Low incidence (~8/100k) but high prevalence (35/100k) due to long survival

   ▸ Can have several localisations:

      ▸ Pancreas, liver, intestine, lung…

   ▸ Due to slow growing are often **discovered late** and when already spread

   ▸ They show good uptake for DOTATOC

RADIO-GUIDED SURGERY IN NEUROENDOCRINE TUMORS

▸ **Surgery** is the gold-standard treatment for NETs (even if metastasised)

  ▸ **Complete asportation** crucial for outcome ➜ RGS!

▸ Today, **γ-RGS** is used in NET, also for:

  ✓ Lymph node discrimination

  ✓ Hidden lesions identification

  ✓ Recurrent operations

  ✓ Infiltrations identification

RADIO-GUIDED SURGERY IN NEUROENDOCRINE TUMORS

▸ Common characteristics of today NET **γ-RGS**:

   ▸ Detector:

      ▸ Commercial gamma probe

   ▸ Radio pharmaceutical:

      ▸ Somatostatine analogues marked with In, I, Tc

      ▸ One recent attempt to use ^{68}Ga (β^+ decay)

   ▸ Approach:

      ▸ Search of the known lesions + "systematic scan" to look for possible unknown ones

   ▸ Results and limitations:

      ▸ Very good capability of **discovering hidden lesions** (i.e. in stomach and small bowel)

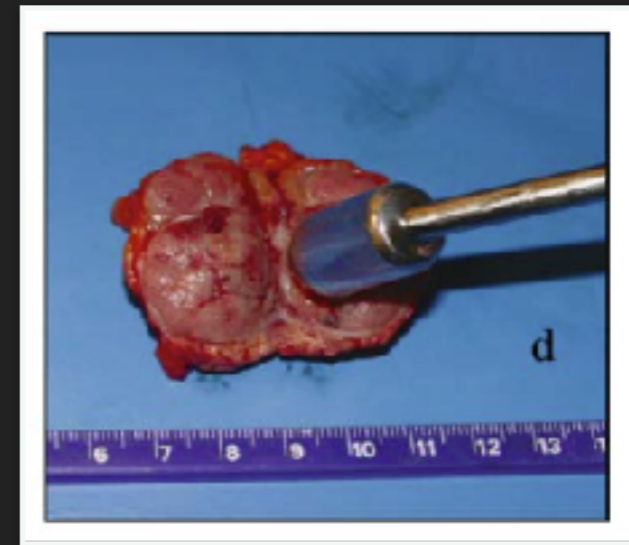   ▸ Reduced utility in areas with greater physiological **background**:

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    ‣ Very good capability of **discovering hidden lesions** (i.e. in stomach and small bowel)

    ‣ Reduced utility in areas with greater physiological **background**:

physiological DOTANOC uptake

We found that lesions in the pancreas and peripancreatic lymph nodes were difficult to detect with the probe as a result of high relative background counts. In such cases,

helpful in confirming the location of a single lesion with a TBR of 43.6 (WHO grade 1 insulinoma). We did not find that the probe was helpful for detecting liver lesions: in 3 patients with liver metastases found on ^{68}Ga-DOTATATE PET/CT, the background count for the liver was high, with an average of 499.7 ± 89.0, and target lesions therefore could not be distinguished. Resection was guided by ultrasound.

EX–VIVO TESTS ON NET SAMPLES

Trial in progress

▸ Collaboration protocol with IEO (Milano)

  ▸ We are enrolling 5 **patients** affected by Neuro Endocrine Tumor with demonstrated uptake for DOTATOC (pre-op PET)

  ▸ Patients are **injected** ~24h before surgery with a PET-like dose of DOTATOC

  ▸ **Surgery** is performed **normally**, and we have the opportunity to test with the probe the counts on excised samples (tumor, healthy tissue nearby…)

  ▸ Our findings are compared with the ones from anatomo-pathologists
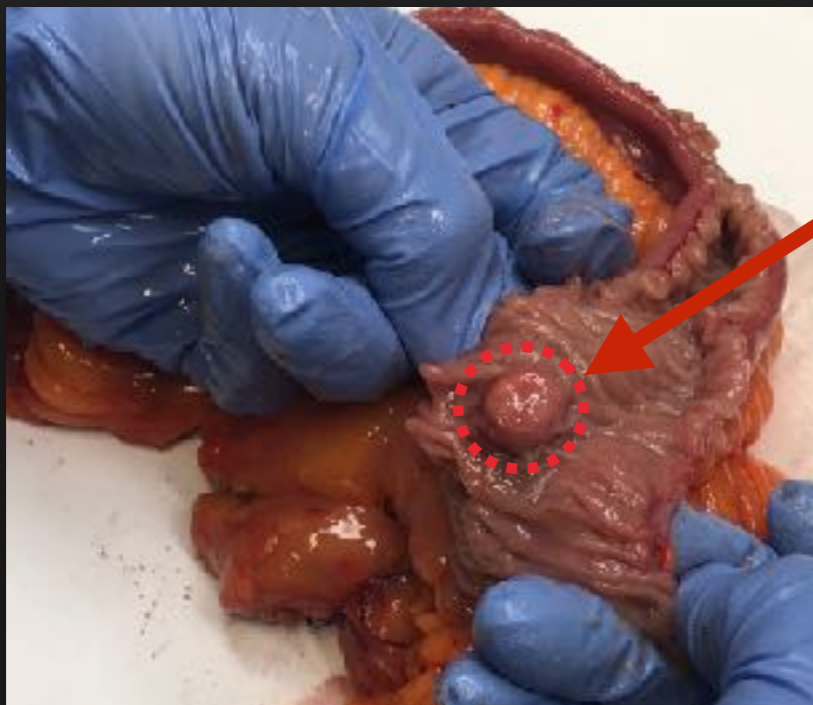
EX-VIVO TESTS ON NET SAMPLES

Trial in progress

▸ With respect to the meningioma ex-vivo tests, we are now in a more realistic situation

   ▸ In these kind of surgery, a ~50cm segment of ileum is usually excised

      ▸ We are thus in a ~ **signal + background** configuration!

EX–VIVO TESTS ON NET SAMPLES

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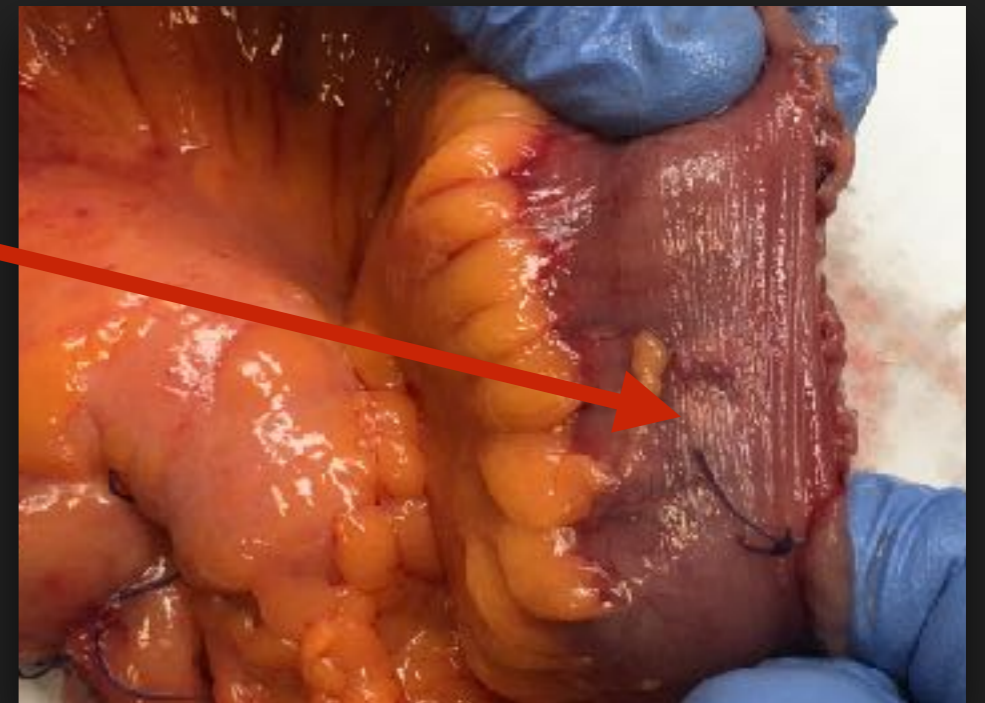   ▸ We are thus in a ~ **signal + background** configuration!

Main lesion

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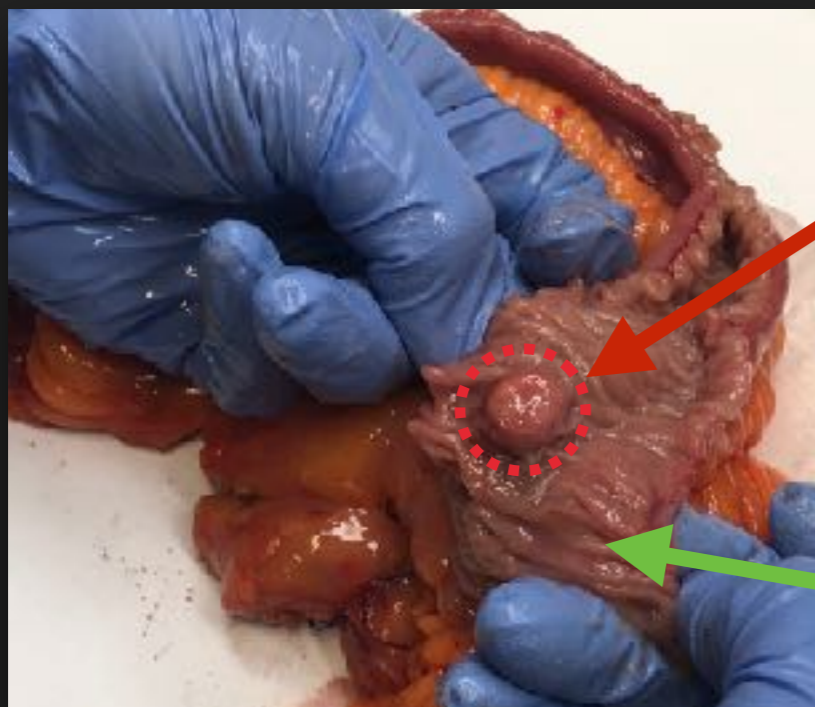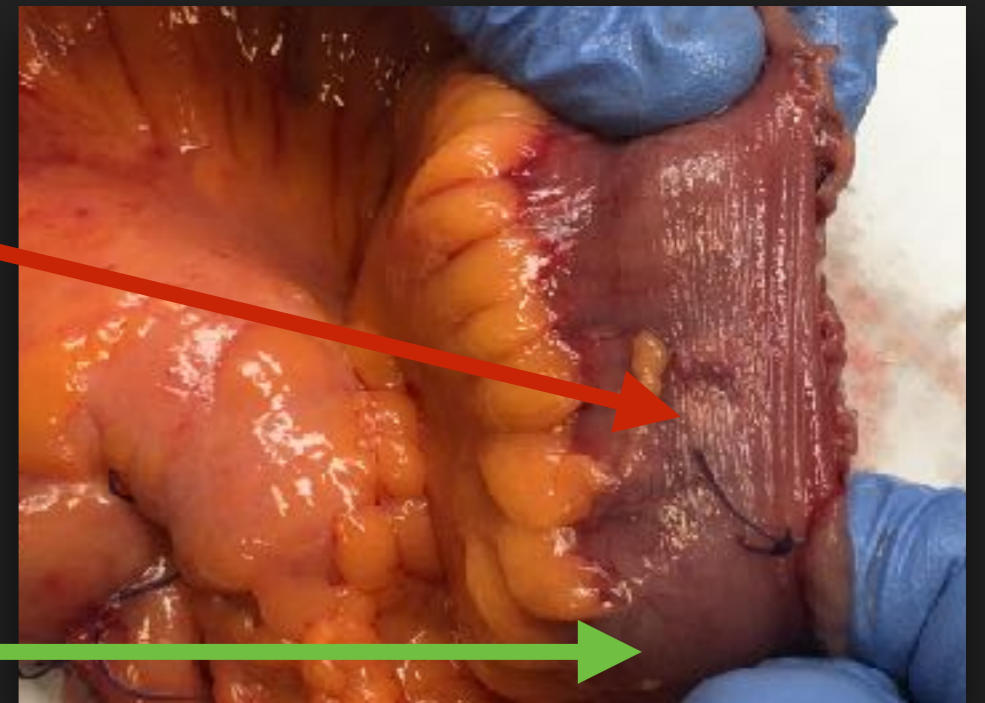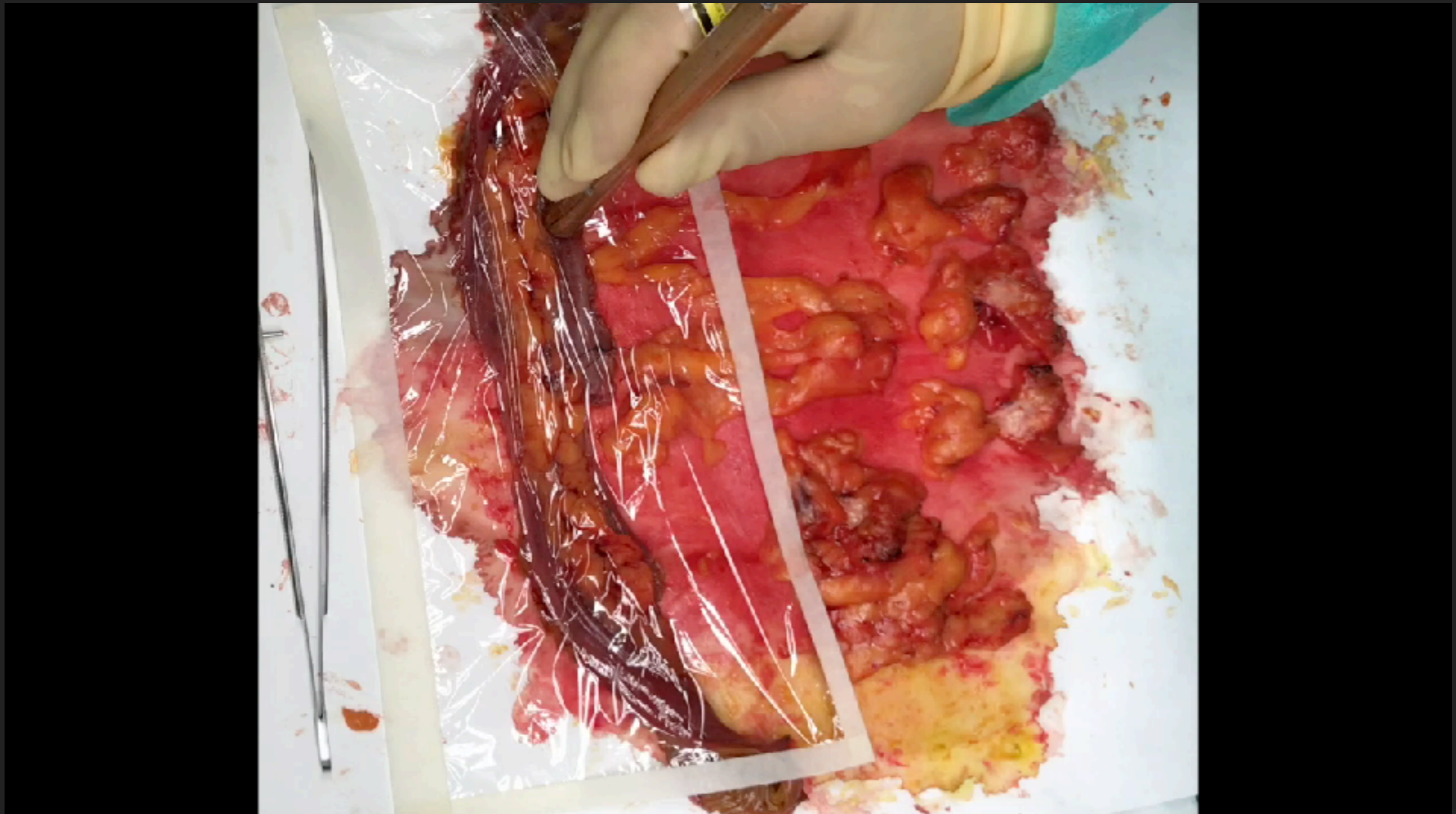   ▸ We are thus in a ~ **signal + background** configuration!

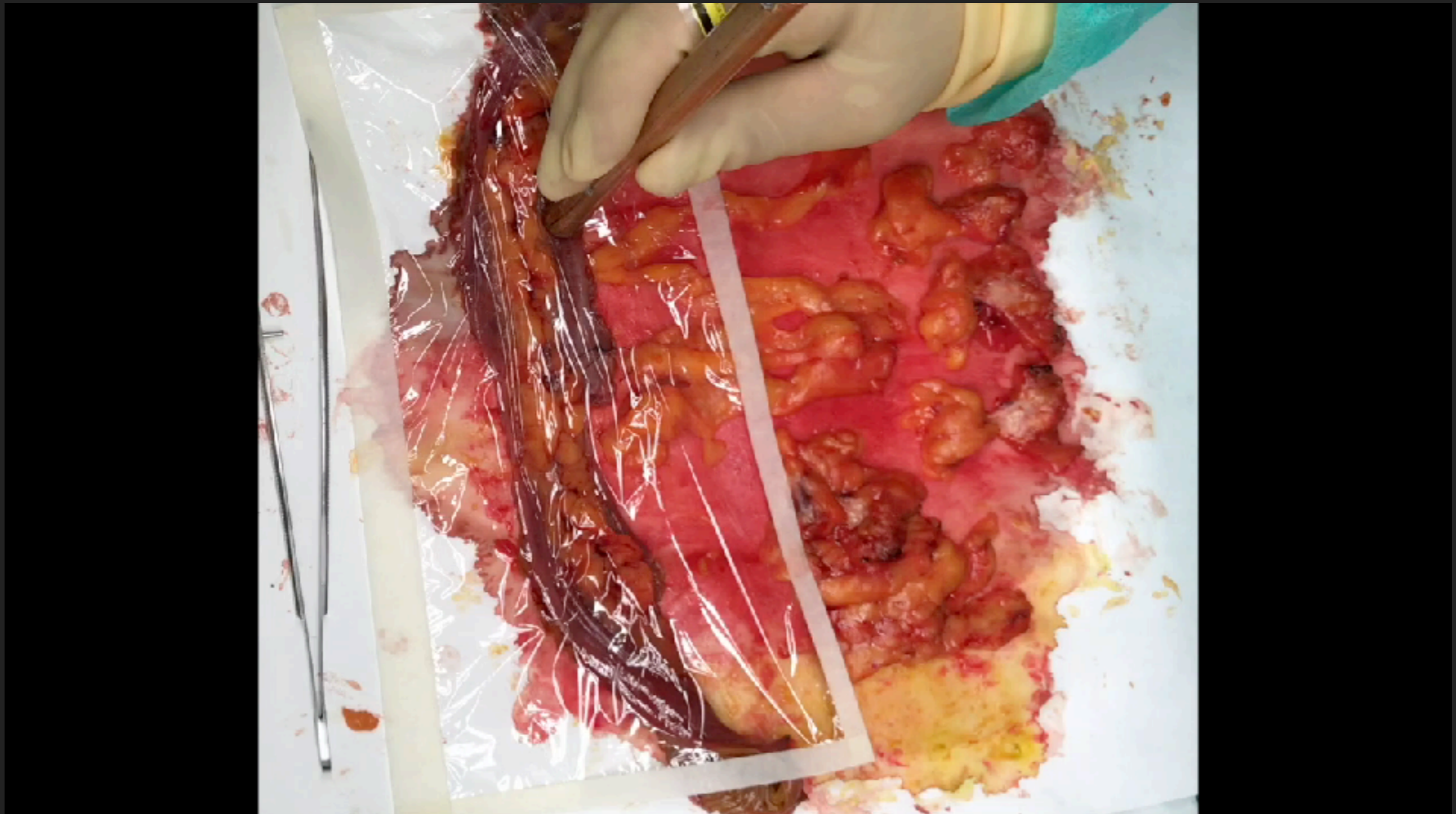**Main lesion**

Healthy intestine

EX–VIVO TESTS ON NET SAMPLES

EX-VIVO TESTS ON NET SAMPLES

EX–VIVO TESTS ON NET SAMPLES

Trial in progress

▸ Goals of the test:

- ▸ Ability to **identify** known lesions, and look for unknown (e.g. lymph nodes)

- ▸ Extract "cuf-off" values (cps) for possible RGS application

- ▸ Assess the behaviour of the probe in a **~S+B** configuration

    - ▸ Counts on lesion

    - ▸ Counts on background

        - ▸ D.I.Y. **real application case**: hiding a part of tumor under healthy tissue

background counts on healthy intestine:

9,96 ± 0,77 cps
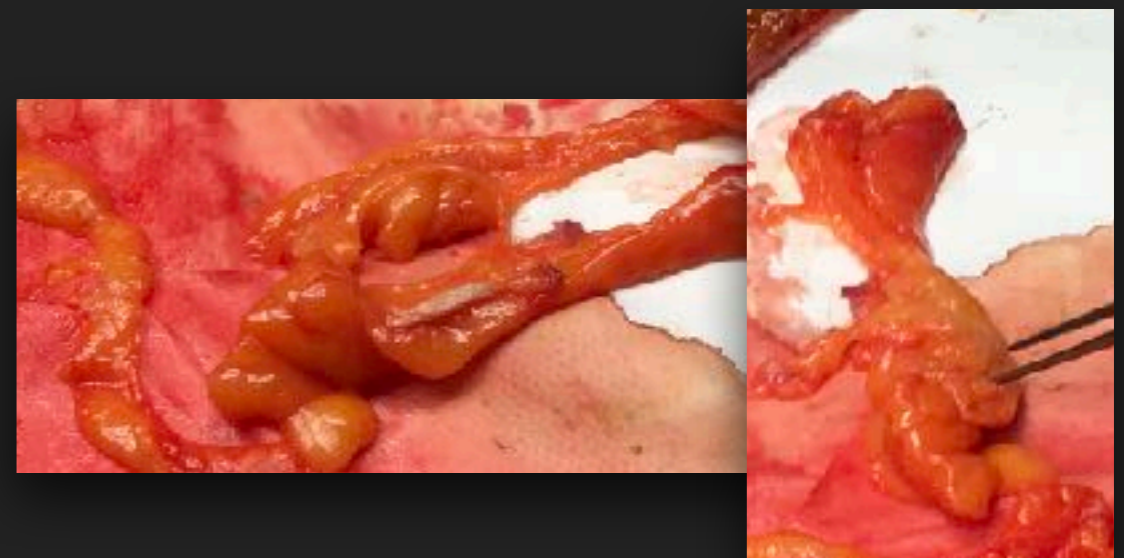
SUMMARY

▸ So far, we identified **two** possible **application cases** in which ^{90}Y-DOTATOC RGS could give a remarkable contribution

  ▸ **Gliomas** and **Neuro-Endocrine Tumors**

▸ First ex-vivo tests on **Meningioma** were fundamental to assess the **feasibility** of the whole procedure, the **radio protection** impact and the **probe performances**

  ▸ Their success also contributed to **trigger enthusiasm** in medical staff that led to the starting of the second collaboration protocol

▸ Ex-vivo tests on NETs have already started and are planned to last for the next months

  ▸ They will be fundamental to test the technique in an almost realistic scenario

▸ Next step:

  ▸ **In-vivo** tests: ongoing contract with Nucleomed for probe certification

  ▸ Collaboration with Sant'Orsola hospital (BO) to use ^{68}Ga-PSmA in **prostatic cancer** (laparoscopic approach)

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