Surgery of the thyroid gland

- How to minimize surgical complication

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Aim of surgical management of thyroid disease (thyroid cancer, Graves' disease, etc)

- Complete removal of tumor
- Minimizing recurrence
- Prevention of complications : lifelong disability
  - recurrent laryngeal nerve injury
  - hypoparathyroidism

- excellent survival rate of most differentiated thyroid cancer
- prevention of complication

  : as important as complete removal of the tumor

Painful post-thyroidectomy complications to both surgeons and patients depending on the situation

1. Expanding hematoma by arterial bleeding
   - can lead to death of the patients by airway obstruction
2. Bilateral RLN injury
   - airway obstruction and dysphonia
3. Unilateral RLN injury
   - inconvenient
   - the most common thyroidectomy related malpractice lawsuit
   - even temporary paralysis can be very painful in professional voice user
4. External branch of superior laryngeal nerver injury
   - easy voice fatigue, decreased pitch, inability to project voice

Surgery of thyroid gland

- Recent advances in intraoperative parathyroid gland mapping and localization with Near-Infrared Autofluorescence (NIR AF)
- Recent advances in IONM

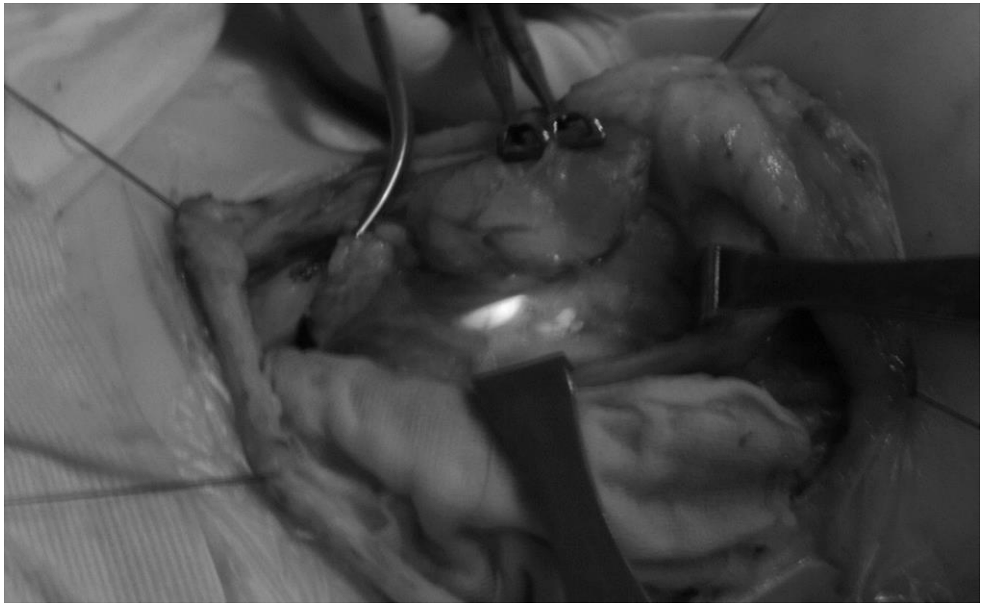
  - endotracheal EMG tube

  - Non-endotracheal EMG tube

    ; needle electrode

    ; skin adhesive electrode

Parathyroid gland mapping and localization using autofluorescence



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9th IRSS, Oct. 26-27, Seoul, Korea

Post-thyroidecotmy hypoparathyroidism

- The most common complication of total thyroidectomy

  - temporary : ~ 46% / permanent : ~ 6.6%

- **Typical Sx and Sn**

  - perioral numbness, acral paresthesia (hand, foot)
  - muscle cramp
  - Trousseau sign of latent tetany (carpopedal spasm)
  - Chvostek's sign
  - laryngeal spasm
  - seizure
  - mental change - anxiety, confusion
  - QT Interval prologation
  - cardiac arrest

Long-term effects of postoperative hypoparathyroidism in benign thyroid disease

BJS

Original article

Mortality in patients with permanent hypoparathyroidism after total thyroidectomy

M. Almquist, K. Ivarsson, E. Nordenström, A. Bergenfelz

First published: 17 April 2018 | https://doi.org/10.1002/bjs.10843 | Cited by: 6

- The risk of death in benign thyroid disease (hazard ratio 2.09)
  - a twofold higher among patients with permanent hypoparathyroidism after TT than patients without permanent hypoparathyroidism

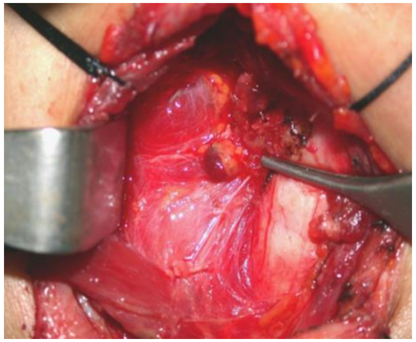
- The reason : unclear
  - the use of large, supraphysiological doses of active vitamin D?
  - lower PTH levels?

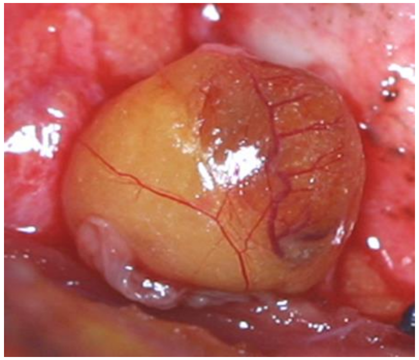
Skills of intraoperative parathyroid identification
- basic requirement for surgeons to be equipped

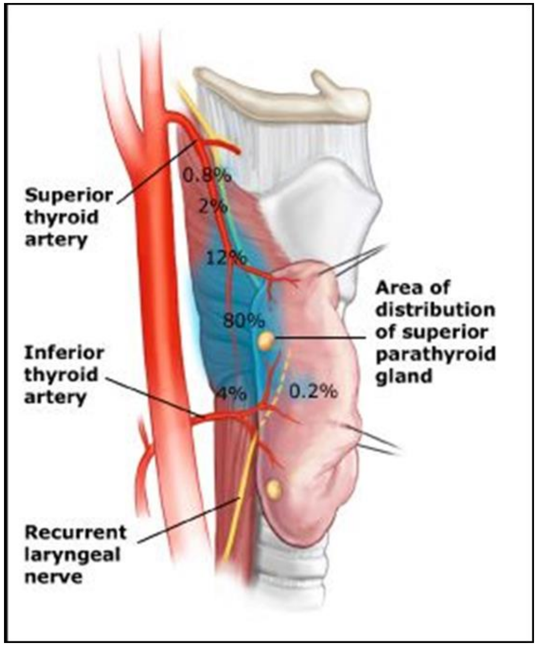
- Less experienced surgeons in thyroidectomy

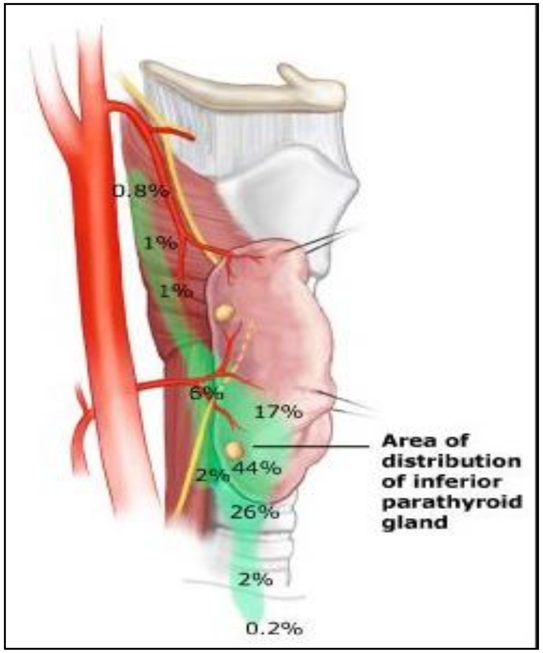
  - difficult to localize the parathyroid gland

  : due to small size, inconspicuous coloring, variable location of PG









Intraoperative parathyroid identification and preservation
- the must procedure to learn

- Highly experienced surgeons
  - even the meticulous dissection can also result in inadvertent parathyroid excision during thyroidectomy in 9.1–15%

Lin et al, Laryngoscope, 2002
Lee et al, Layngoscope, 1999
Sasson et al, Arch Otolaryngol HNS

No reliable intraoperative method to identify the normal parathyroid gland during thyroid surgery

- Surgeon's main tool has been an intuitive visual inspection that could be gained through extensive experiences

  - subjective, often inconclusive

Near-infrared techniques for intraoperative real-time localization of parathyroid gland using auto-fluorescence

- 2 types of commercialized equipment – approved by FDA in 2018

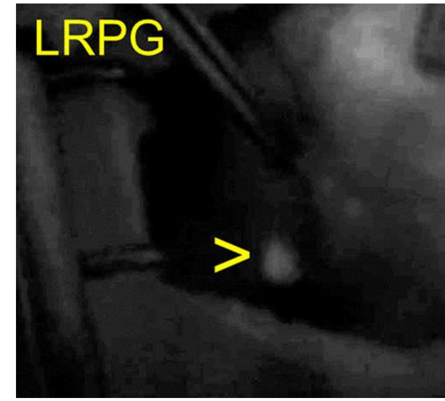
  - Fluobeam 800® as NIR AF imaging system

  - PTeye as NIR AF fiber probe-based system (spectroscopy)

Fluobeam

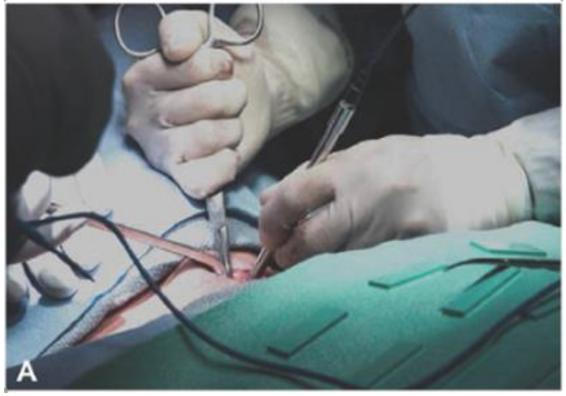
PTeye

Fluobeam - commercialized NIR AF imaging system



- Can visualize parathyroid gland and surrounding tissues
- Needs both operating light and fluorescent room light turned off to get images
  - as the intensity of the AF from parathyroid gland is considerably weak
- To use the Fluobeam, it is necessary to maintain the operation room dark
  - can interrupt the work flow
  - a drawback

PTeye - commercialized NIR AF fiber probe based system



(Thomas G. Surgery, 2019)

- Pteye probe
  - needs tissue contact and conducts point-by-point measurements
  - provides real-time quantitative information
  - works even in the presence of operating light, room light and head light

- Drawbacks
  - does not provide spatial information on the operation site
  - identifies only exposed parathyroid gland
    : can not identify non-exposed parathyroid gland

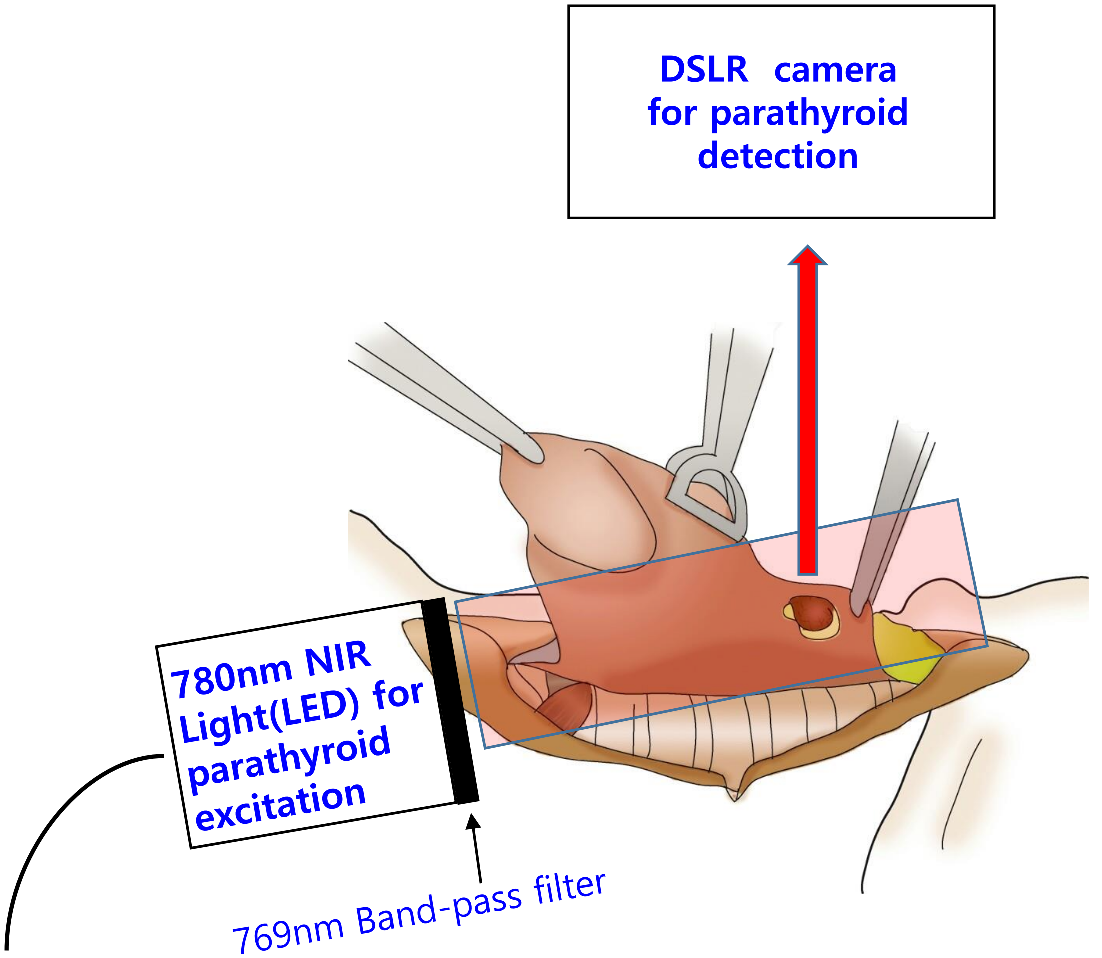
Development of Lab-built NIR AF imaging system and probe system by Kosin Head and Neck Team

- usefulness of our imaging and probe techniques in parathyroid gland mapping and localization

- Near Infrared Autofluorescence (NIR AF) Imaging system using DSLR camera

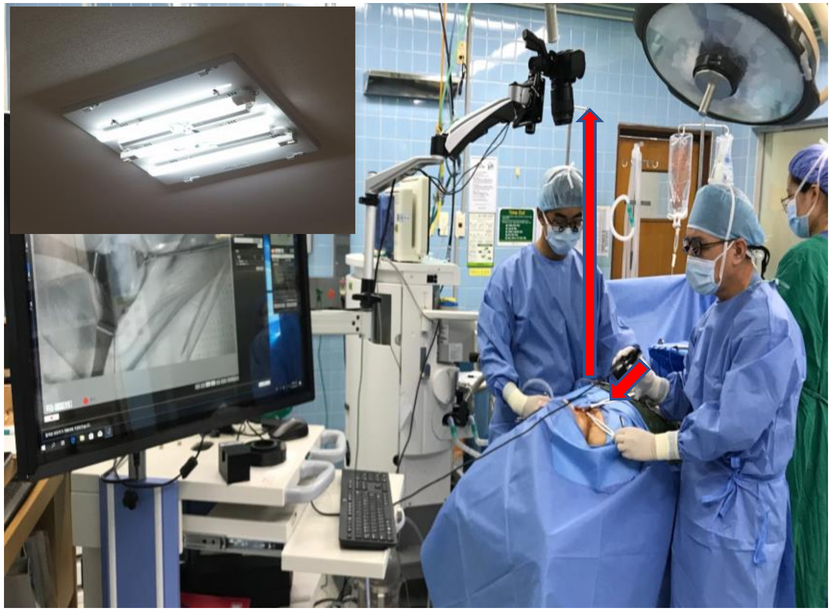
NIR AF probe

Schema of NIR AF imaging system using DSLR camera



Our NIR AF imaging system

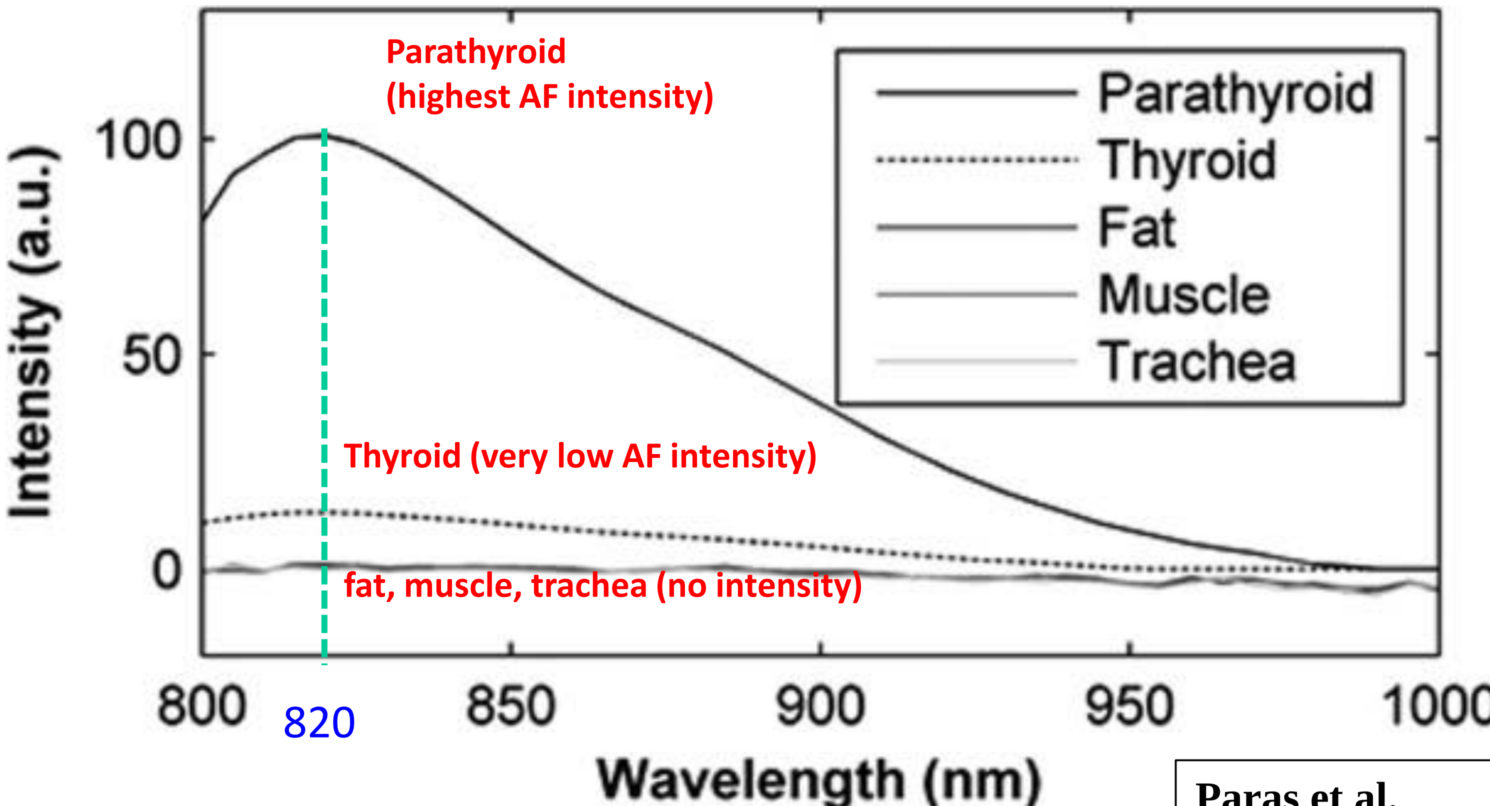
- uses AF : no need to use any exogenous contrast dye
- works in the presence of fluorescence light turned on (operating light turned off)
  : enables us to maintain the work flow



- Commercialized Fluobeam
- needs both operating light and fluorescent light turned off

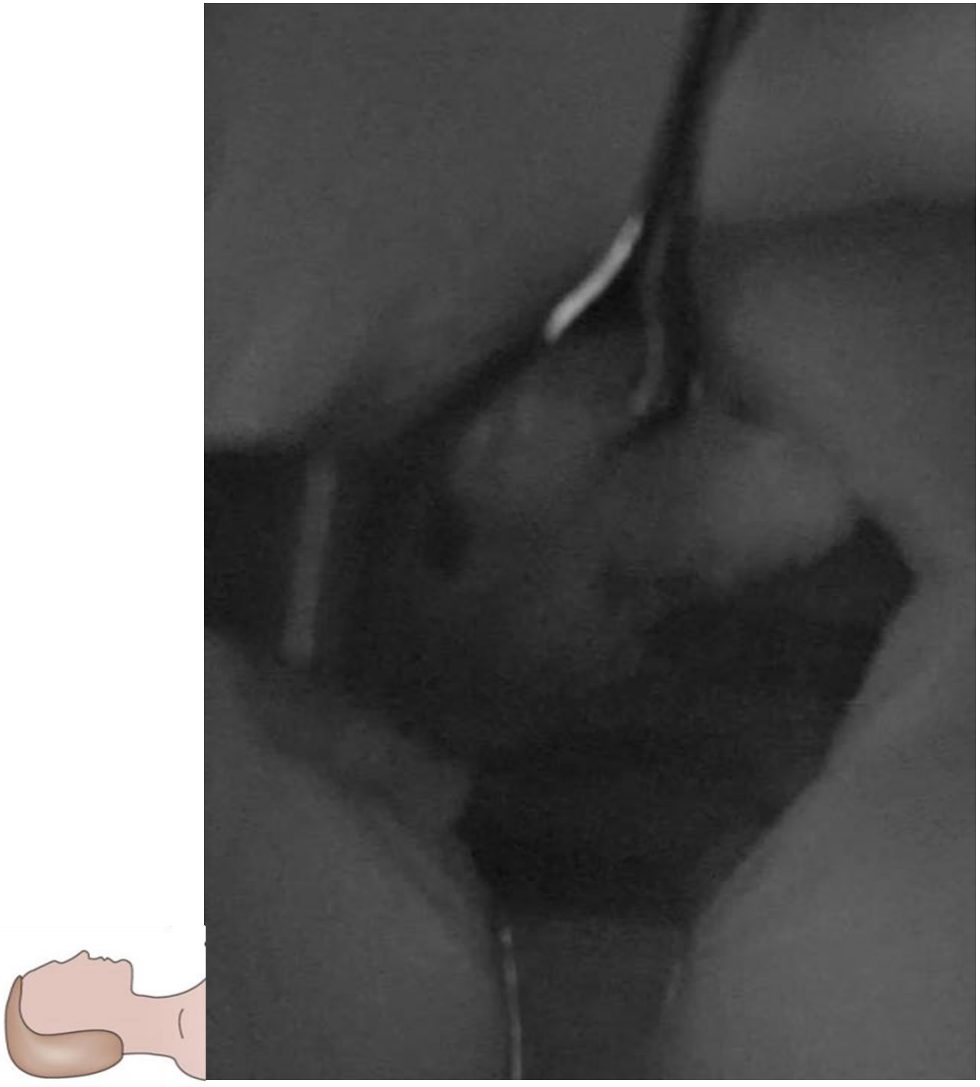
Comparison of NIR auto-fluorescence intensity in neck organs (Paras et al, 2011 of Vanderbilt group)

- **NIR AF** can discriminate parathyroid gland from surrounding tissues



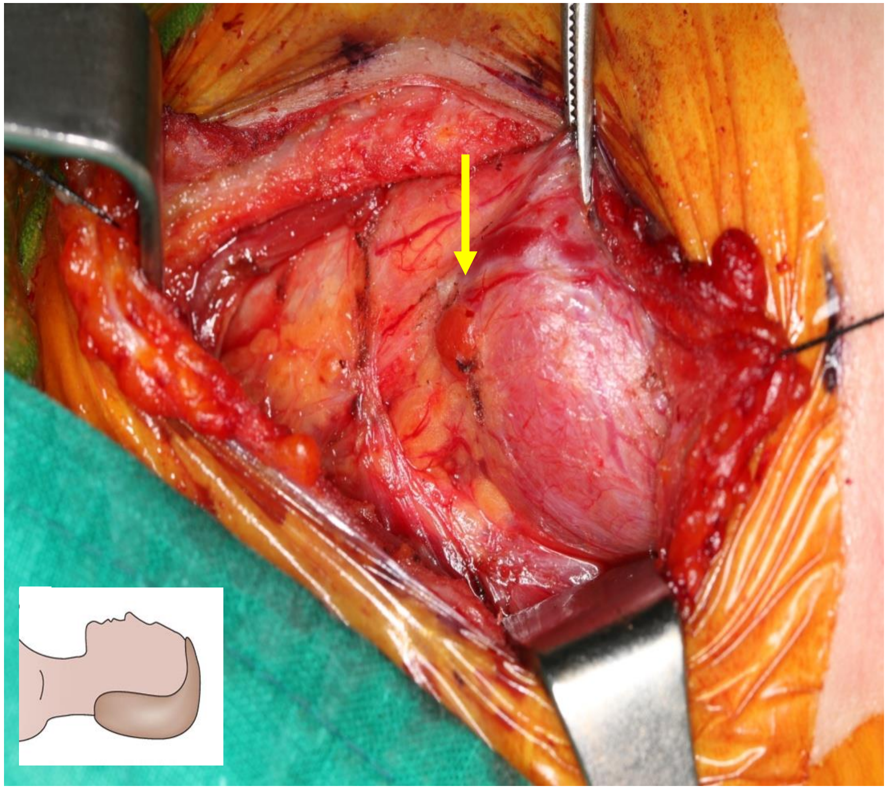
Paras et al.
J Biomedical Optics, 2011

Ideal NIR AF image for parathyroid gland mapping

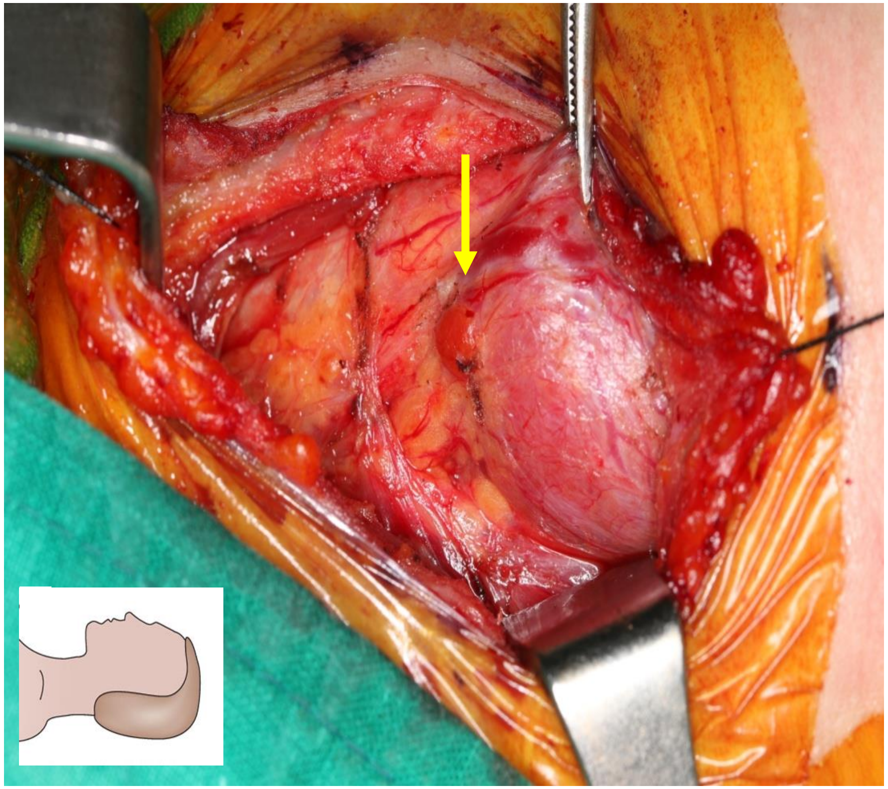


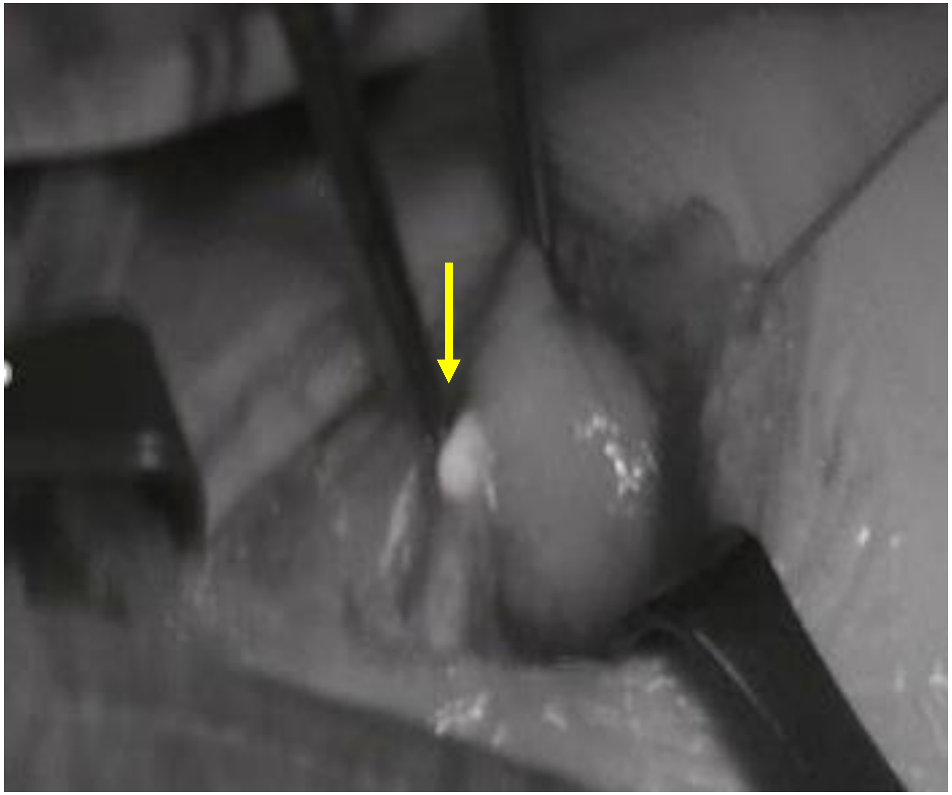
- parathyroid gland
  : the strongest fluorescence
  : secretory granule
- thyroid gland
  : weak fluorescence
- surrounding fat, LN, and muscle
  : no fluorescence

No confidence for parathyroid gland?
- get confidence with the use of NIR AF imaging



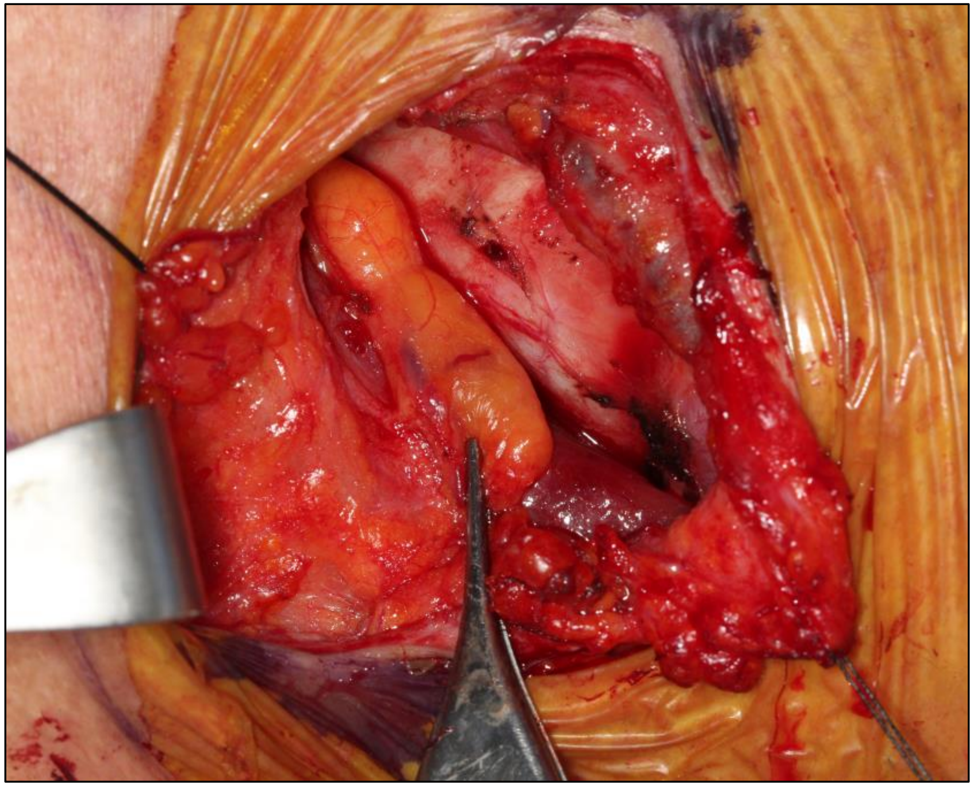
No confidence for parathyroid gland?
- get confidence with the use of NIR AF imaging





Is this a parathyroid gland?

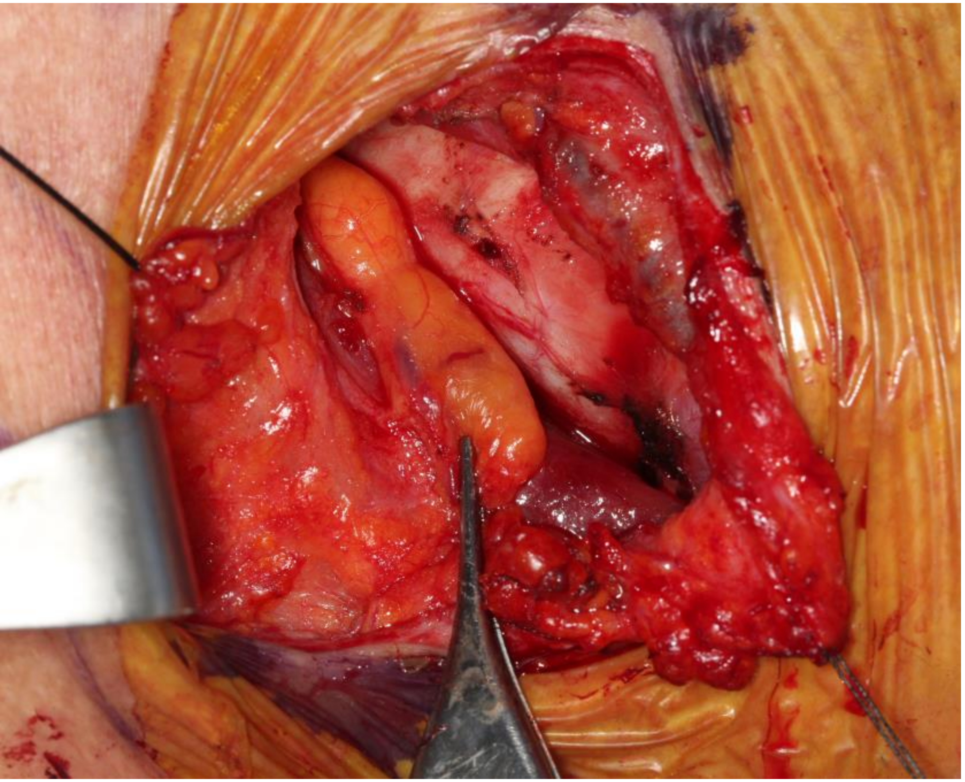
- equivocal by your naked eye

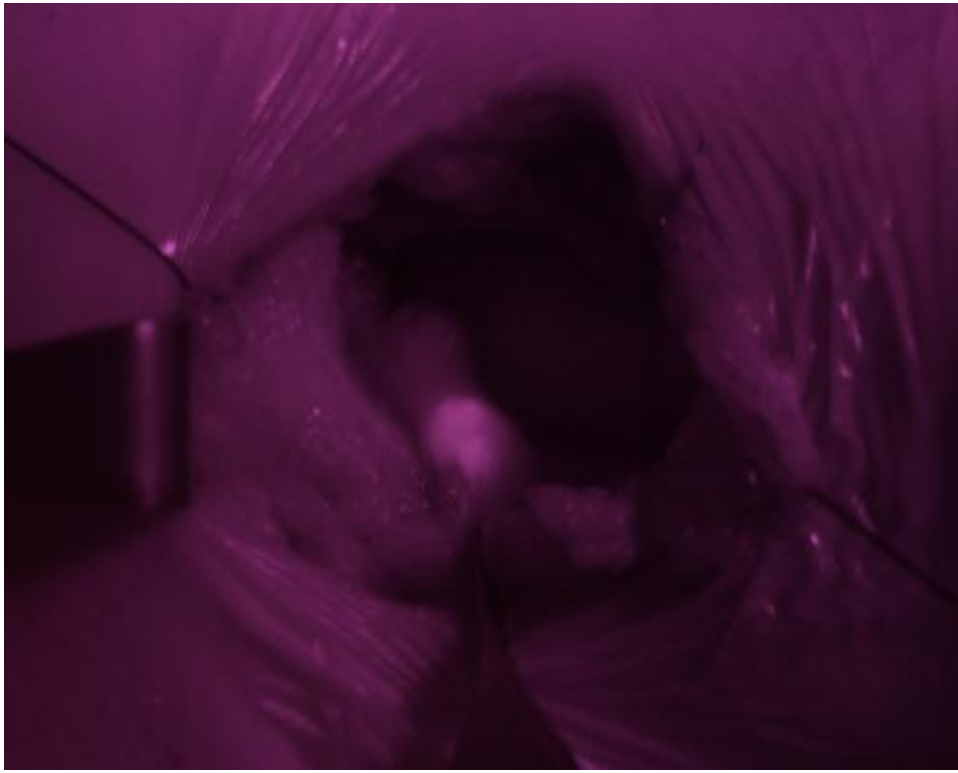


Is it a parathyroid gland?

- equivocal by naked eye

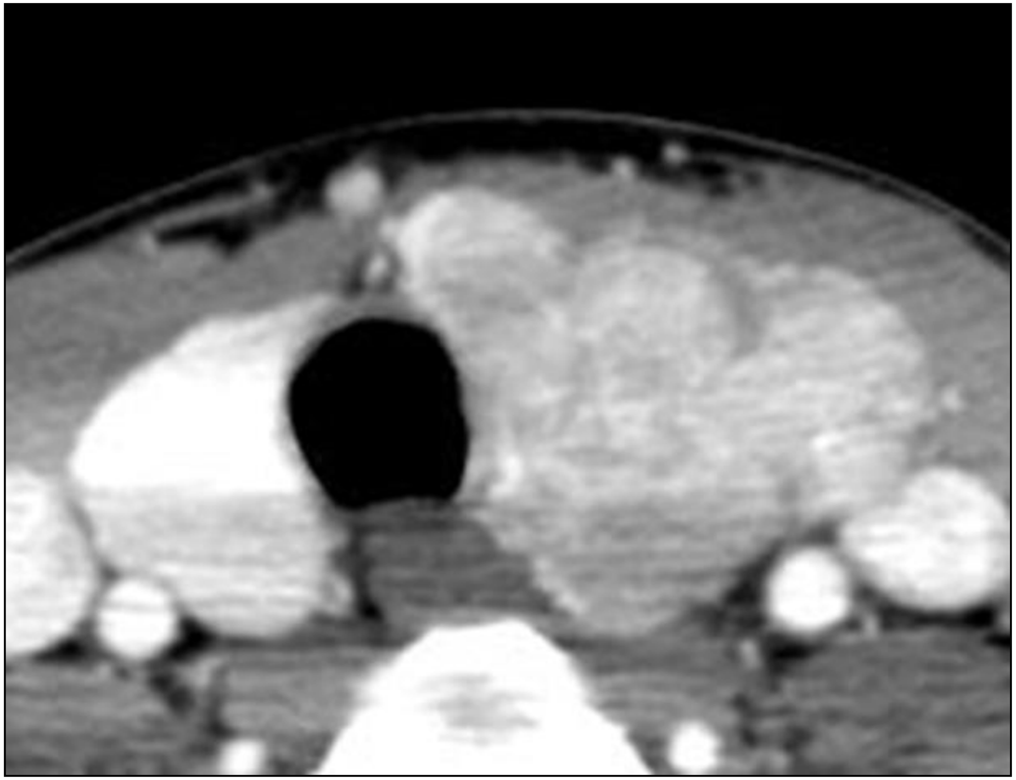
- unequivocal by NIR AF imaging

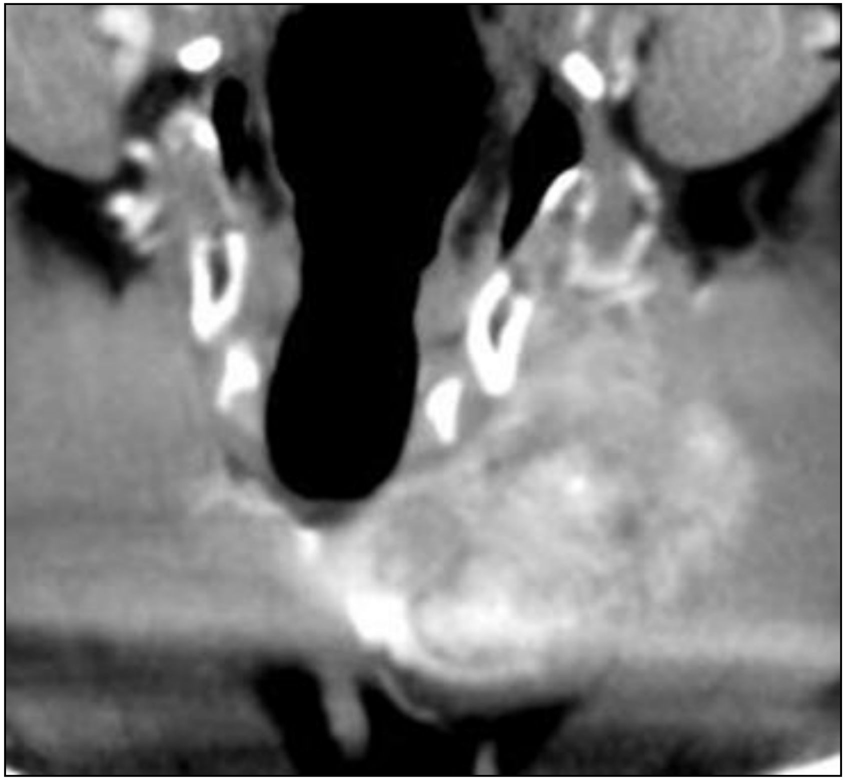


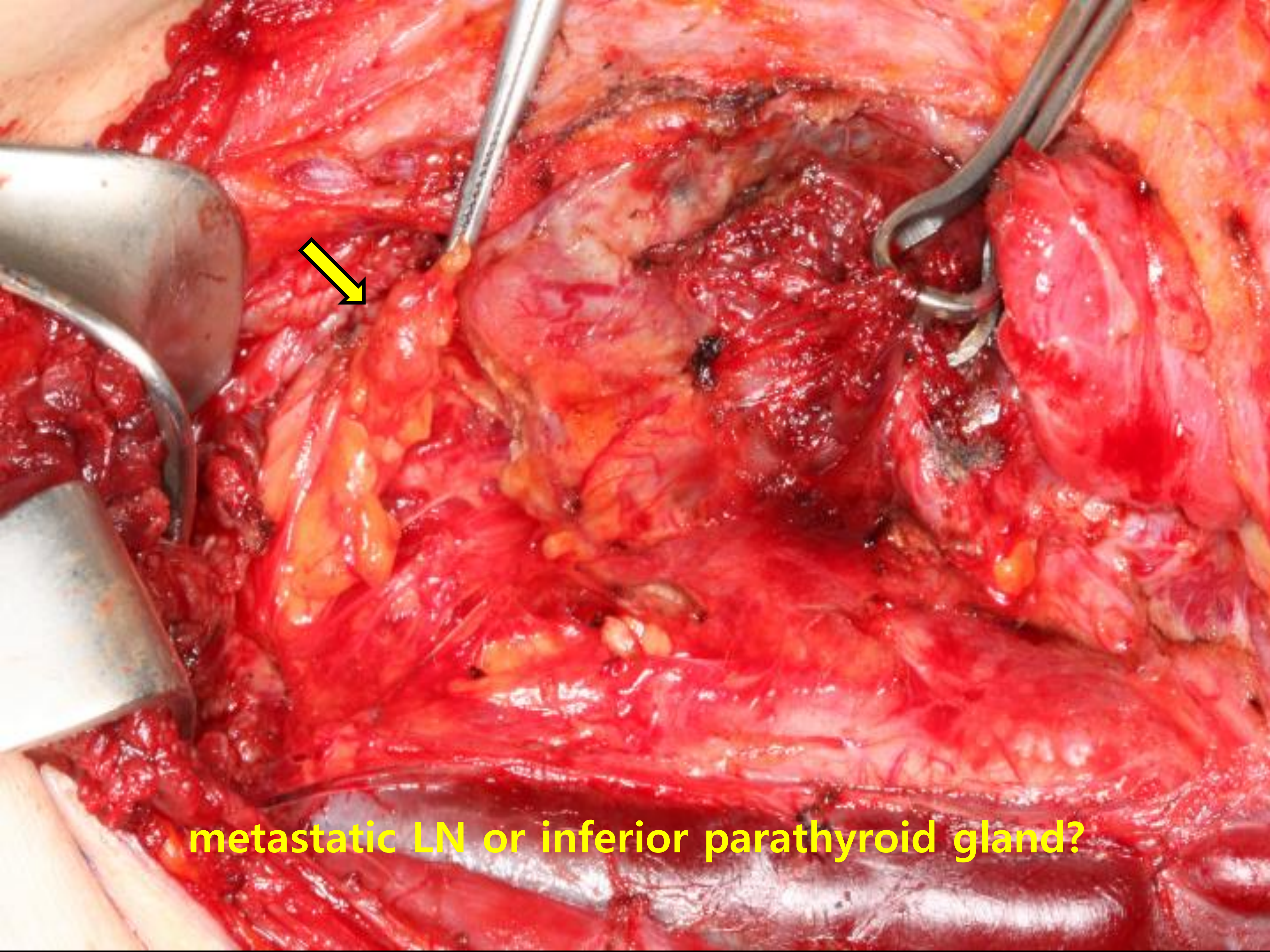


Left advanced PTC (4.5 cm) with left neck metastasis

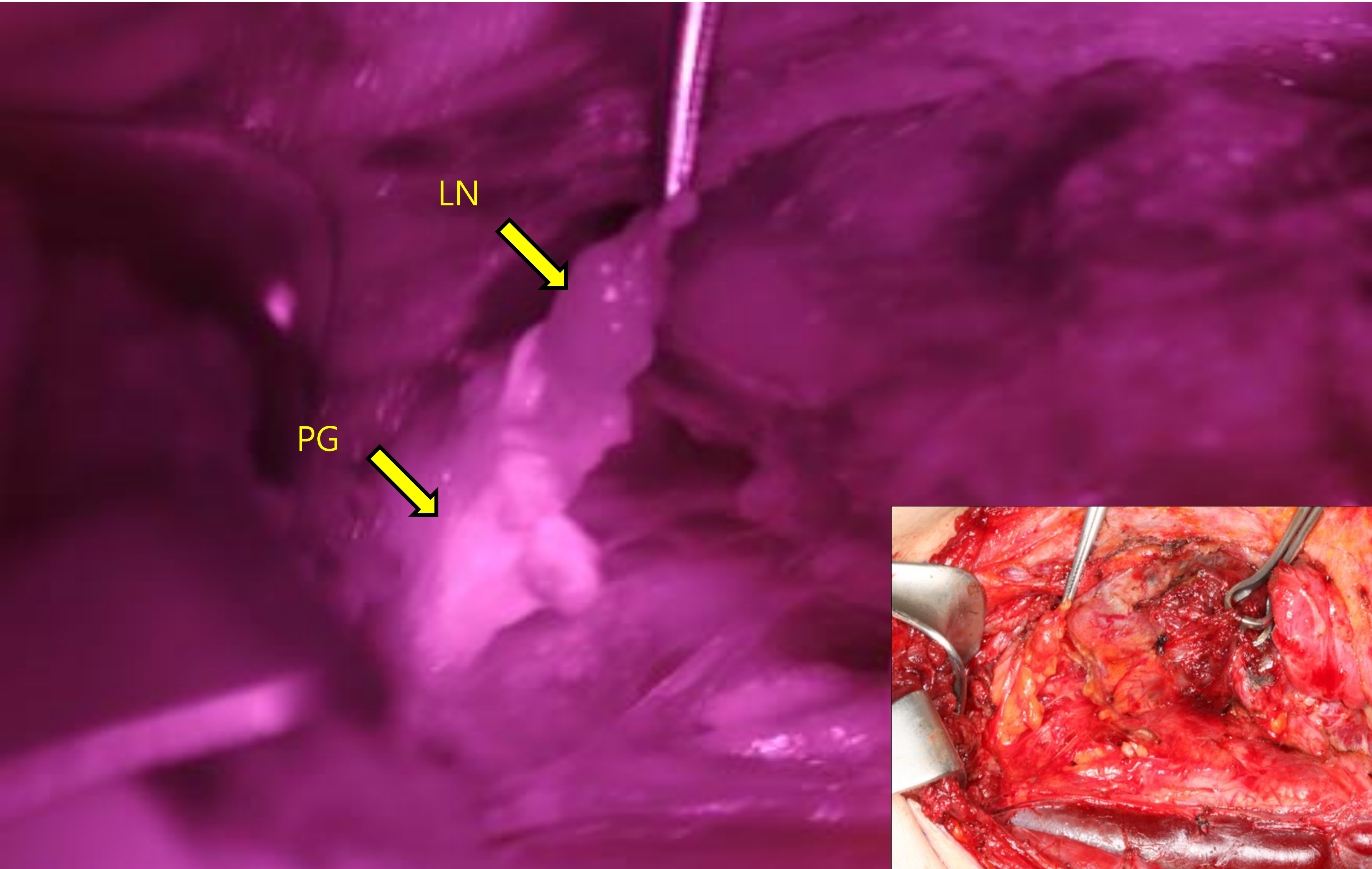
(cT3N1b), 오0우 (M/33)





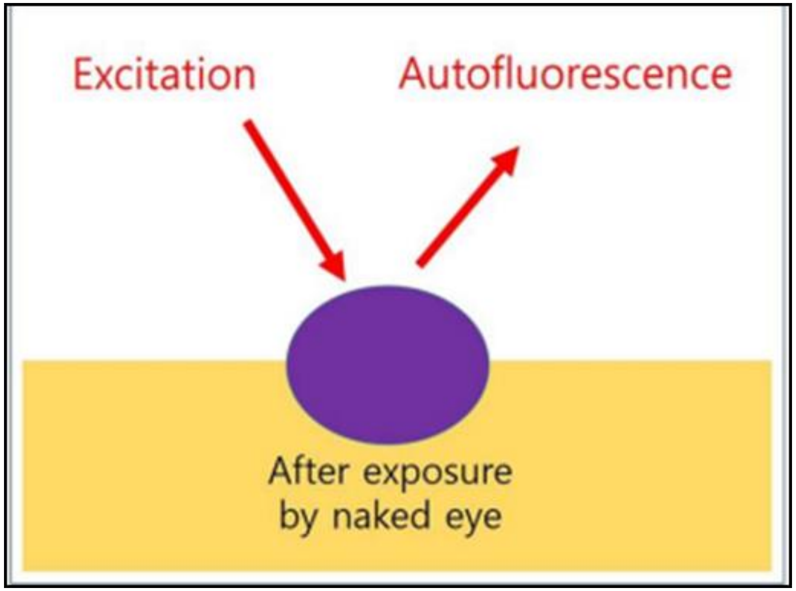

metastatic LN or inferior parathyroid gland?

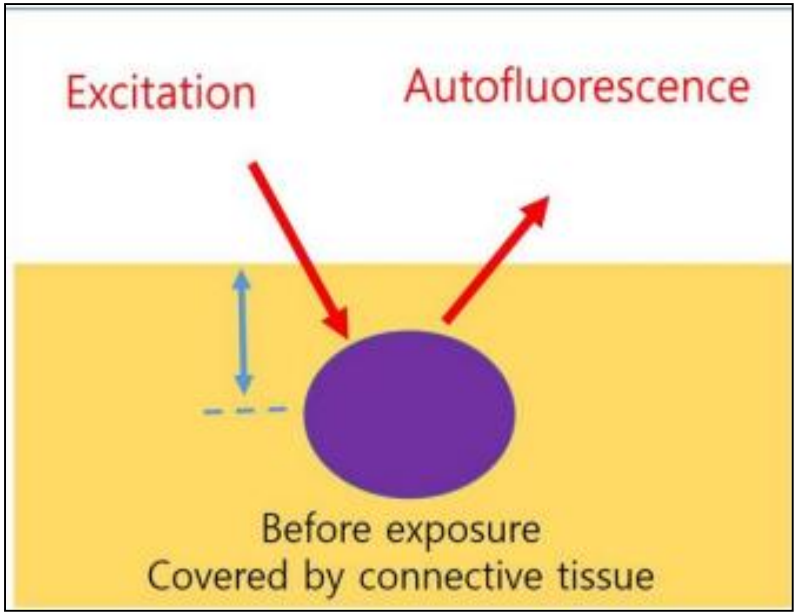
Discrimination of the parathyroid from the metastatic LN by NIR AF imaging system



Endpoint of intraoperative parathyroid gland imaging

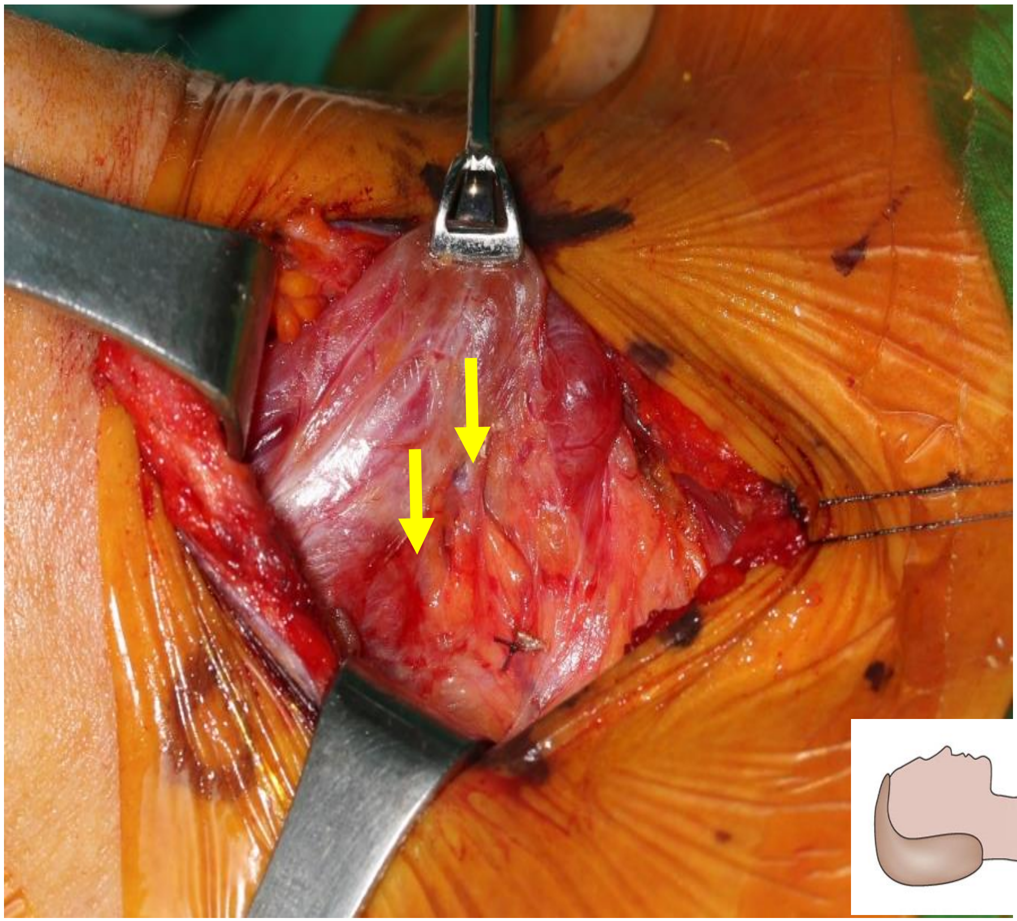
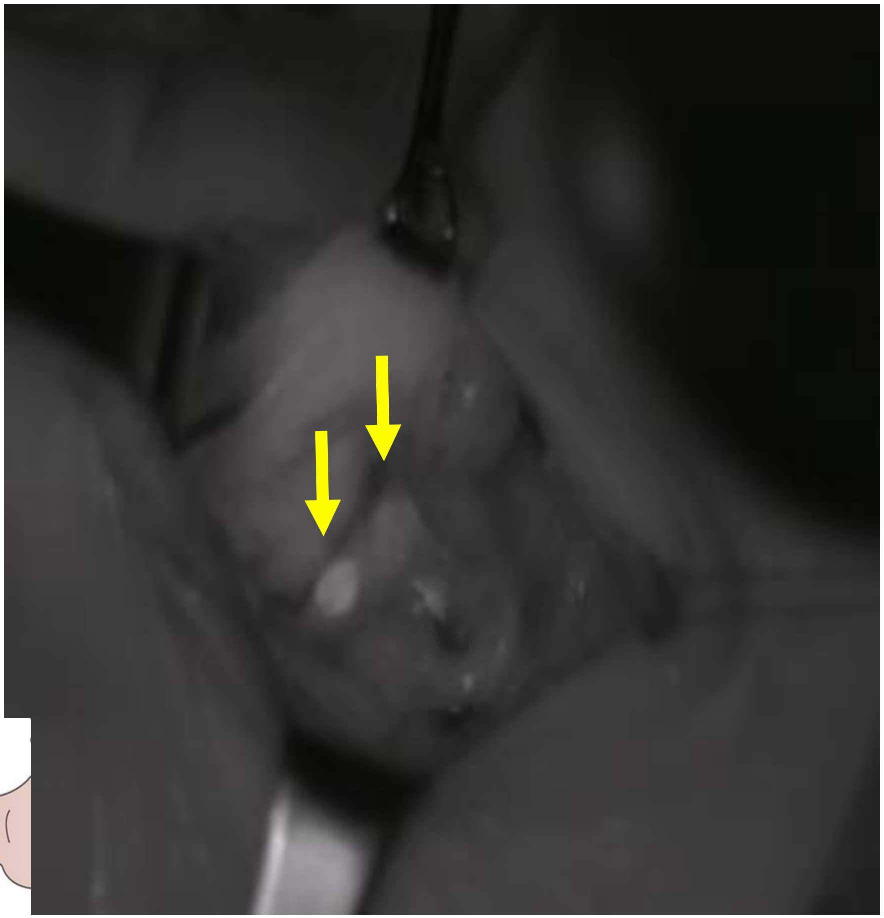
- not only to detect the exposed gland but also to preserve its function
- Just identifying the exposed parathyroid gland with NIR AF
  ; can be meaningful in most surgical situation
- Early localization of the parathyroid gland buried by fat tissues
  - more important for surgeons
  - for preservation of the parathyroid gland function

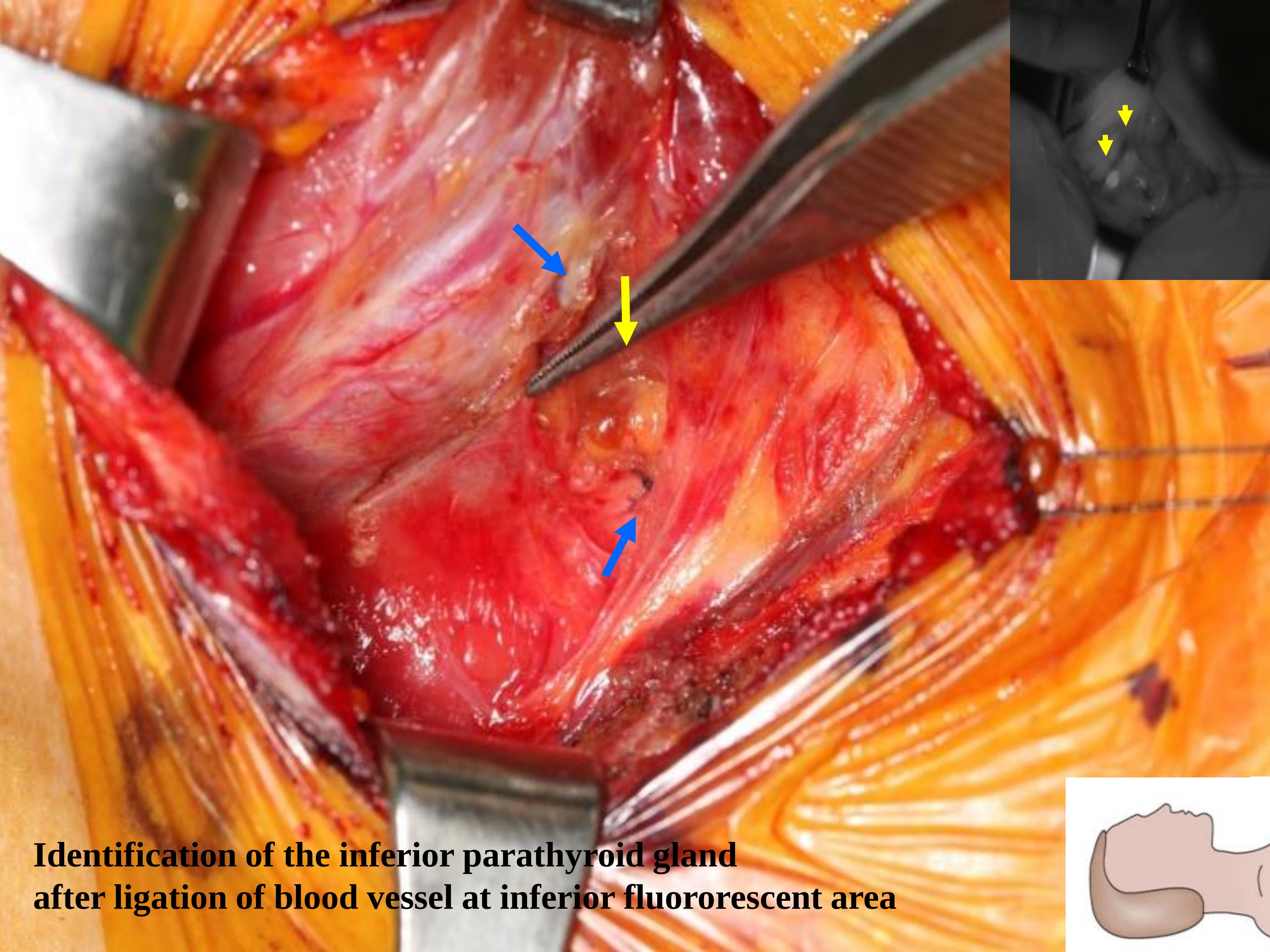




Case. Can we detect a parathyroid gland when it is covered by connective tissues or vessels?

- autofluorescence image : 2 fluorescent areas with different intensity
- superior fluorescent area : covered by connective tissues
  inferior fluorescent area : covered by blood vessels

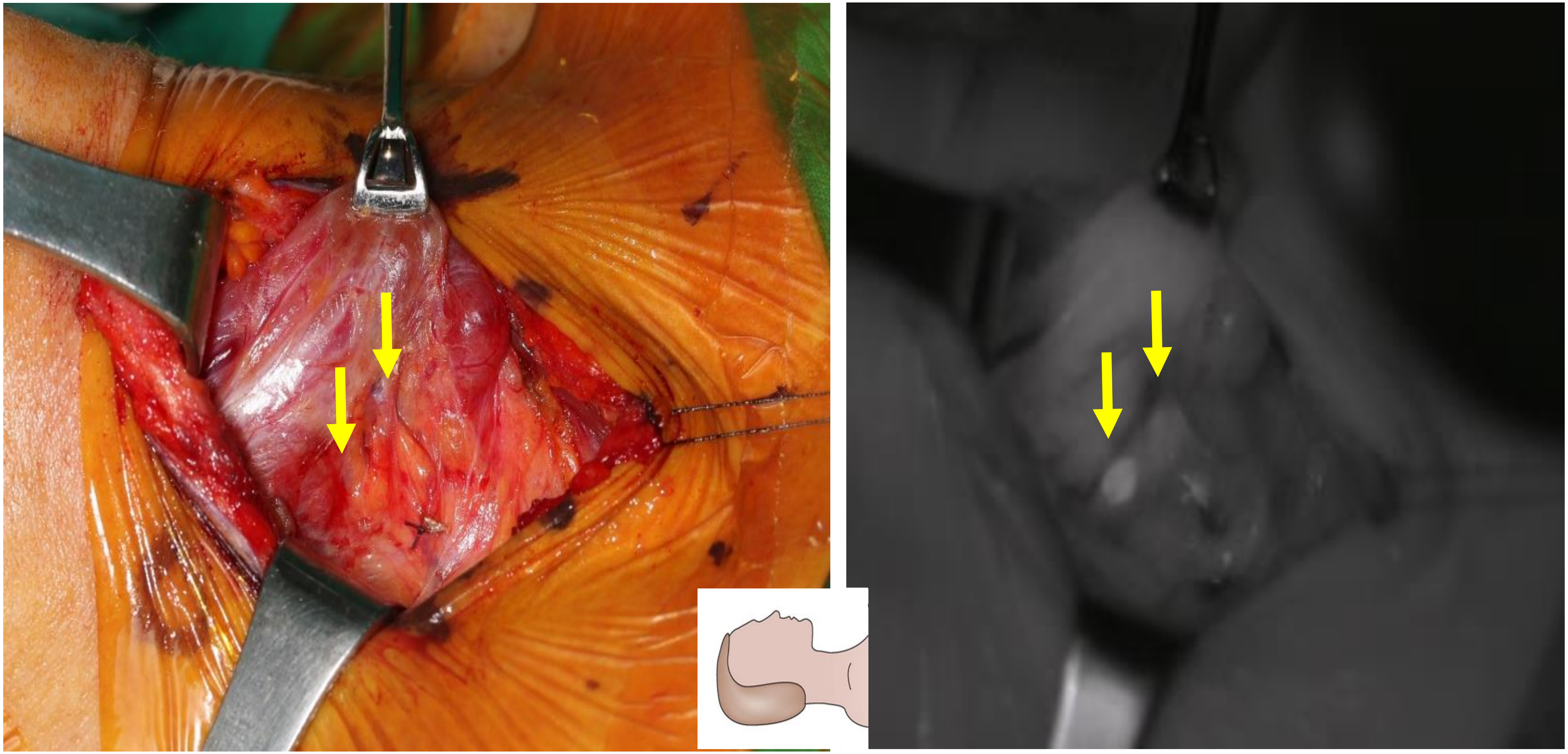





Identification of the inferior parathyroid gland after ligation of blood vessel at inferior fluororescent area

- **Identification of superior parathyroid gland after dissection of connective tissue at superior fluororescent area**

- Even the parathyroid glands covered by connective tissues or blood vessels can be detected with our imaging technique



Conceptualization of the parathyroid gland mapping

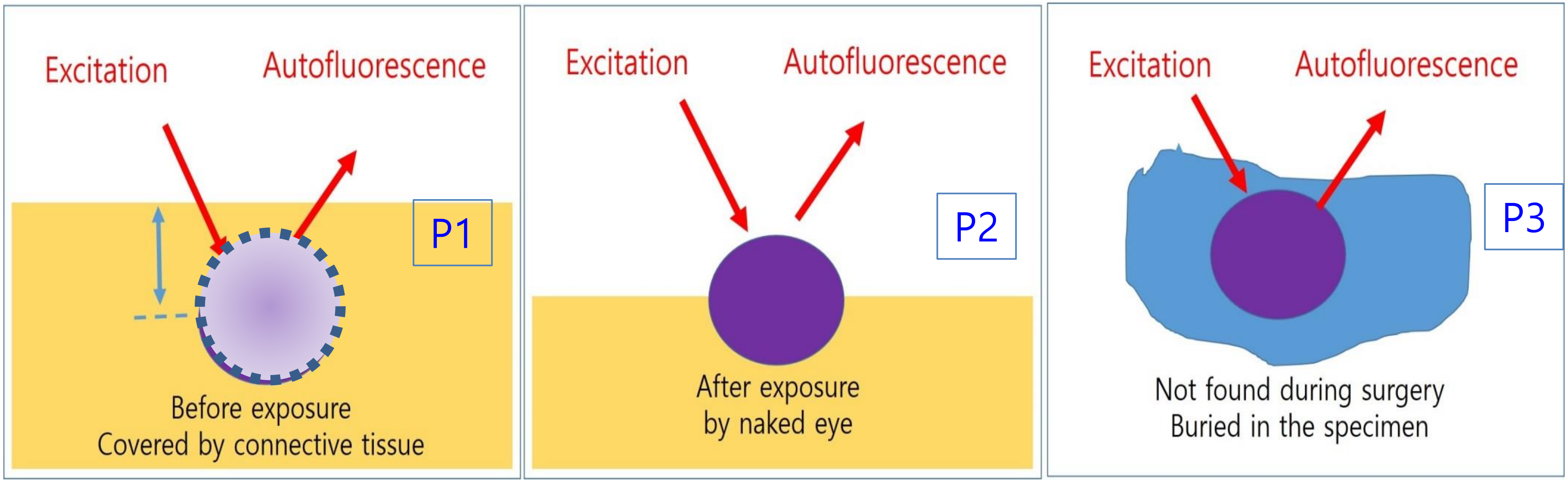
- **definitive identification of parathyroid gland through localization process for parathyroid gland which was initially not visualized by naked eye**

● Parathyroid gland mapping

Stage P1 - taking images before visual identification by surgeons

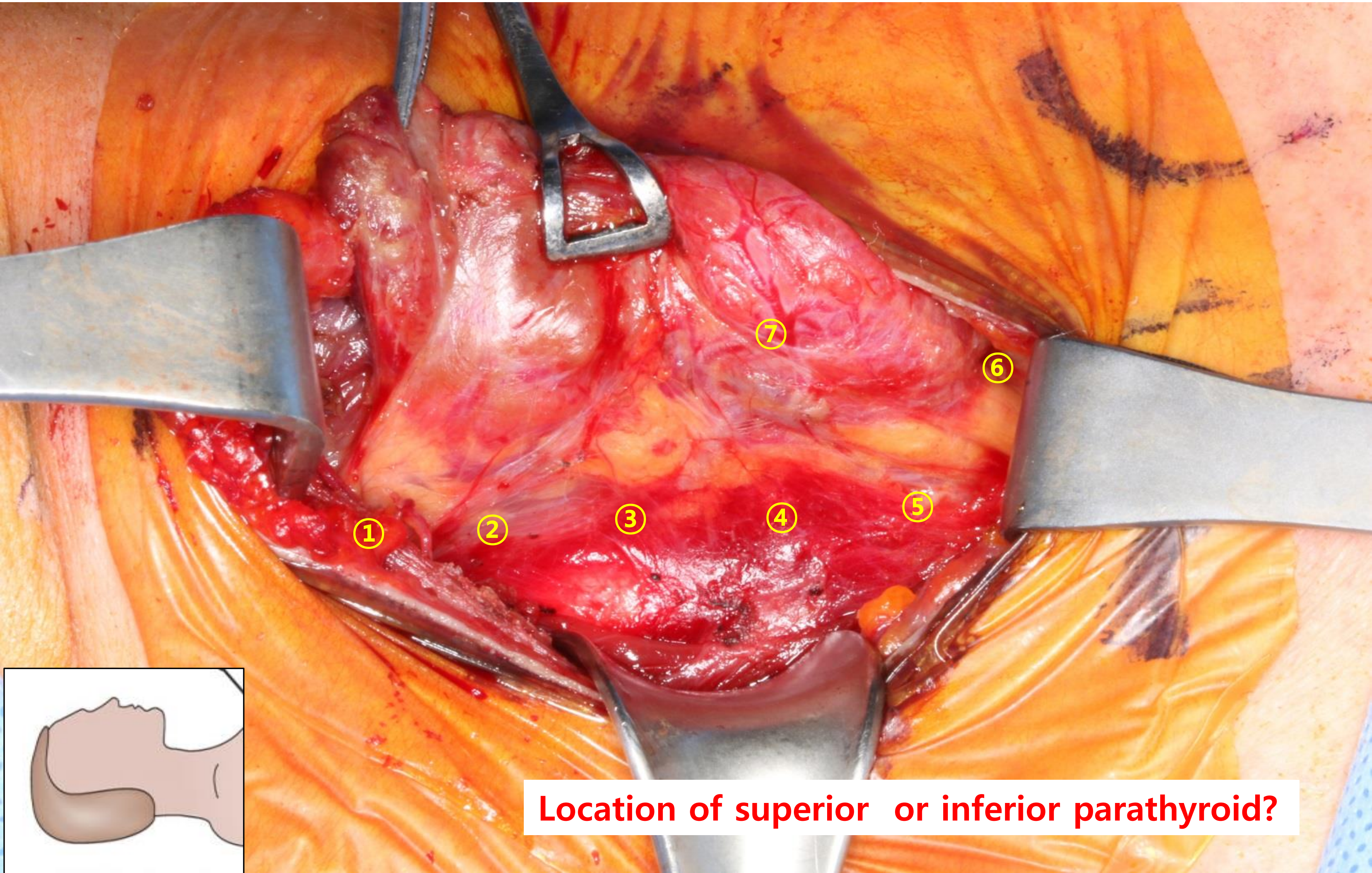
Stage P2 - taking images after visual identification by surgeons

Stage P3 - taking images in the removed specimen

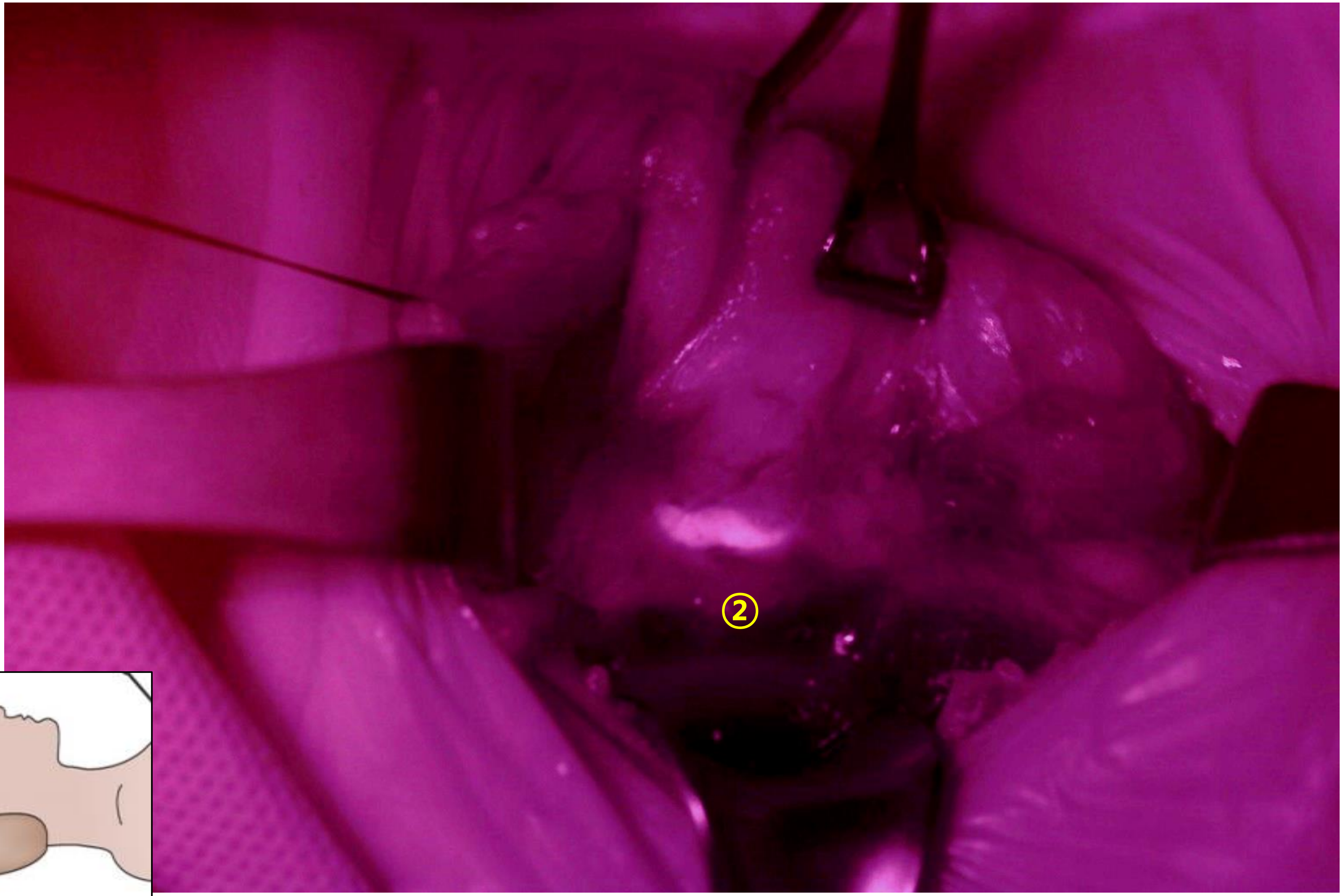


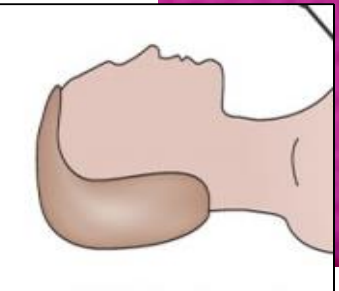
Cases of parathyroid gland mapping

Case. Before visual identification of parathyroid gland by surgeons

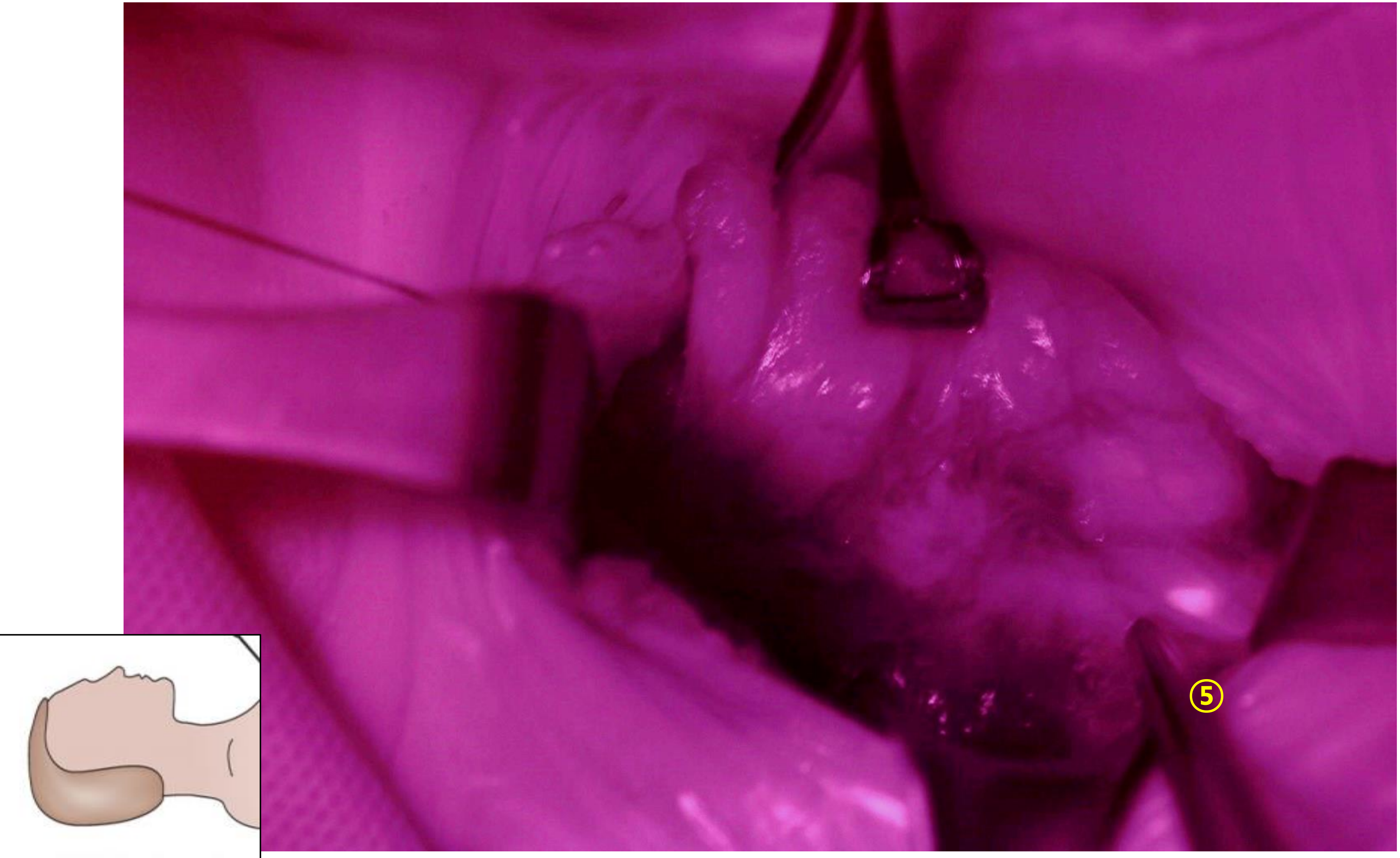


Localization of right superior parathyroid gland
(still covered by fatty connective tissues)
with NIR images



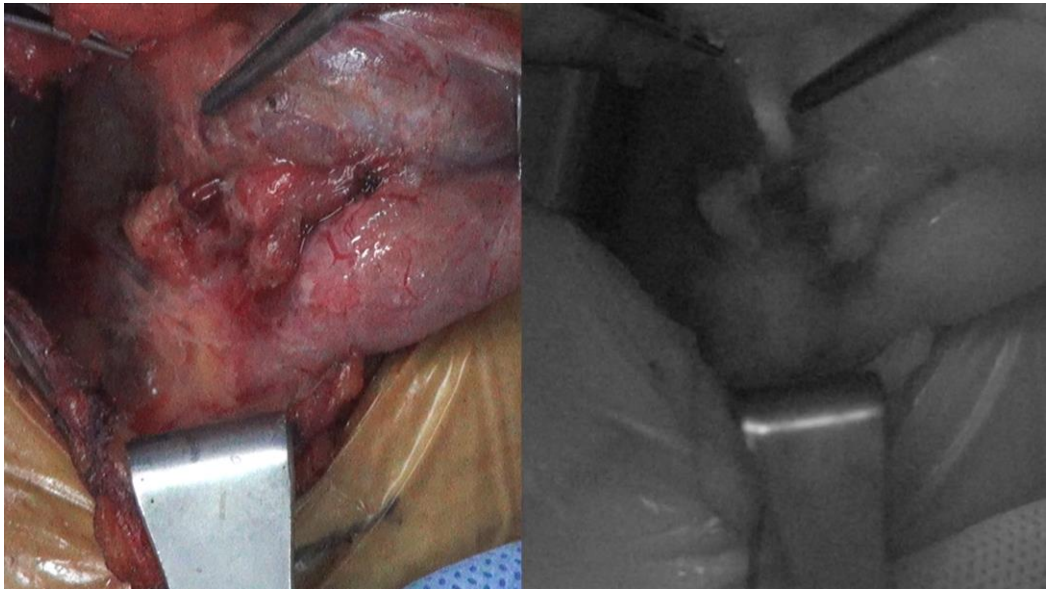


Localization of right inferior parathyroid gland (still covered by adipose tissues) with NIR imaging



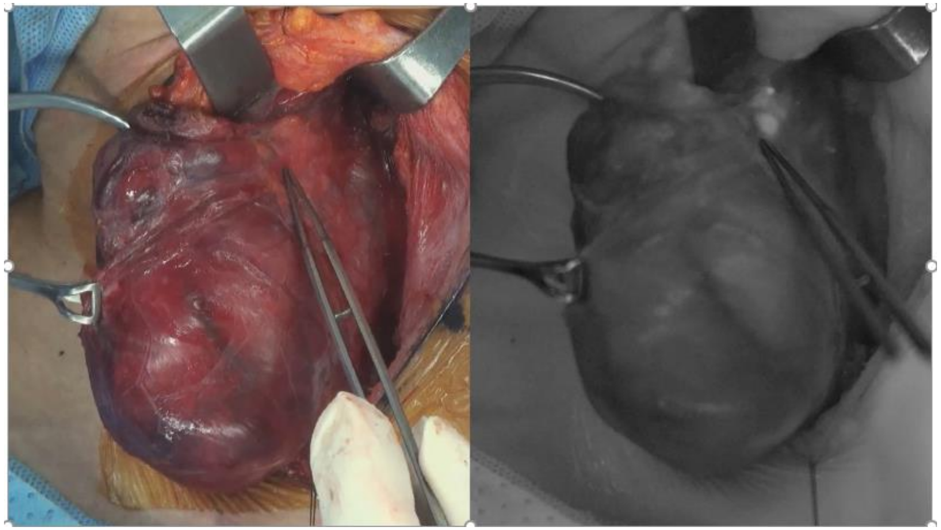
Upgraded the prototype to improve spatial information

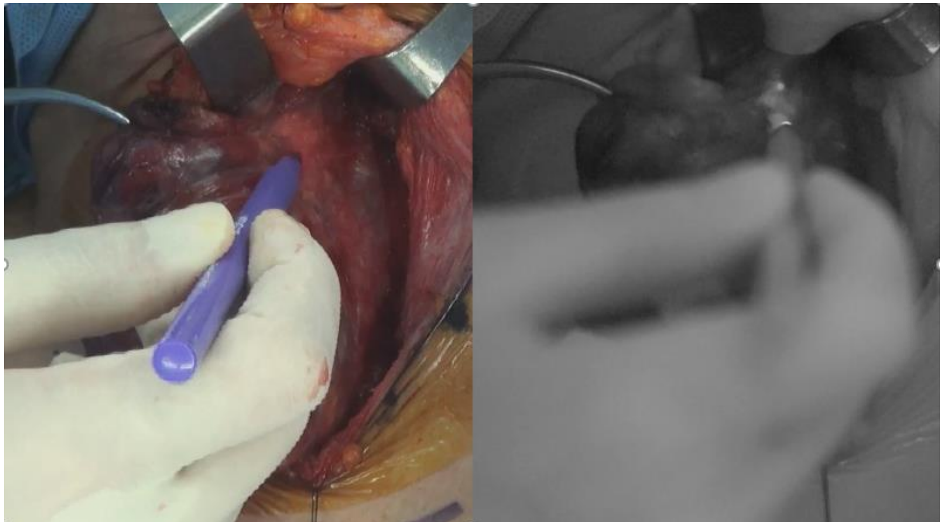
- Added a video camera to facilitate anatomical guidance
  - can display both white light and NIR light images together



- AF image of sup. parathyroid gland hidden by connective tissue

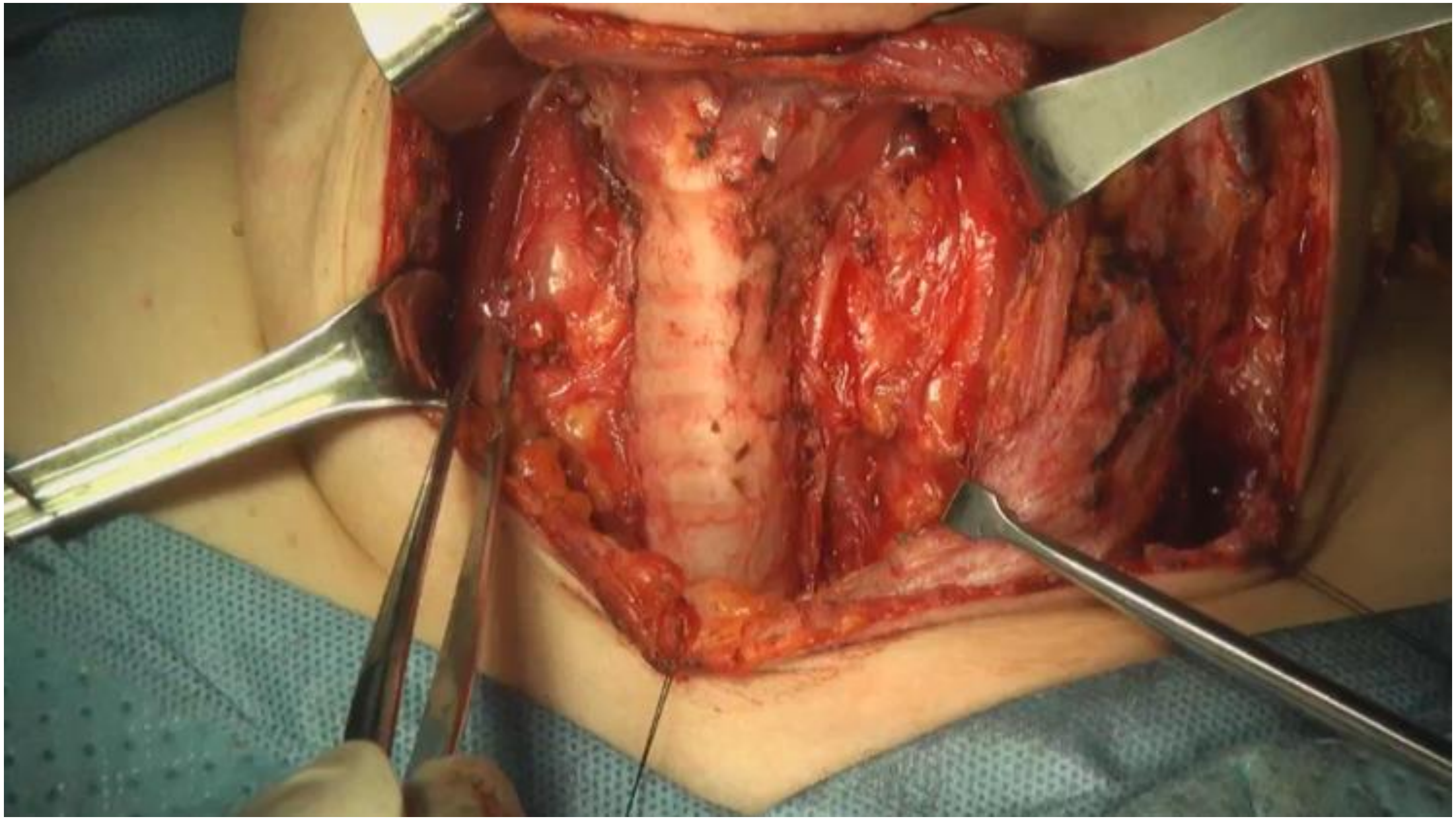
Mapping by marking the potential location of non-exposed parathyroid gland based on NIR system





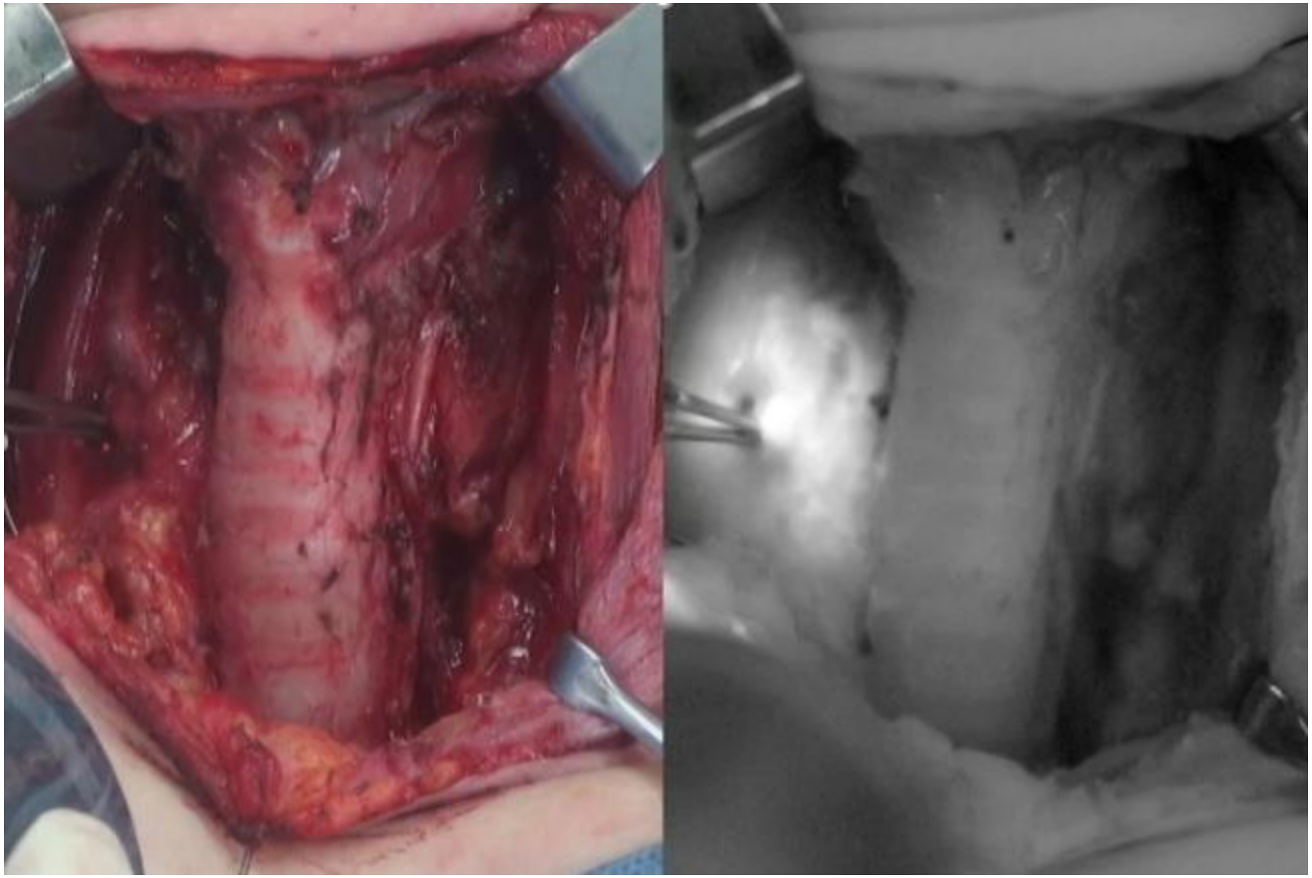
ICG angiography coupled with NIR AF imaging system - to assess the perfusion of parathyroid gland

- preservation of parathyroid glands
  - not necessarily mean the preservation of the function

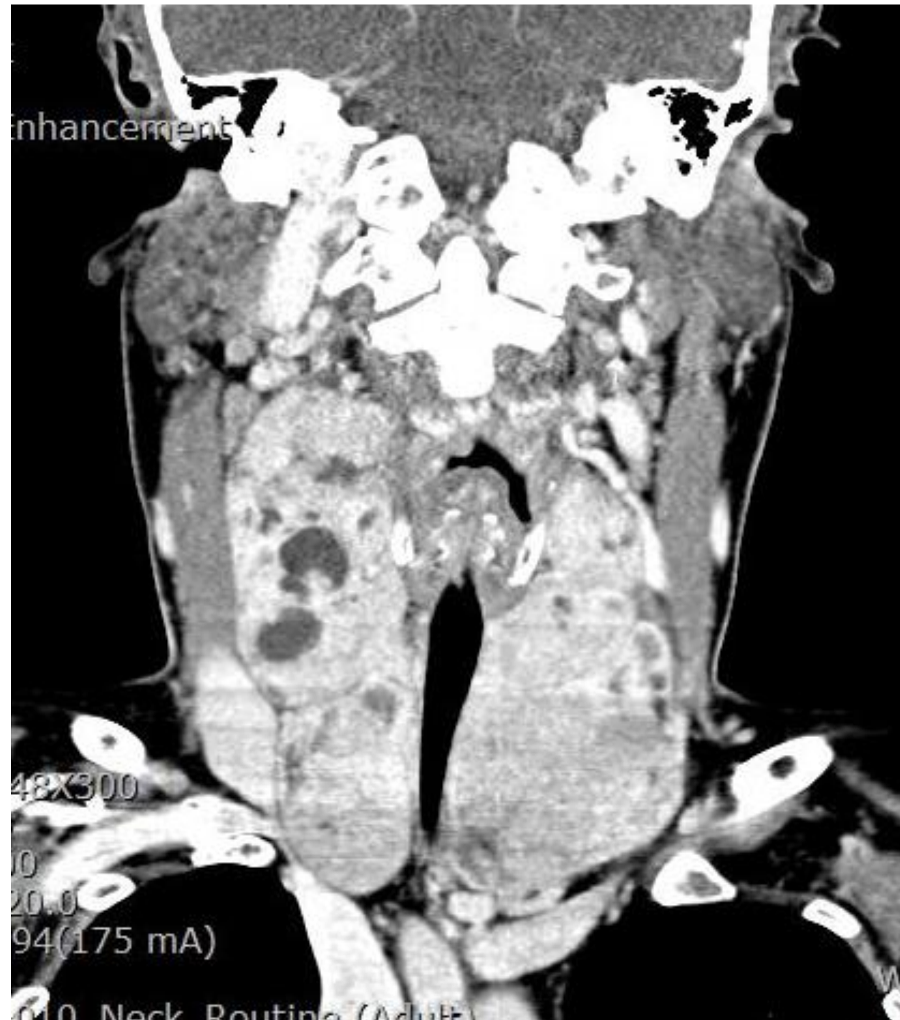


ICG angiography with NIR AF imaging system

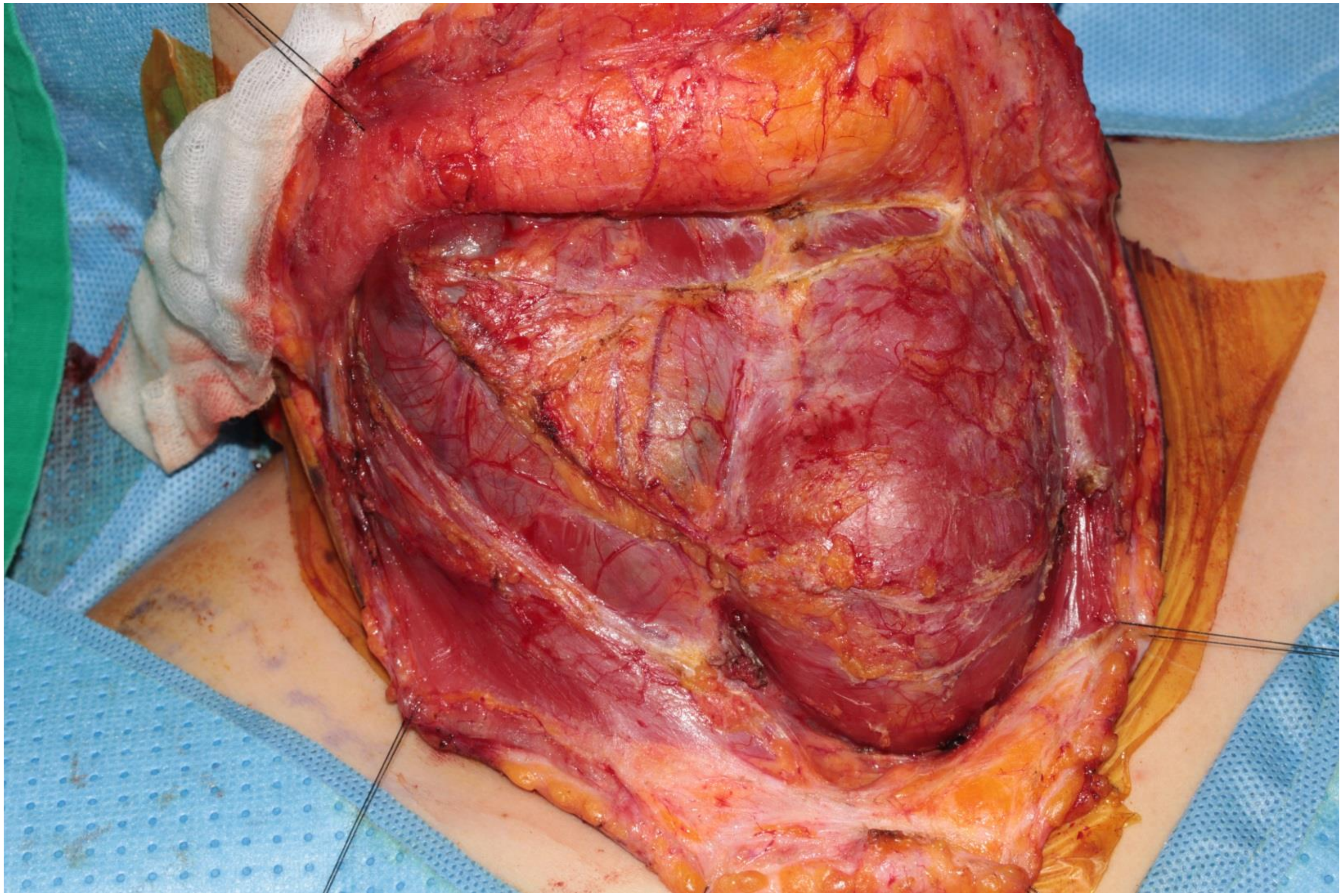
- Right inferior PG : good blood flow and good perfusion
- Left superior PG : good perfusion even in the presence of congested color



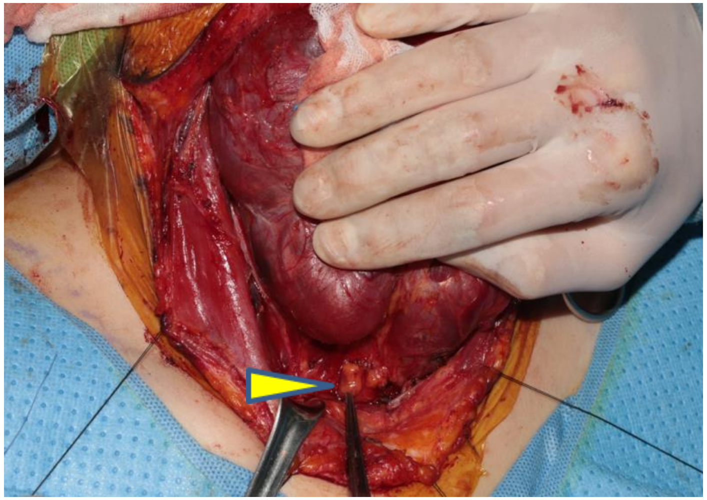
A case of huge multinodular goiter
- 이 0 연 (F/30)



Total thyroidectomy

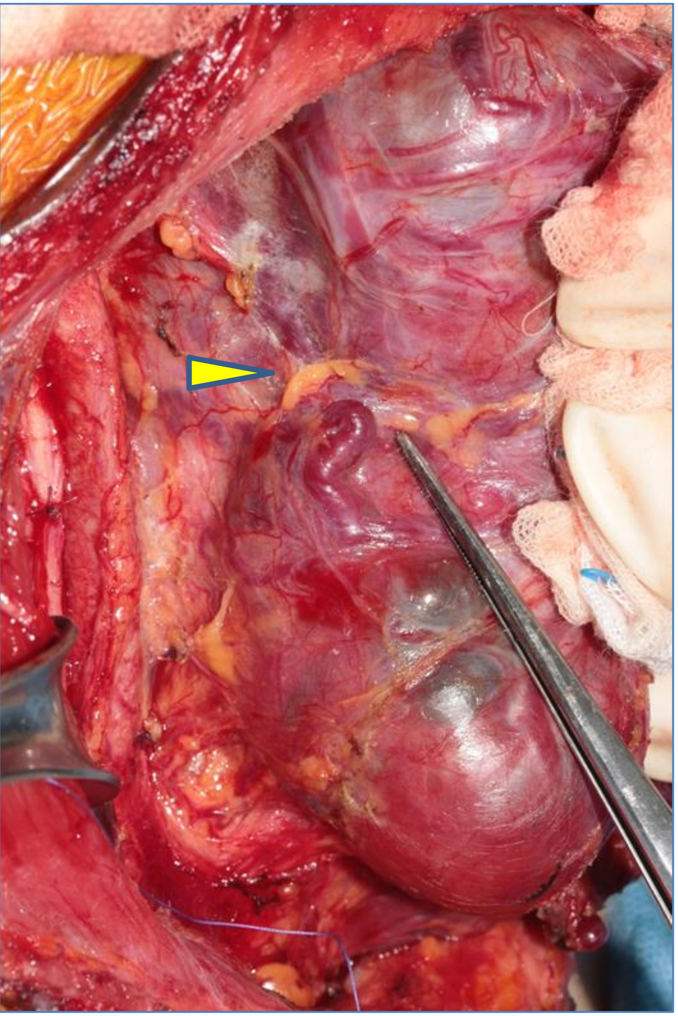


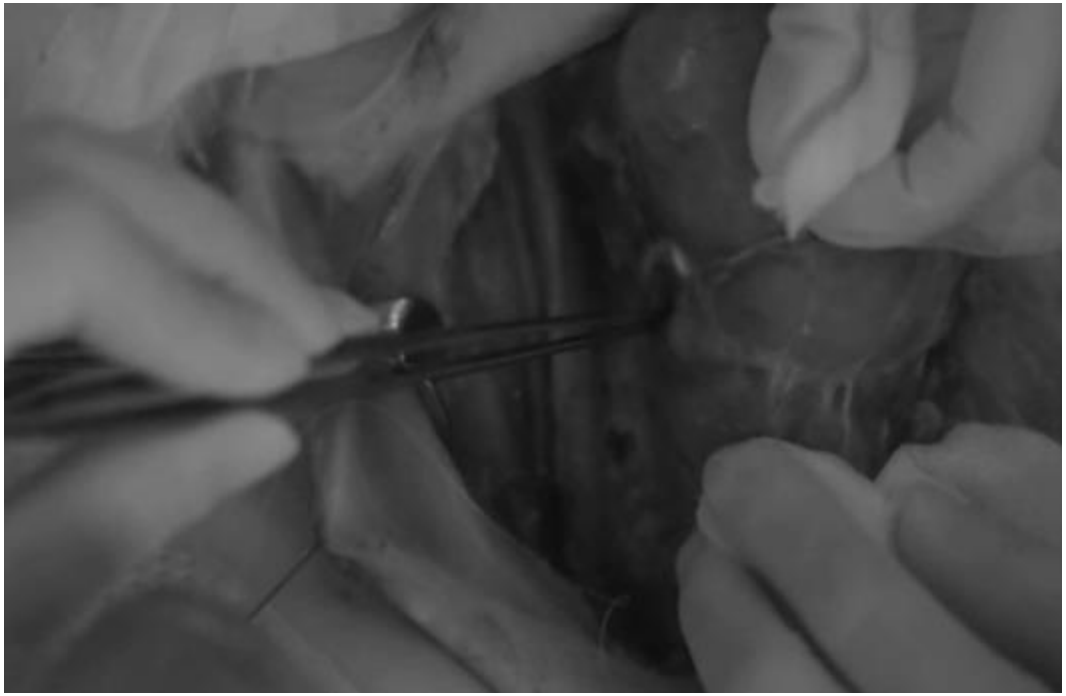
Right inferior parathyroid gland mapping with NIR AF guidance



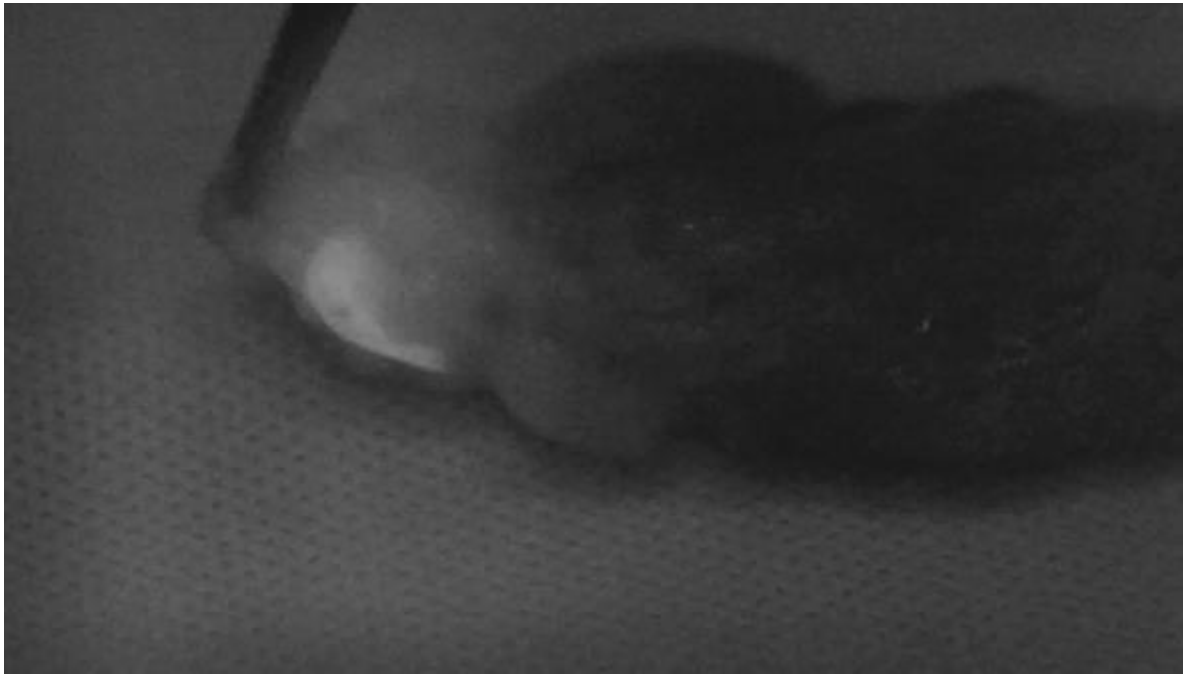
- Preserved
inferior parathyroid gland

A small right superior parathyroid
- mapped very easily from the huge thyroid goiter



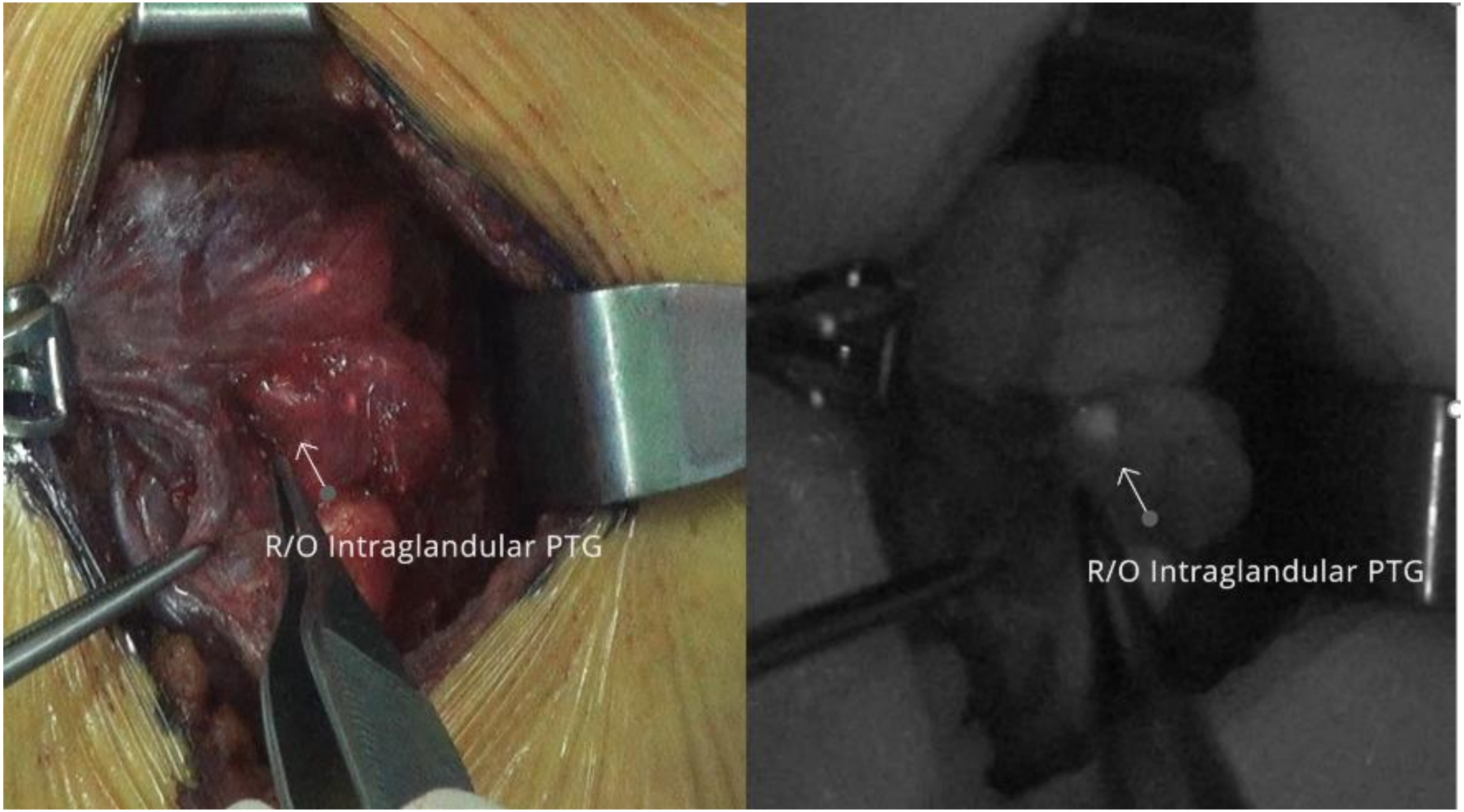


Case. Identification of inadvertently removed parathyroid gland from central neck dissection specimen



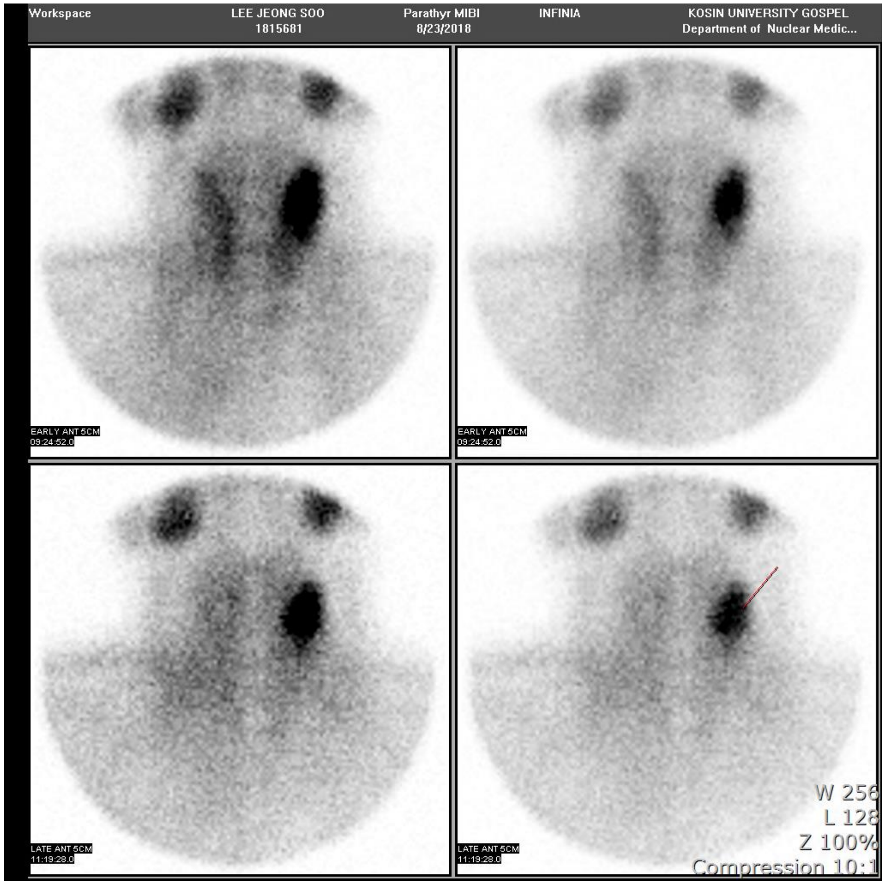
- The parathyroid gland
  : identified from the CND specimen with NIR AF imaging
  : auto-transplanted

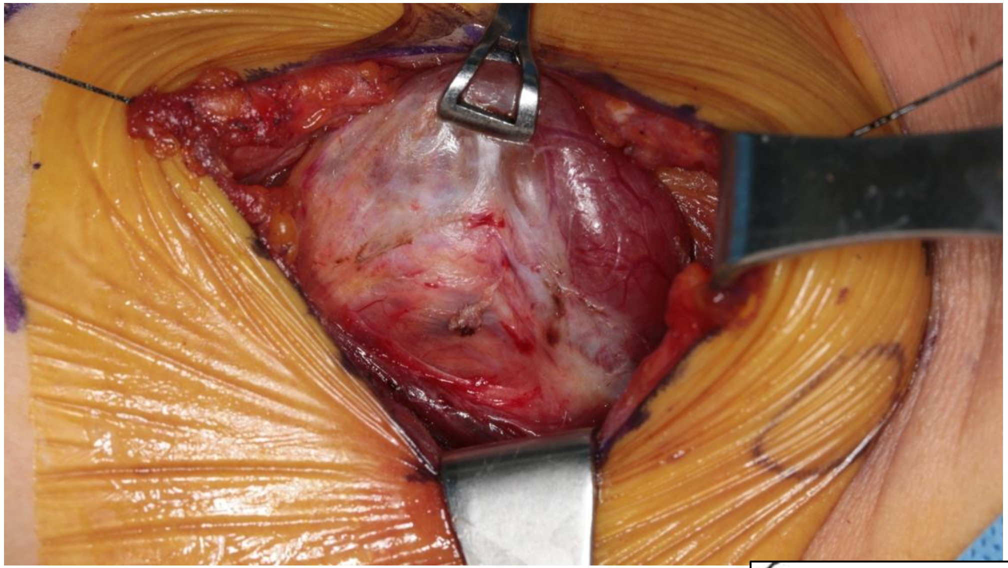
Case. Intrathyroidal parathyroid gland

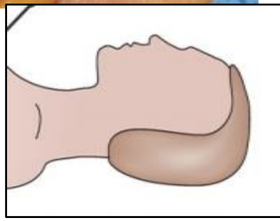


Parathyroid adenoma mapping with NIR AF imaging

Case. Adhesive superior parathyroid adenoma





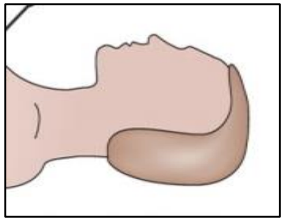


- mobilized left thyroid lobe
- **no parathyroid adenoma : identified yet**

- **iPTH level : 141**
- **Serum calcium : 11.7**

Localizing parathyroid adenoma with NIR light

- discernible, shining adenoma
  when it is stimulated by NIR light



Removal of the parathyroid adenoma

Early localization of parathyroid gland with NIR AF before visual identification by surgeon (PG mapping) : possible in 92% by imaging in our series

Table 1. Accuracy of Parathyroid Gland Mapping

	Stage P1		Stages P1, P2		Stages P1, P2, P3	
Characteristic	n/total	%	n/total	%	n/total	%
Sensitivity	64/69	92.75	68/69	98.55	69/69	100
Specificity	1/1	100	1/1	100	1/1	100
Positive predictive value	64/64	100	68/68	100	69/69	100
Negative predictive value	1/6	16.66	1/2	50	1/1	100
Accuracy	65/70	92.85	69/70	98.57	70/70	100

Stage P1, imaging before identification of the gland by direct visualization; stage P2, imaging after identification; stage P3, imaging in the removed specimen.

- Excluded naturally exposed parathyroid gland during initial dissection

Kim et al. JACS, 2018

Efficacy of NIR AF imaging for preserving parathyroid function

- Benmiloud et al, Surgery (2018)

  - NIR AF use during total thyroidectomy significantly

    : reduced postoperative hypocalcemia (from 20.9% to 5.2%)

    : improved inadvertent resection of parathyroid (from 7.2% to 1.1%)

    : reduced autotransplantation rate (from 15% to 2.1%)

- Dip et, JACS (2019)

  - randomized controlled trial comparing white light with NIR AF for parathyroid gland identification during total thyroidectomy

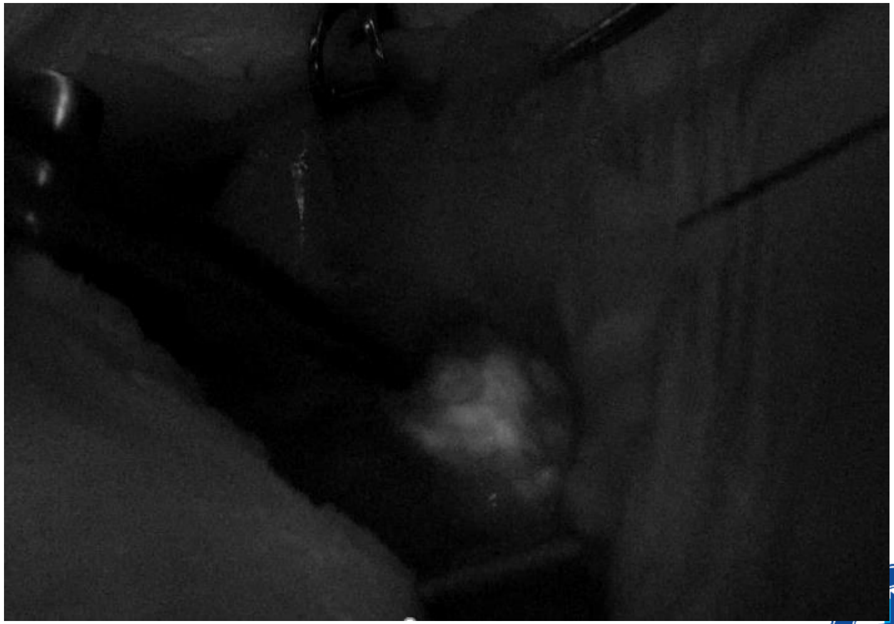
    : temporary hypocalcemia (from 16.5% to 8.2%) ($p < 0.103$)

    : reduced severe hypocalcemia (11.8% to 1.2%) ($p = 0.005$)

Limitations of the NIR AF technique

- False positive from brown fat or colloid nodule
- False negative from limited penetration

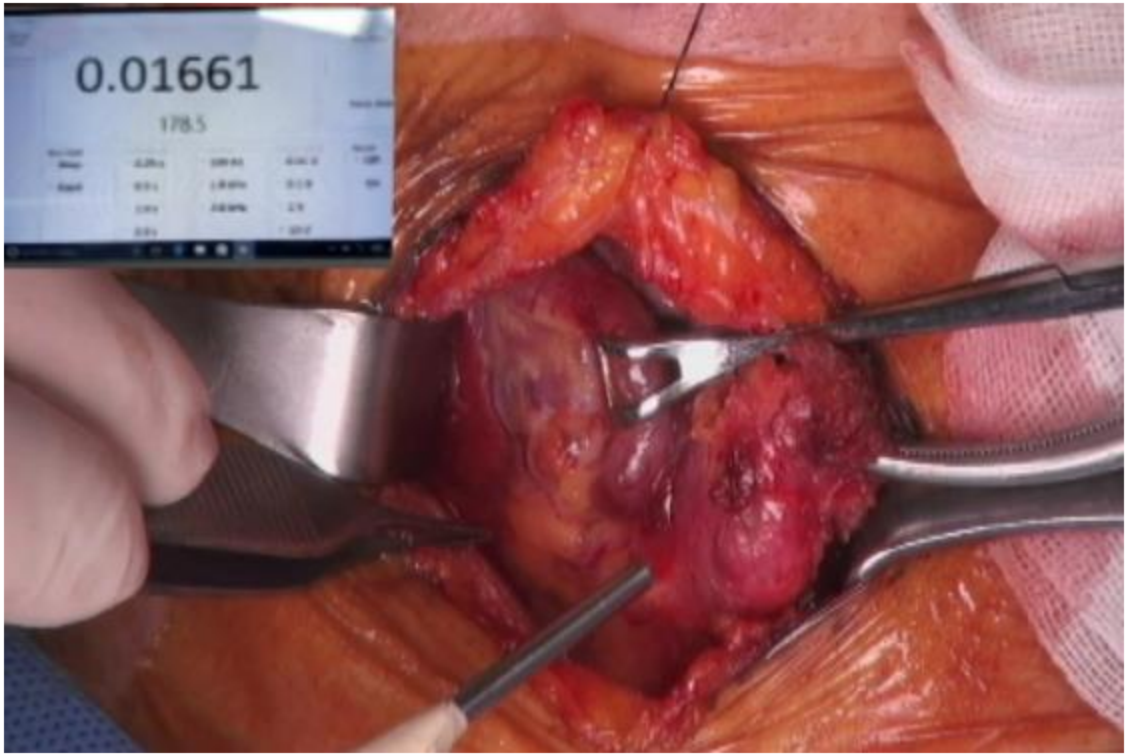
  due to fatty tissues, blood vessels or intrathyroidal parathyroid gland
- There is a learning curve for the correct interpretation of the images



Parathyroid identification with Lab-built NIR AF probe

NIR AF probe

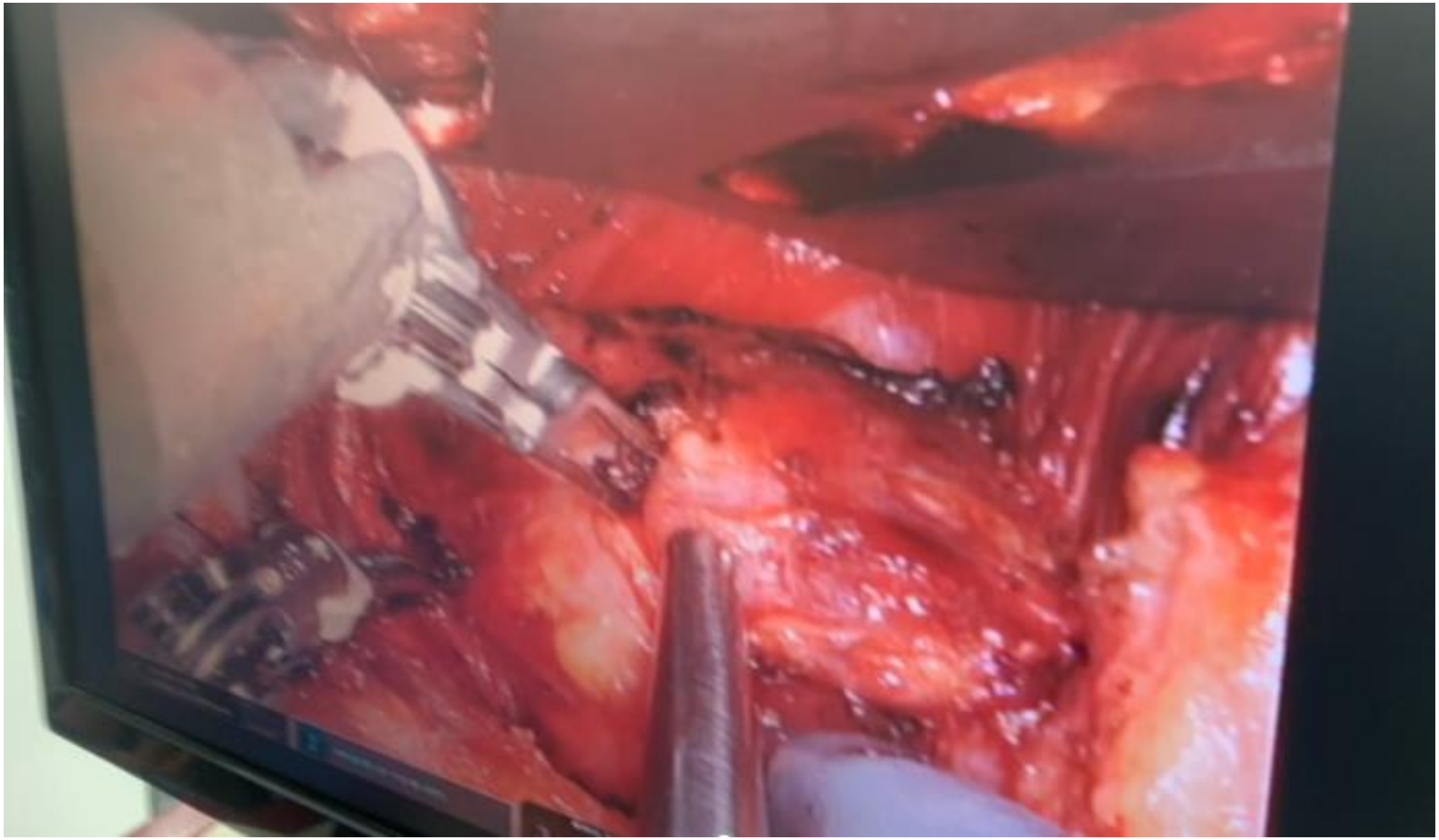
- can be used in the presence of fluorescence light, operating light, and even head light
- can provide an audio and visual display to indicate parathyroid gland



- **AF intensity**
  - **thyroid : 0.3**
  - **fat : 0.2**
  - **trachea : 0.01**
  - **muscle : 0.05**
  - **Parathyroid : 1.7**

- parathyroid showed 6-fold higher intensity than the thyroid
  - made it possible to differentiate parathyroid gland from other tissues

Application of NIR AF probe to robotic thyroidectomy



Summary

- NIR AF imaging with DSLR camera is a very useful tool for the early localization of the parathyroid gland before visual identification by surgeons
- Parathyroid gland mapping and localization is possible with high accuracy rate using NIR AF imaging
- Parathyroid AF will be increasingly used in thyroid and parathyroid surgery in the near future

Intraoperative Neuromonitoring (IONM)

Monitoring systems

1. The **recording side**

- involves the endotracheal tube recording electrodes, its recording electrode ground, and associated connections at the interface-connector box and monitor.

2. The **stimulation side**

- includes the stimulation neural probe, its grounding electrode, and associated connections to the interface box-connector and stimulation current pulse generator within the monitor.

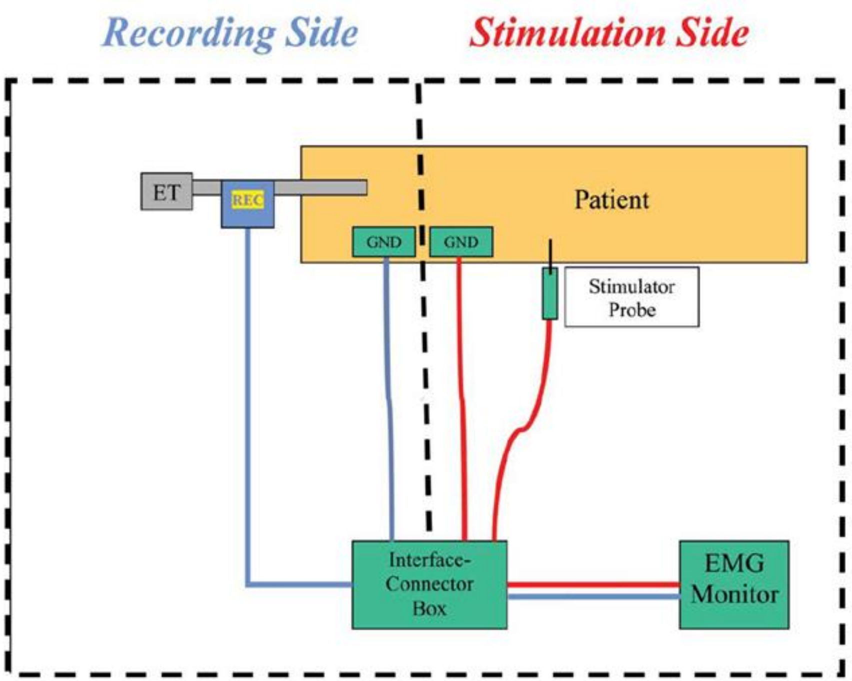
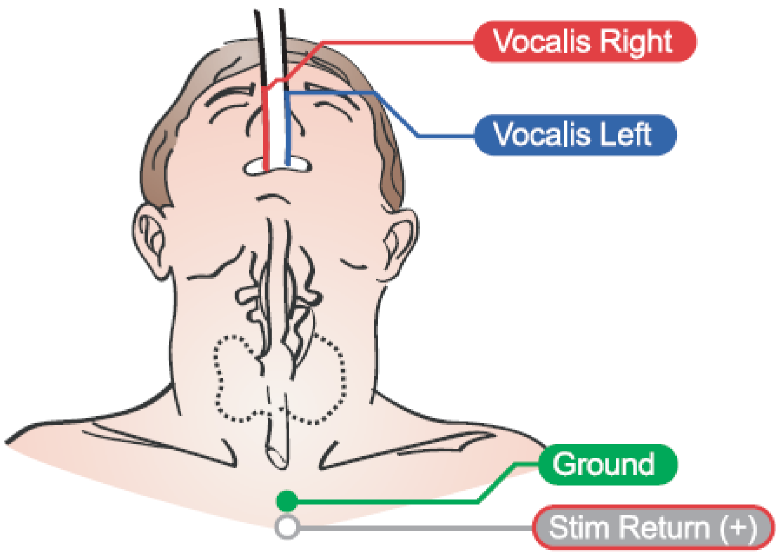
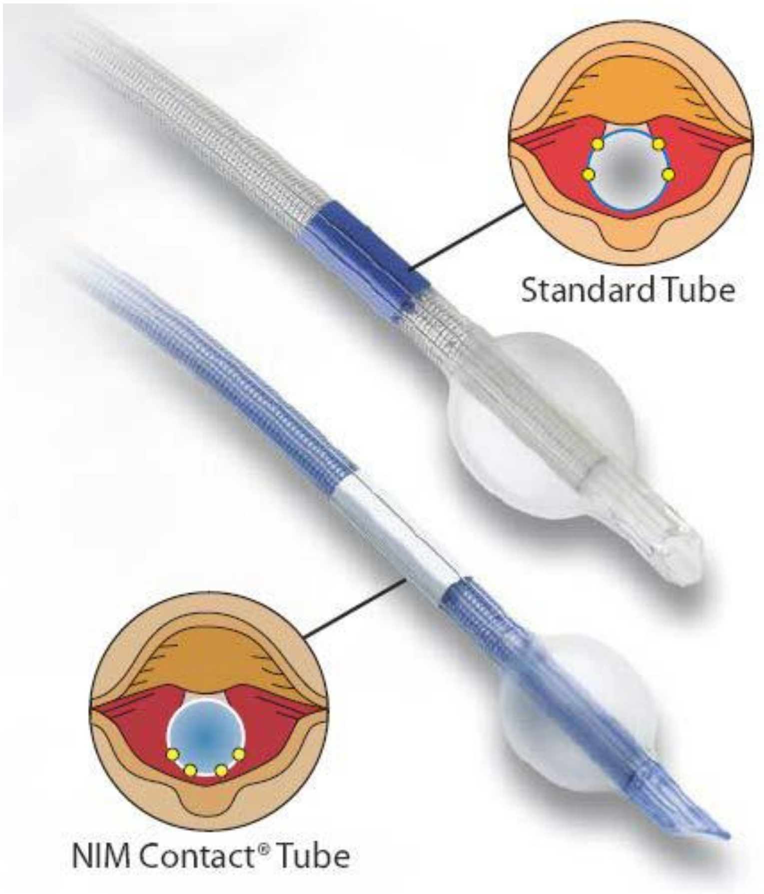


Fig. 2. Basic monitoring equipment setup. ET = endotracheal tube; REC = recording electrodes; GND = ground electrodes; EMG = electromyography.

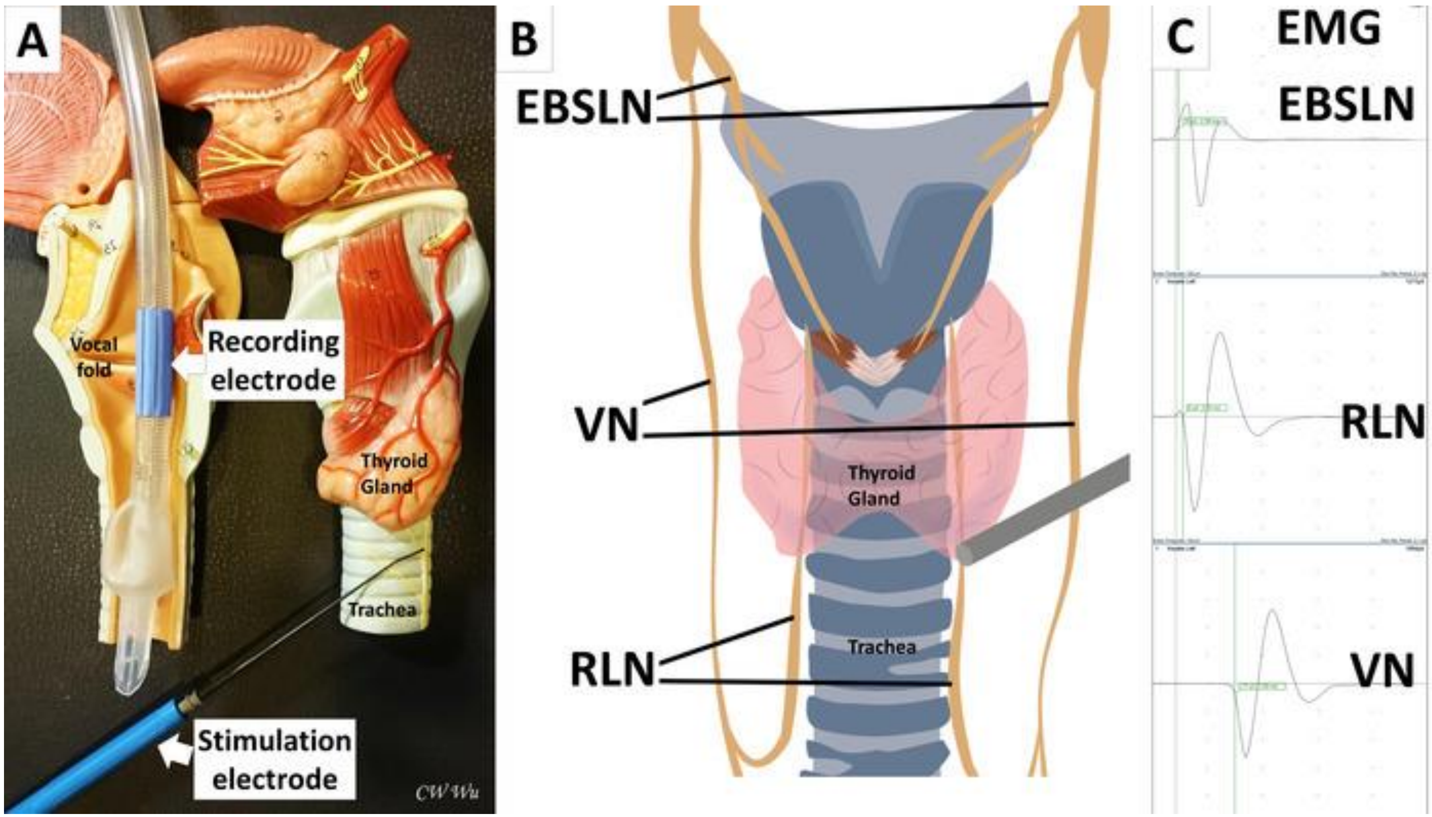
Standards of equipment

EMG Endotracheal Tube

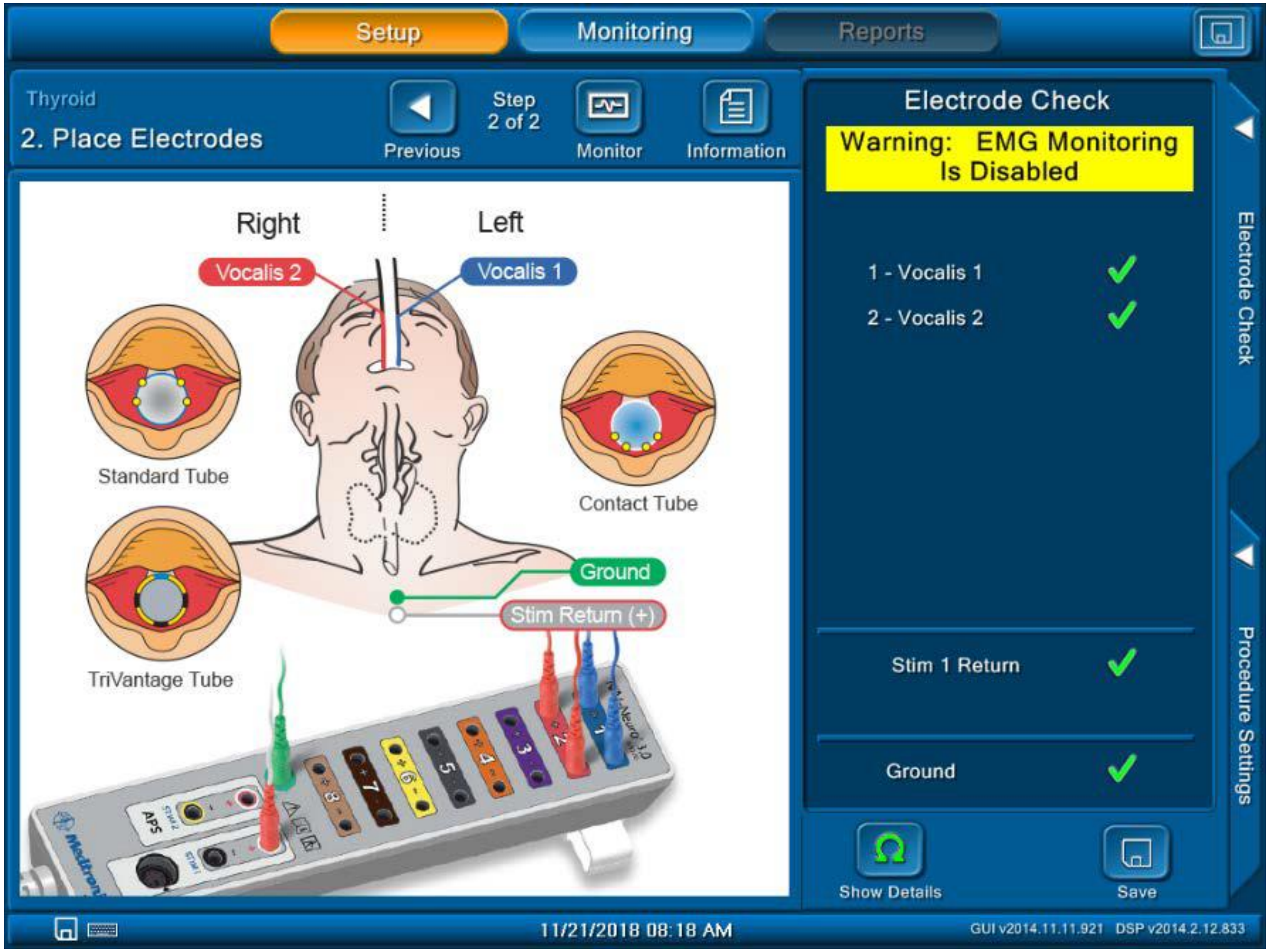




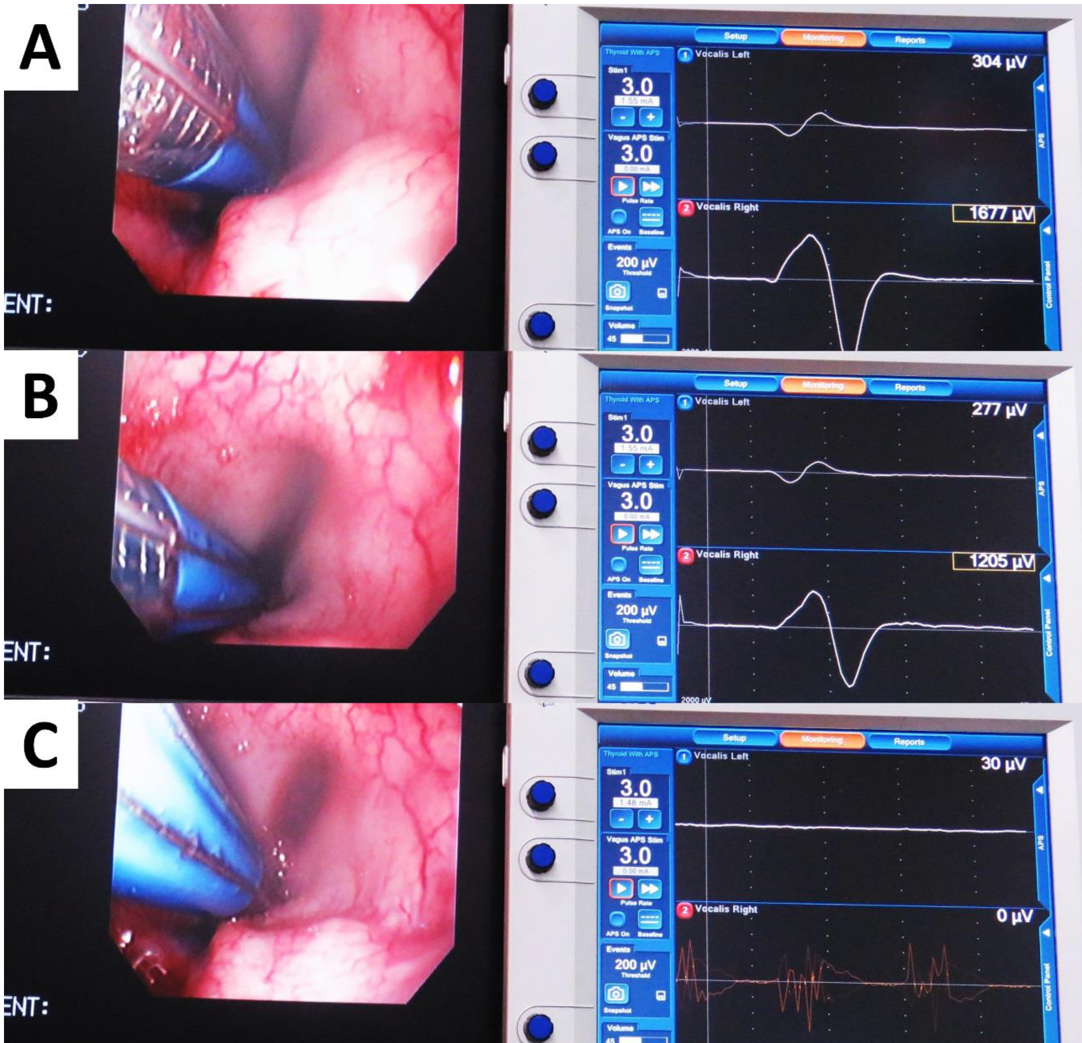
EMG endotracheal tube placement



Check proper position of electrode



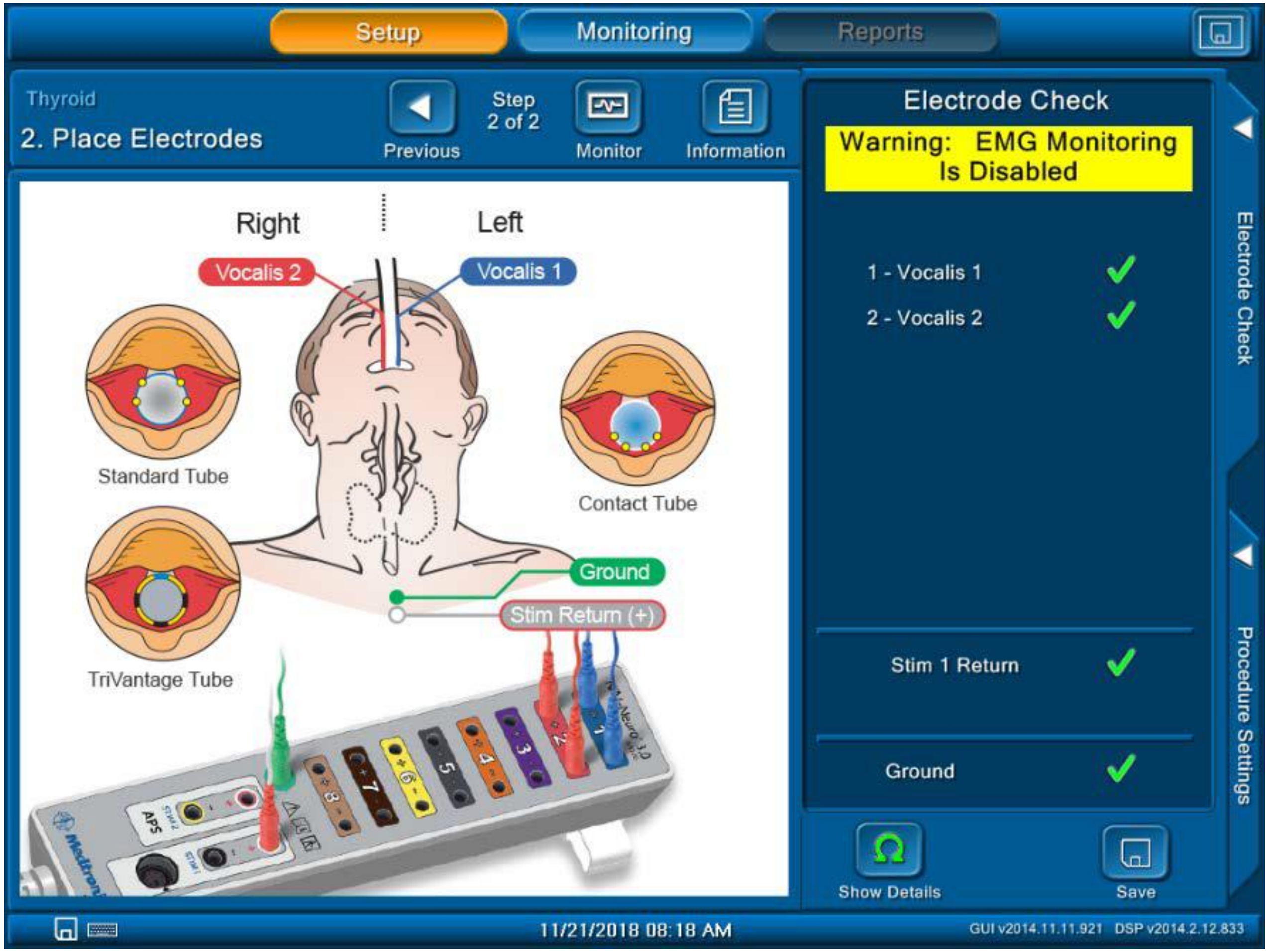
EMG Endotracheal Tube Placement



Wu, et al.
J Vis Exp2019

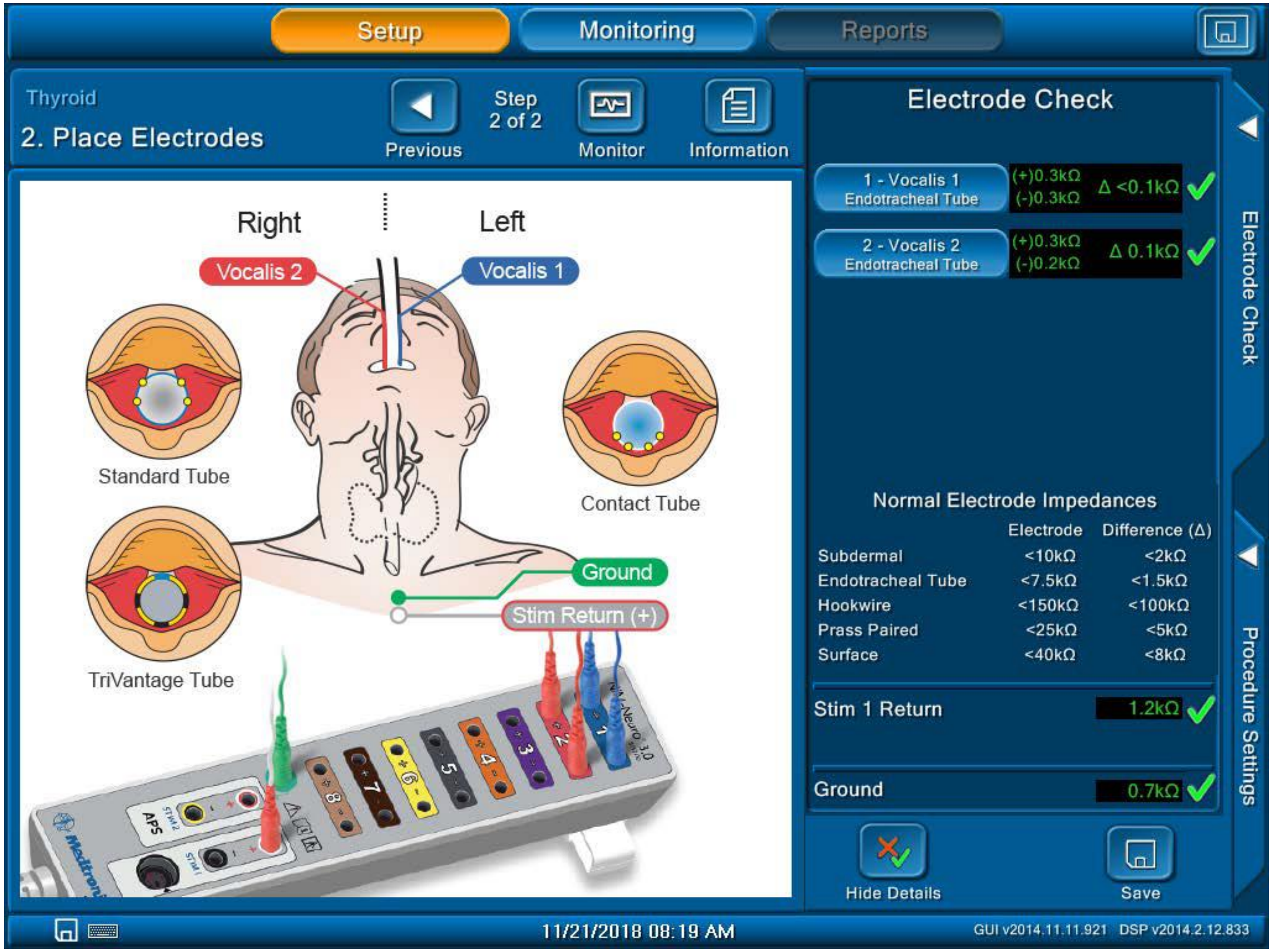
EMG monitor : Monitor Assessment

Check proper position of electrode



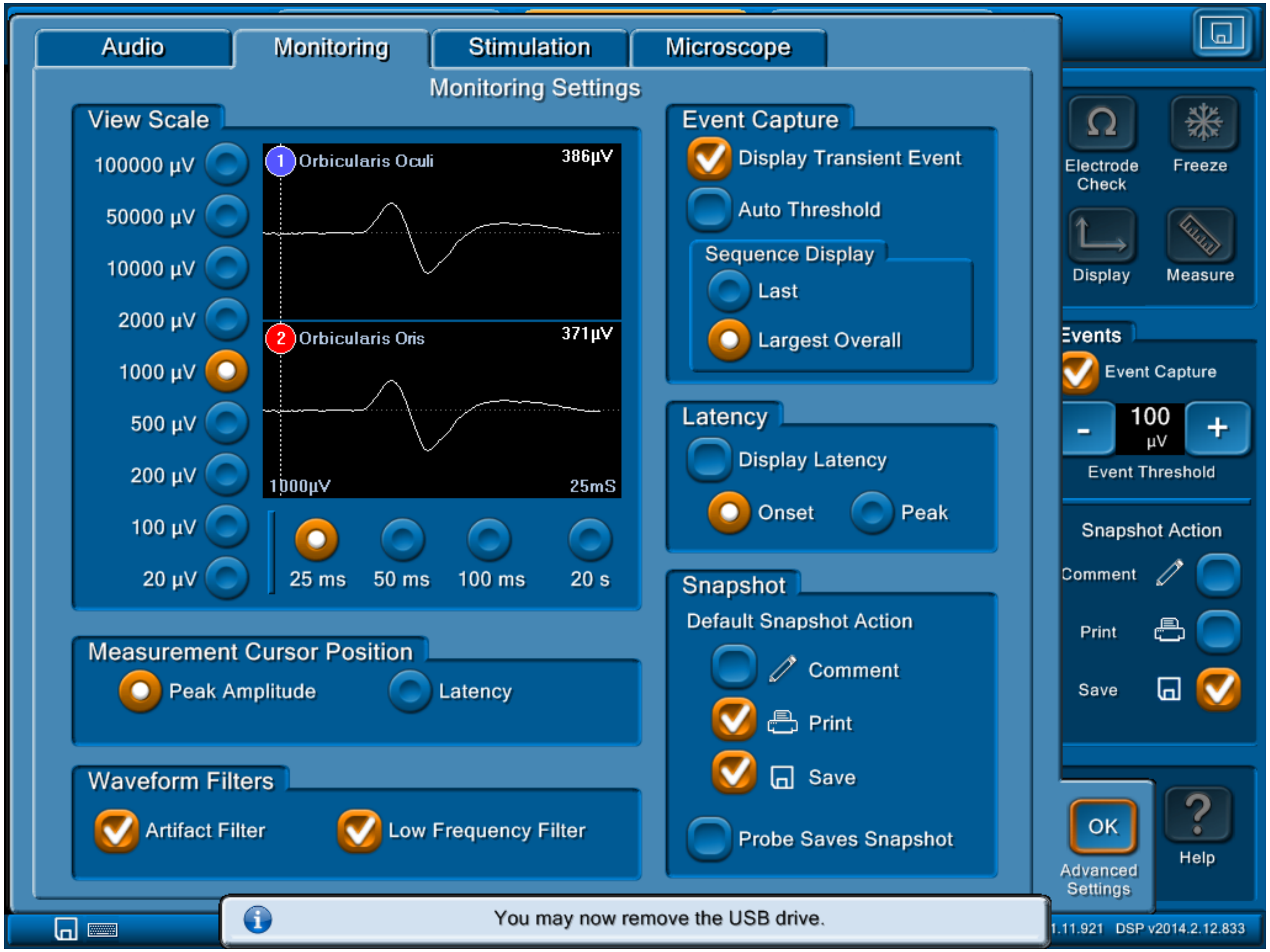
EMG monitor : Monitor Assessment

- Impedance (<5.0 kΩ),
- impedance imbalance (<1.0 kΩ)

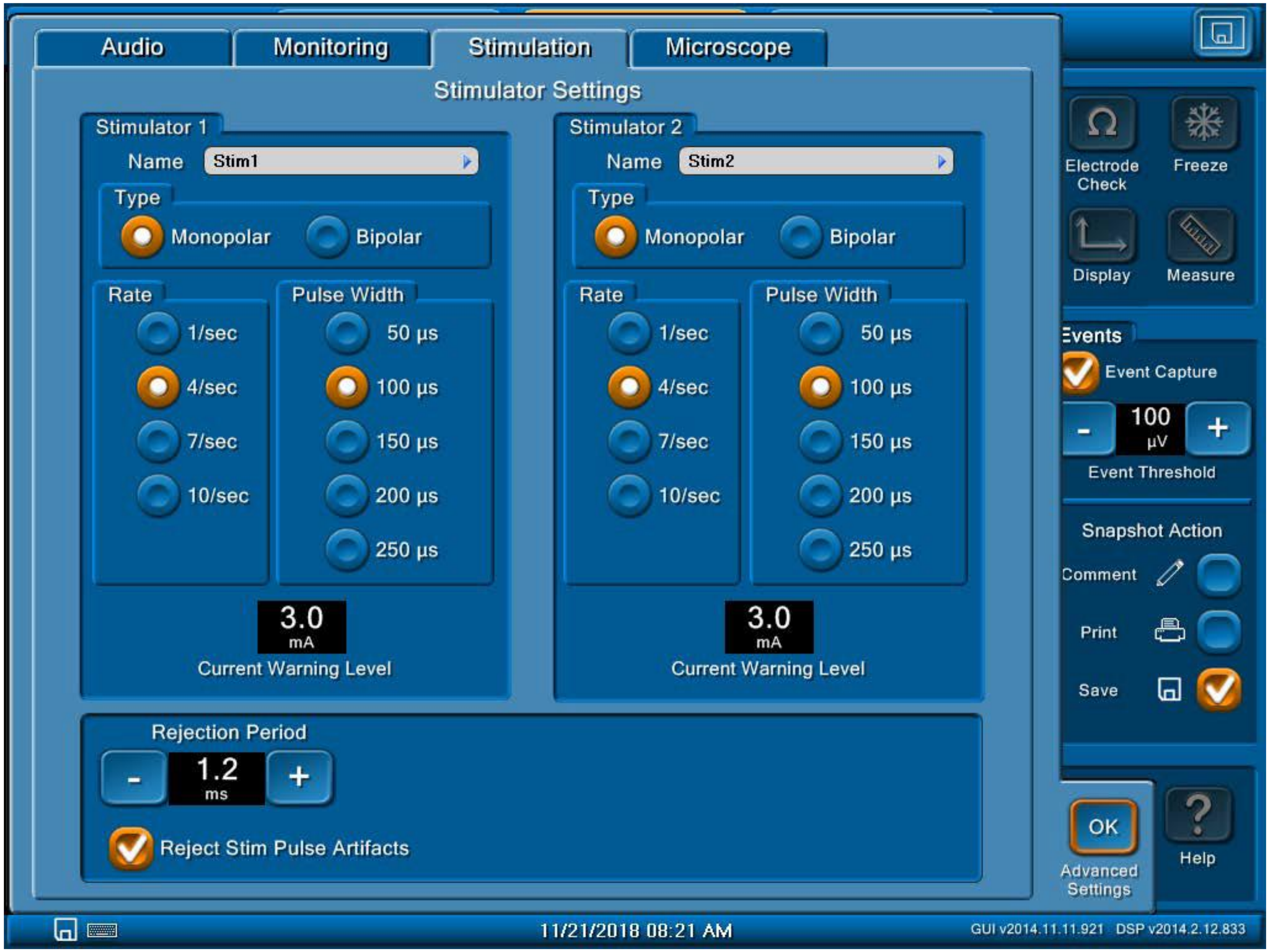


EMG monitor : Monitor Assessment

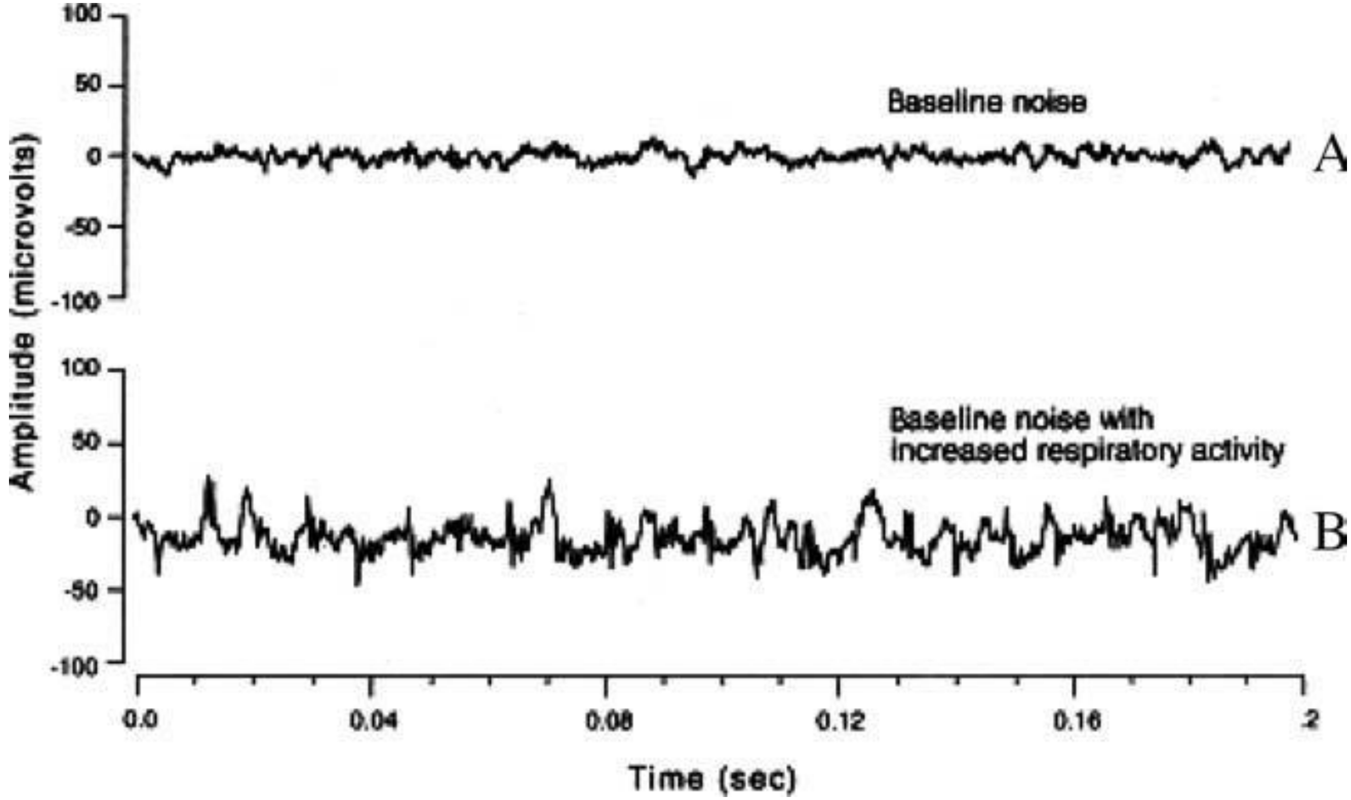
EMG monitor : Monitor Assessment



EMG monitor : Monitor Assessment

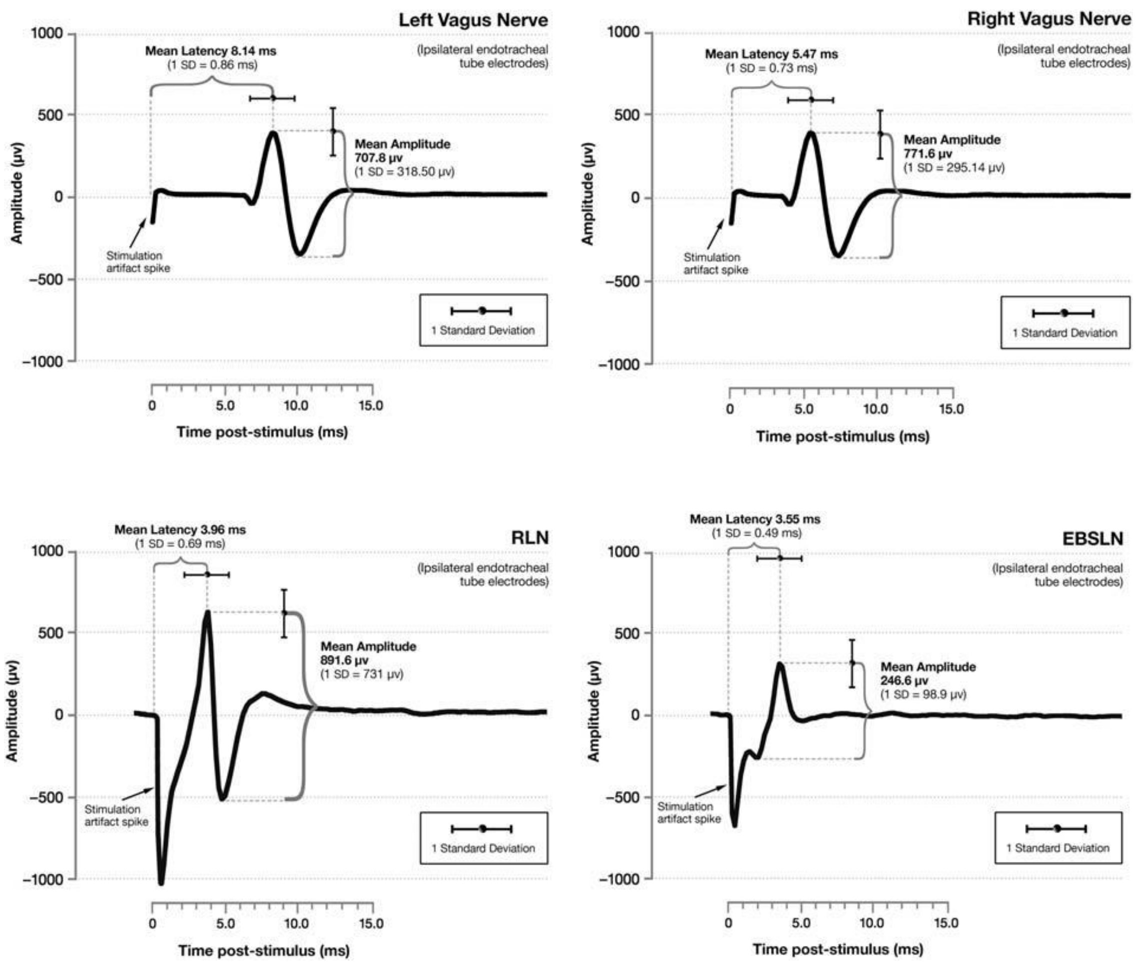


EMG monitor : Monitor Assessment



Randolph, et al. Laryngoscope 2011

EMG monitor : Monitor Assessment

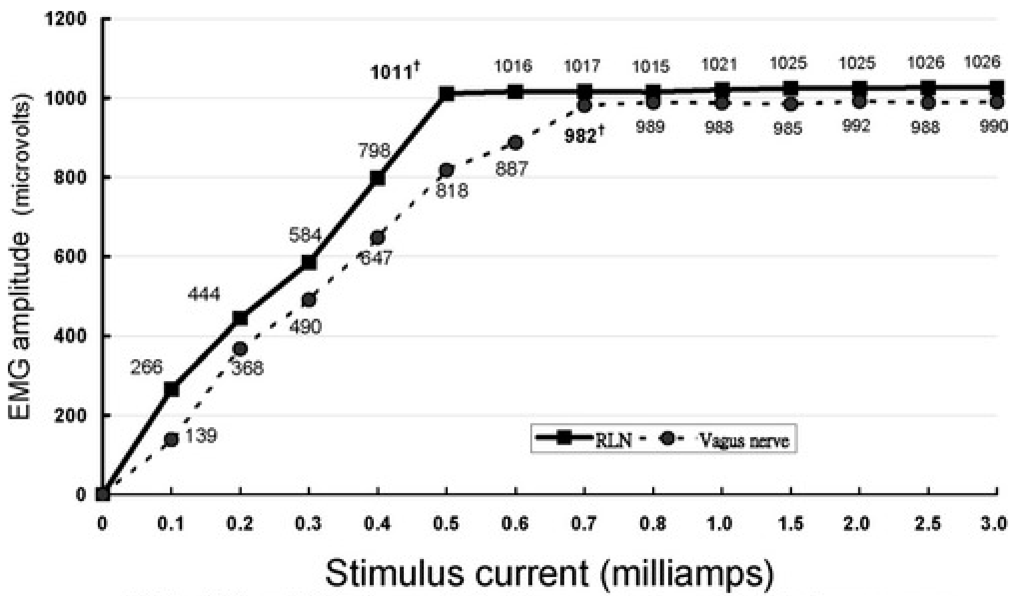


Optimal Intensity of Stimulation

- Idea is to use minimum current intensity (mA) to induce maximal response (μA)
- If stimulus current is too high, it may cause false-positive signal by shunt effect

Equipment Set Up

Correlation of Stimulus Current Intensity and EMG Response

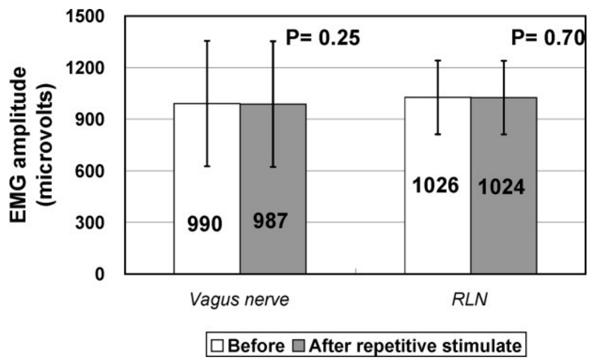


*data of 0.1 and 0.2 mA was obtained from selected nerves which have response.
†approximately maximal response occur.

Nerve Stimulation : Background

- Supra-maximal stimulation
  : to get constant EMG amplitude

- 3mA, 100μs pulse, 4Hz frequency, for 10 minutes
  : no electrophysiological or cardiopulmonary effects



Wu, et al. Head & Neck 2010

- No vagal side effects during or after continuous VN stimulation

Scheneider, et al. Am J Surg. 2010

Suggested Optimal Stimulus Current

- Vagus Nerve
  - with nerve exposure : 2-3 mA
  - without nerve exposure : 3 mA

- Recurrent Laryngeal Nerve
  - with nerve exposure : 1-2mA
  - without nerve exposure : 2-3 mA

- EBSLN : 0.5 –1 mA

Standardized Nerve Stimulation Procedures

- L1 : Preoperative laryngoscopy
- V1: Test of VN before identificationof the RLN
- R1: Test of RLN when it was first identified
- R2: Test of RLN after complete dissection
- V2: Test of VN after complete hemostasis
- L2 : Postoperative laryngoscopy

Equipment/Endotracheal Setup Standard

A. *Endotracheal tube*

- Intubation – short-acting NMB, drying agent
- Electrodes at cords – note depth, no rotation, no salivary pooling
- Position patient – Then verify position via –Glottic Exam or
  – Respiratory Variation
  –Then fix tube position

B. *Equipment*

- Ground electrodes - shoulder
- Monitor: -100µV event threshold
  -stimulation current 1-2 mA
  -impedance (<5 kilo ohms per electrode)
- Separate monitor and electrocautery units

C. *Initial surgical field testing*

- Stimulate ipsilateral Vagus

Nonendotracheal tube based IONM
with needle or skin adhesive electrode

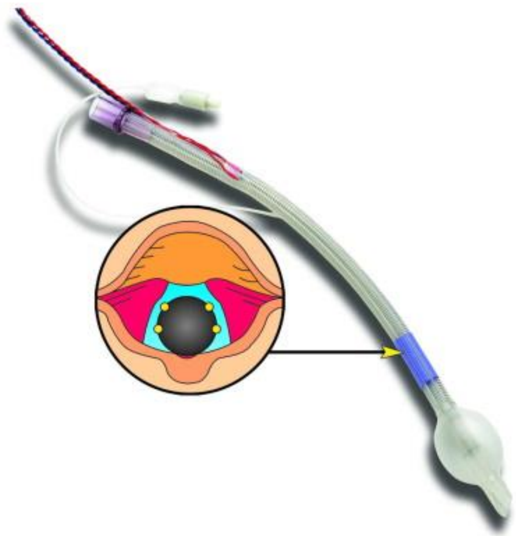
Kang-Dae Lee, M.D.

Department of Otolaryngology – H&N Surgery,
College of Medicine, Kosin University, Busan, South Korea

VI Eurasian H&N cancer Forum, July 11-14, 2019, Moscow, Russia

EMG endotracheal tube based IONM for thyroid or parathyroid surgery

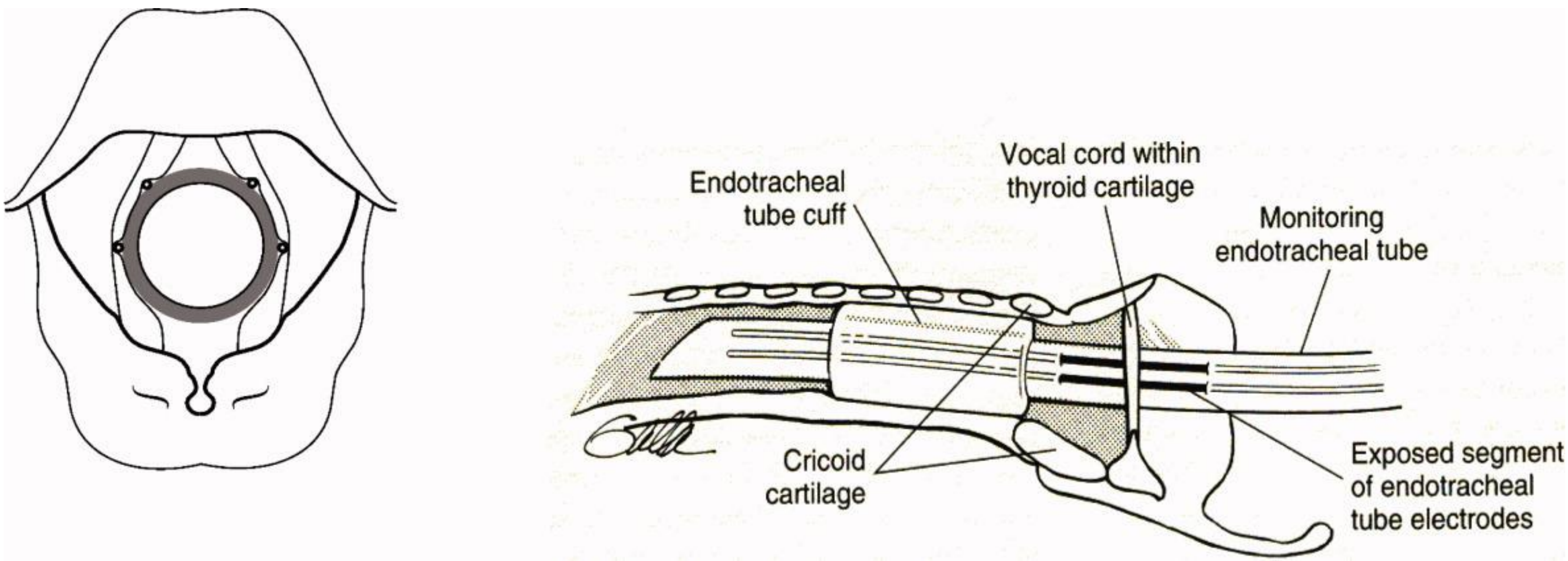
- standard in IONM of RLN and EBSLN
- a useful adjunct for intraoperative laryngeal nerve function assessment
- typically, monitoring is performed by measurement of EMG responses recorded by endotracheal tube (ETT) surface electrodes



Medtronic EMG tube

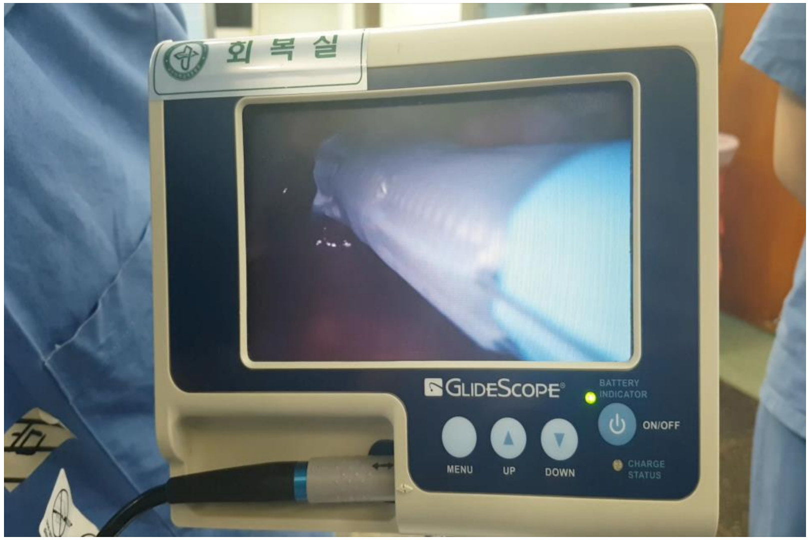
Inomed laryngeal electrode

Monitoring Tubes



- significant equipment problems
  : mostly relating to the endotracheal tube
  : 3.8% ~ 23%

Major problems of endotracheal surface electrode



- False LOS (Loss of signal) of EMG tube

- EMG tube malposition
  - rotation
  - extrusion

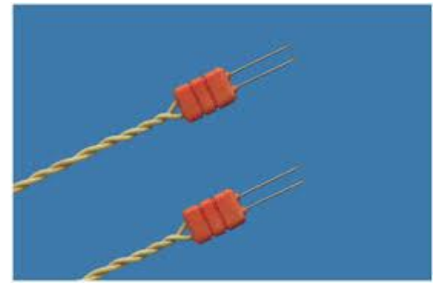
  ; time-consuming readjustment
- Saliva pooling
- Monitoring equipment dysfunction
- Misuse (repeated use) of neuromuscular blocking agent

- To overcome the limitation of EMG endotracheal tube
  - nonendotracheal tube based IONM have been studied

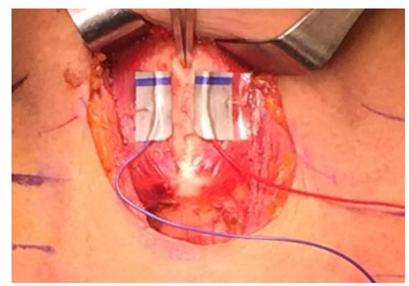
Representative studies on alternative methods of IONM (Prof. Chiang & Prof. Wu, Kaohsiung, Taiwan)

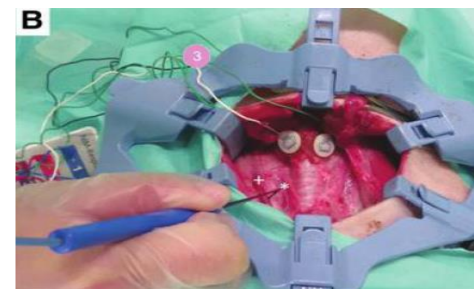
- Intubation with ordinary endotracheal tube instead of EMG tube

- **needle electrode (human study)**

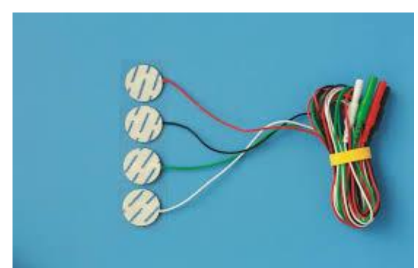


- **anterior laryngeal electrode (animal study)**





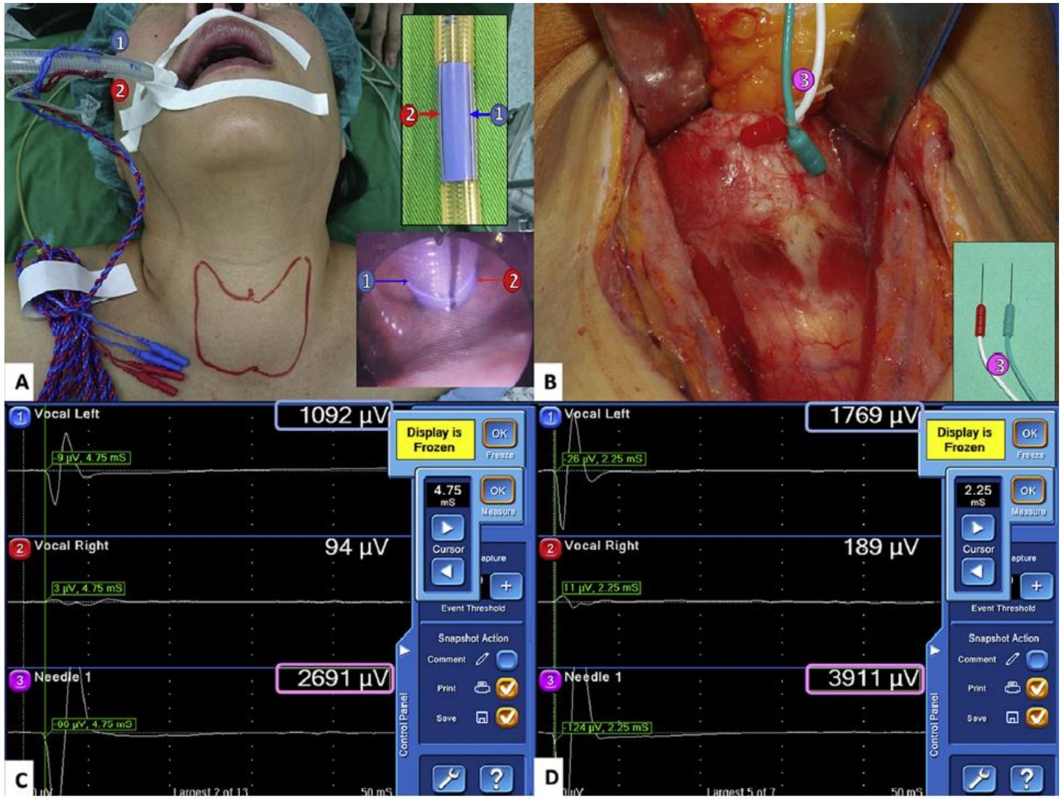
- **skin adhesive electrode to monitor the nerve (animal study)**



Kaohsiung J Med Sci. 2017 Oct;33(10):503-509. doi: 10.1016/j.kjms.2017.06.014. Epub 2017 Jul 22.

Comparison of EMG signals recorded by surface electrodes on endotracheal tube and thyroid cartilage during monitored thyroidectomy.

Chiang FY[1], Lu IC[2], Chang PY[3], Dionigi G[4], Randolph GW[5], Sun H[6], Lee KD[7], Tae K[8], Ji YB[8], Kim SW[7], Lee HS[7], Wu CW[9].

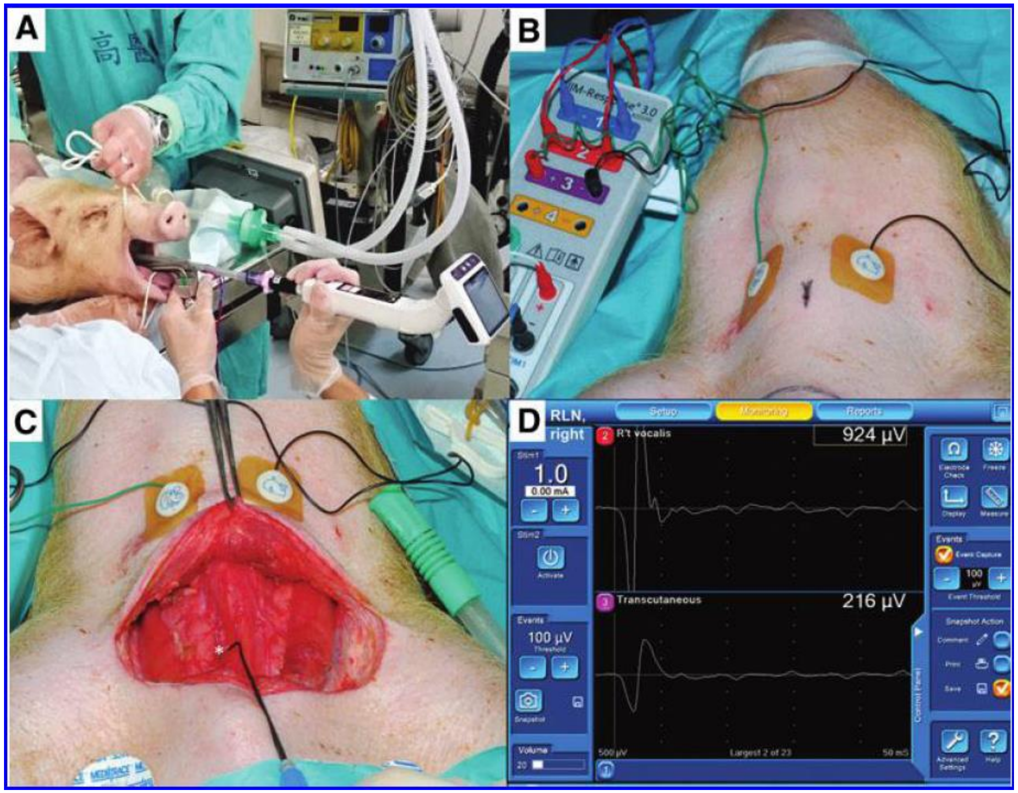


- **surface electrode of EMG endotracheal tube**
- **transcartilagenous needle electrodes in human thyroidecotmy**

Thyroid. 2018 Aug 24. doi: 10.1089/thy.2017.0679. [Epub ahead of print]

Transcutaneous Recording During Intraoperative Neuromonitoring in Thyroid Surgery.

Wu CW[1,2], Chiang FY[1,2], Randolph GW[3,4,5], Dionigi G[6], Kim HY[7], Lin YC[1], Huang TY[1], Lin CI[1], Hun PC[8], Kamani D[3], Chang PY[9], Lu IC[2,9].



•EMG ET

•Skin electrode

- compared surface electrode of EMG tube and adhesive skin electrodes
- demonstrated the feasibility of skin electrode for IONM in a porcine model

Evaluation of feasibility of IONM

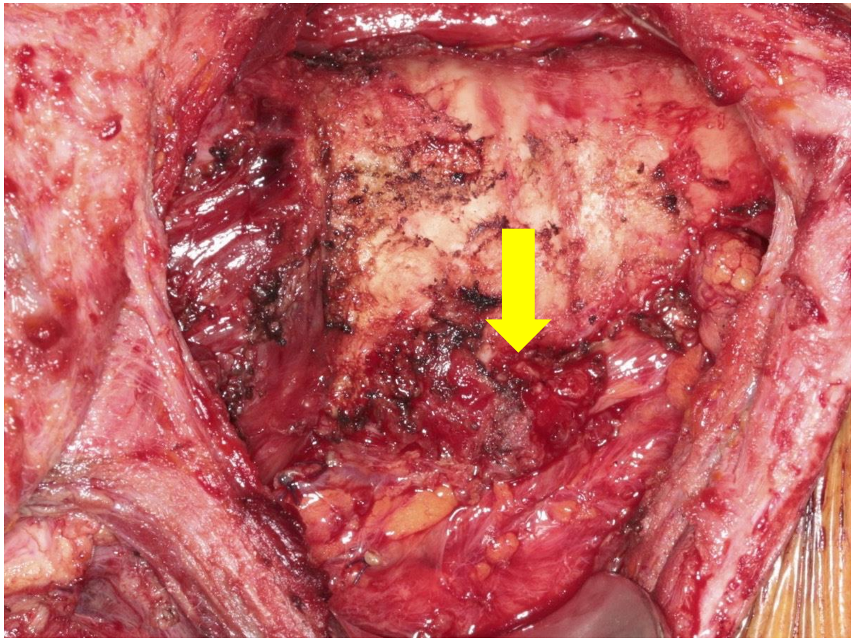
- without EMG endotracheal tube
- with ordinary endotracheal tube in human

1. Transcartilagenous needle electrode
2. Transcutaneous skin adhesive electrode

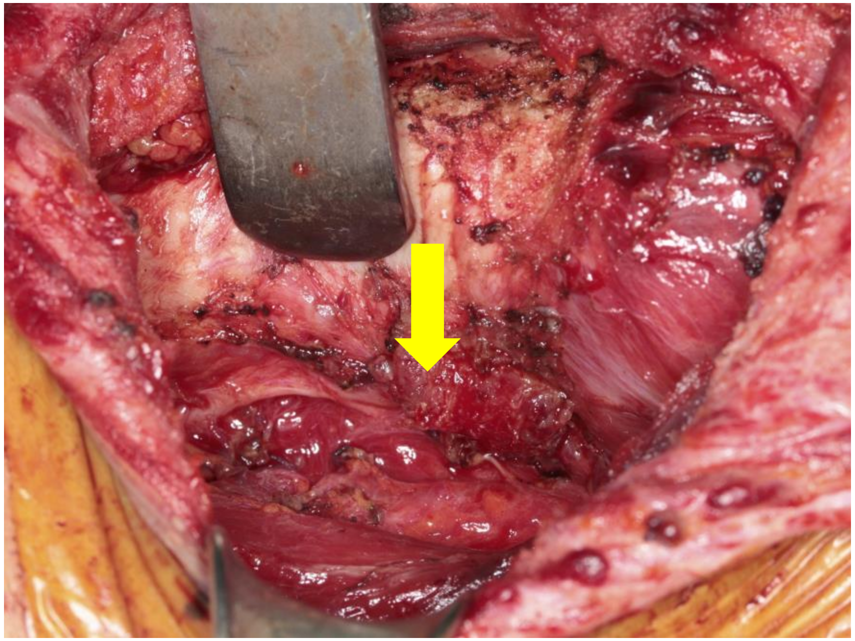
IONM with transcartilagenous needle electrode in Kosin University Gospel Hospital

A Case - bilateral RLN invasion

- Total thyroidectomy with CND
  with right selective neck dissection (II-V)



Right RLN invasion



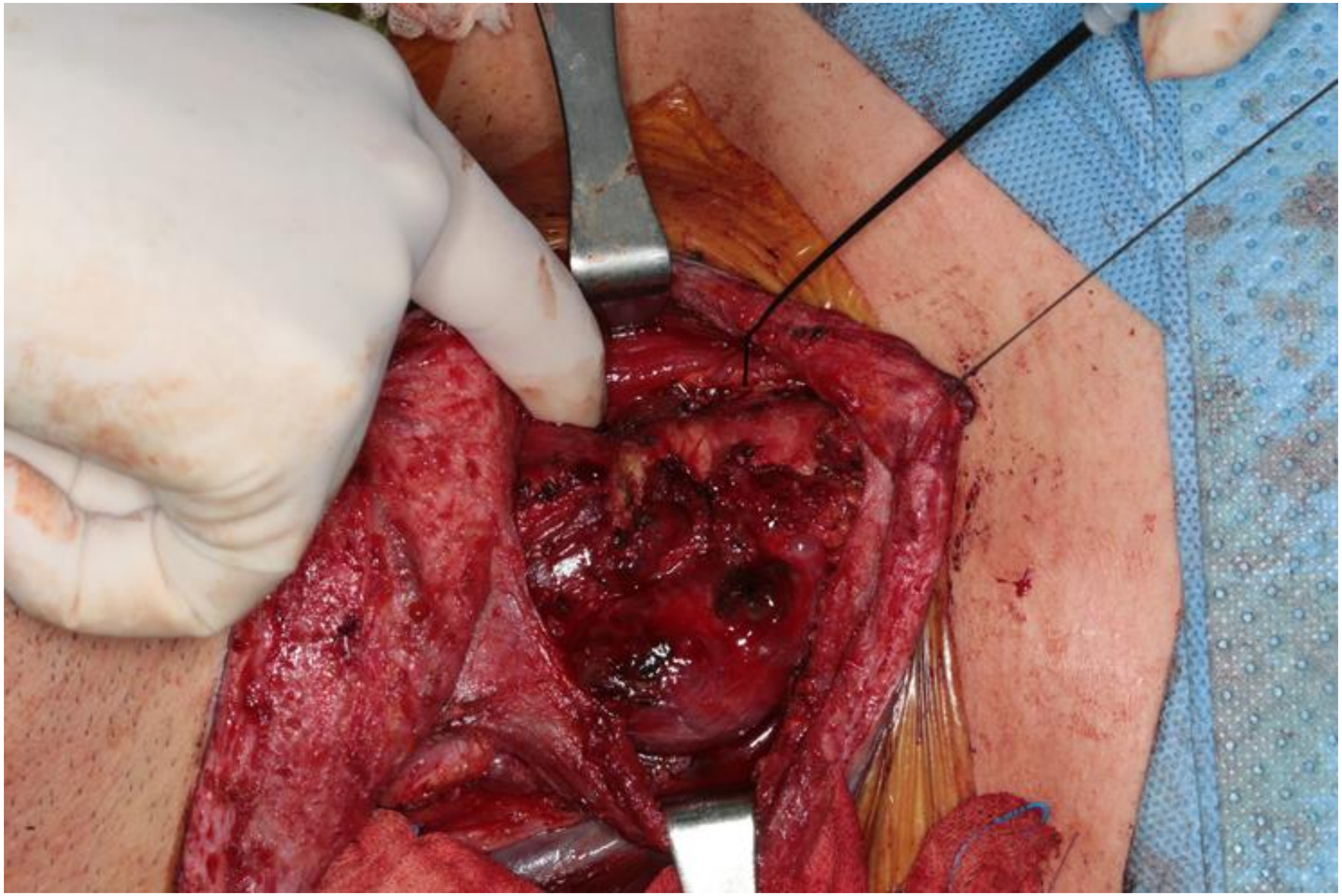
Left RLN invasion

‘LOS’ occurred at both RLN after neck rotation

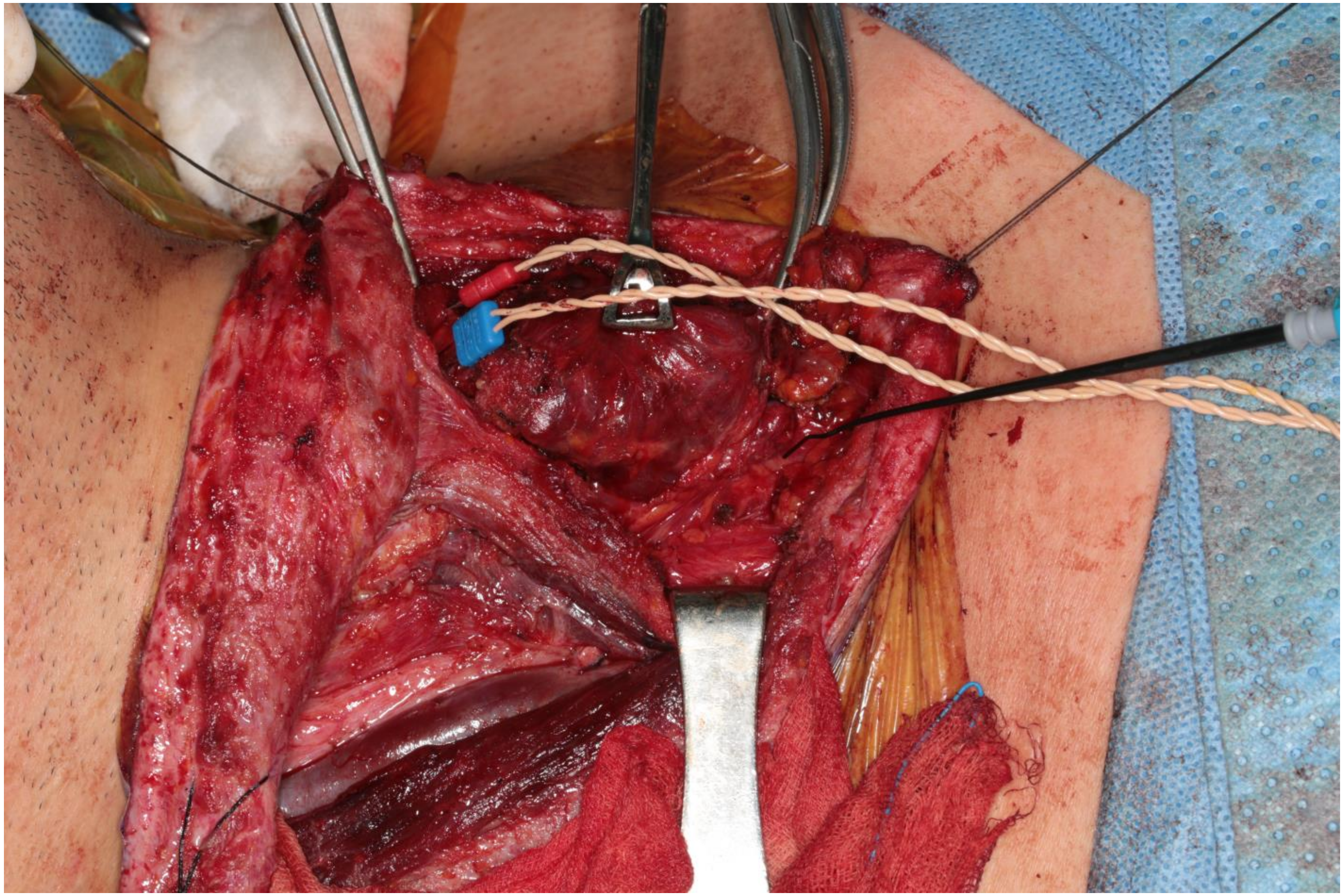
- Due to Bilateral RLN injury?
- Due to Displacement of EMG endotracheal tube?

❖ How can you discriminate false LOS from true LOS?

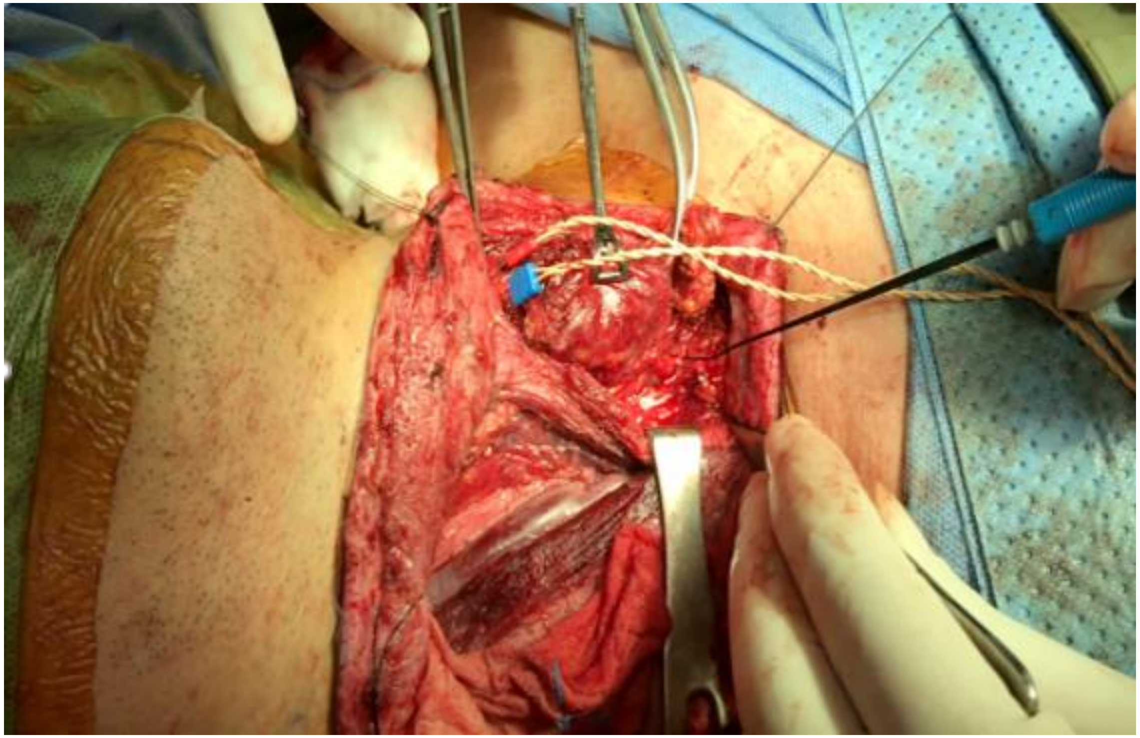
Laryngeal twitching
- one off test for RLN function



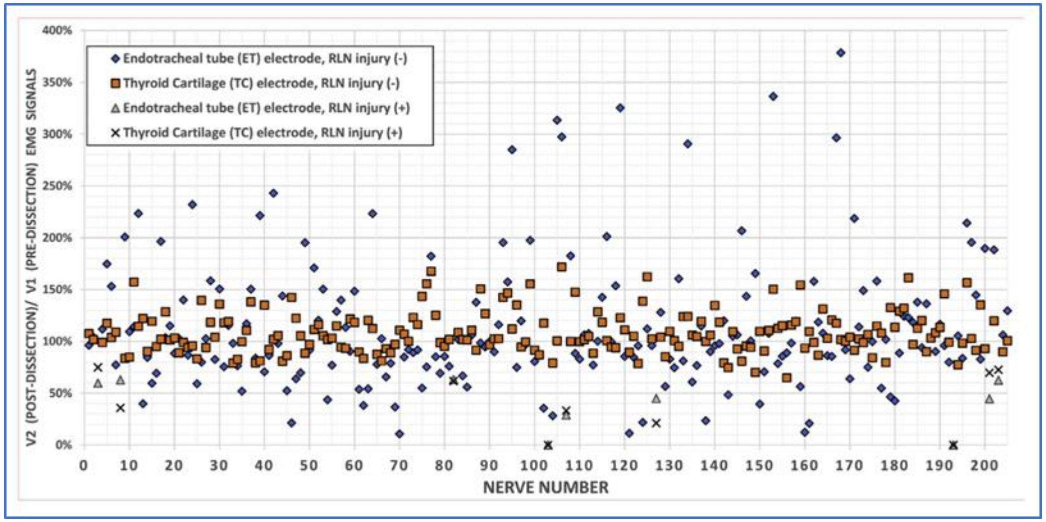
Alternative way of troubleshooting to test RLN function and maintain IONM
- transcartilagenous needle electrode



Transcartilagenous needle electrode
- concluded initial LOS was a false LOS



IONM using needle electrodes



•EMG ET

•Needle electrode

- showed typical biphasic EMG waveform and same latency time

- presented higher amplitude and more stable EMG signals than that of EMG tube

- showed no false loss of signal with needle electrode
  - while IONM with EMG tube showed false LOS in 15%

Chiang et al. Kaohsiung J Med Sci,2017

IONM with transcutaneous adhesive skin electrode

- No reports on human thyroidectomy

IONM with transcutaneous adhesive skin electrode in Kosin University Gospel Hospital

Nerve monitoring with transcutaneous adhesive skin electrode in a patient with non-RLN

Comparison of IONM with EMG endotracheal tube with skin adhesive electrode in 39 RLNs

IONM with transcutaneous adhesive skin electrode

- IONM using adhesive skin electrodes was successful with biphasic EMG signal in all 39 nerves

- although the amplitude was lower in skin electrode than that of EMG tube, latency time of EMG signal was similar

- Advantage of adhesive skin electrodes
  - May prevent false LOS interpretation of EMG tube
  - Very low cost : 5 USD (1/50 of EMG tube)
  - Easy to set (< 1 min)
- Amplitude < 100μV but still with normal biphasic EMG wave

Summary

- Needle electrode and skin adhesive electrode may be used for alternative method of IONM in selected cases, especially in case of

  1. false LOS due to EMG tube displacement

  2. when EMG tube is hard to prepare

Acknowledgement

Sung Won Kim

Hyoung Shin Lee

Jeong-Ho Oh

Department of Otolaryngology-Head and Neck Surgery,

Chulho Oak

Department of Internal Medicine

Yeh-Chan Ahn

Yigeun Kim

Department of Biomedical Engineering Center

Grants : **Marine Biotechnology Program (20150220) funded by the Ministry of Oceans and Fisheries, Korea, and the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2017R1D1A1B03031082**