Brescia, 06/03/2025

**PHD IN INTELLIGENZA ARTIFICIALE IN MEDICINA E INNOVAZIONE NELLA RICERCA CLINICA E METODOLOGICA**

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**XXXVIII Ciclo** Supervisor: Prof. Marco Fontanella

# OPTIMIZING PREOPERATIVE DIAGNOSIS AND TREATMENT OF PITUITARY ADENOMAS USING MACHINE LEARNING AND DEEP LEARNING ALGORITHMS: A RADIOMICS AND VIDEOMICS APPROACH

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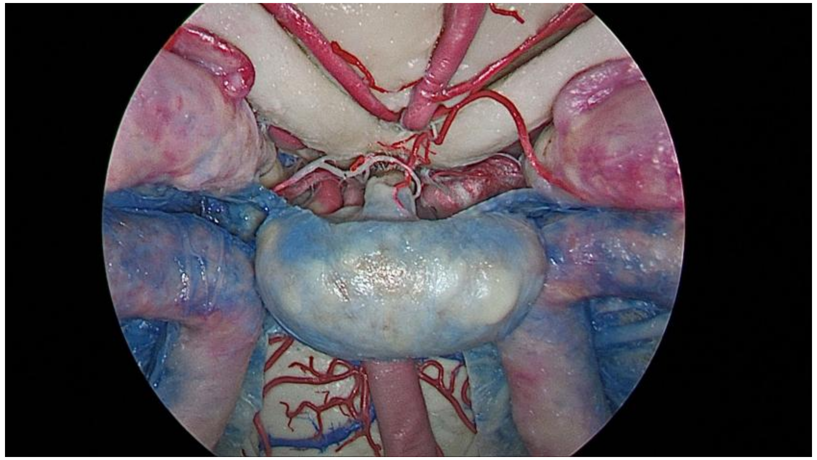
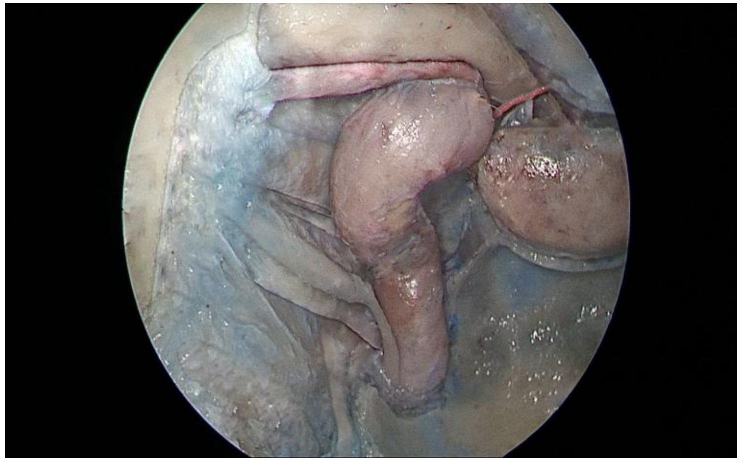
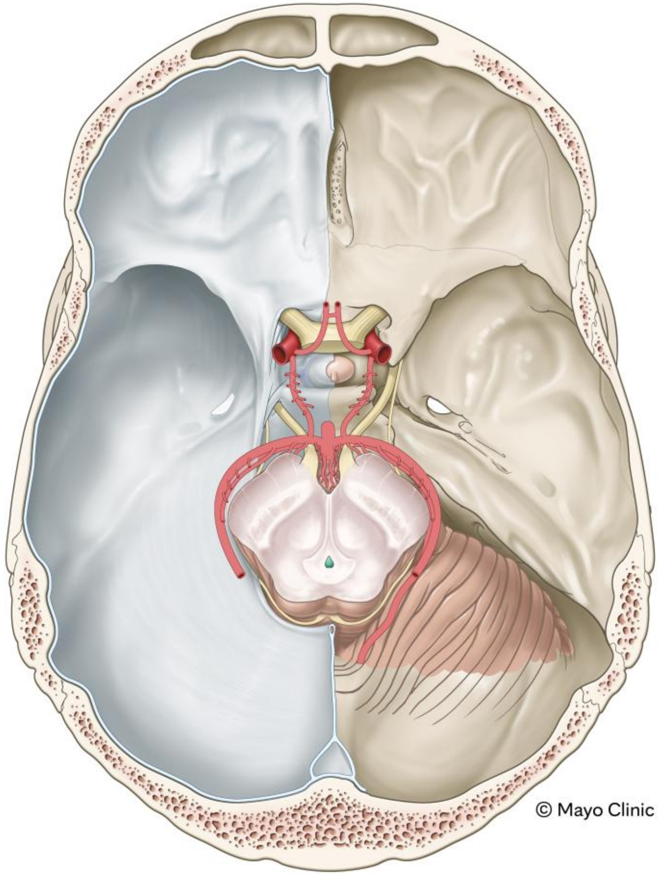
# *BACKGROUND*

- **Sellar** and **parasellar regions** are anatomically complex and contain vital neurovascular structures
- **PAs** are the most common tumors (15% of intracranial tumors, 85% of sellar and parasellar tumors)

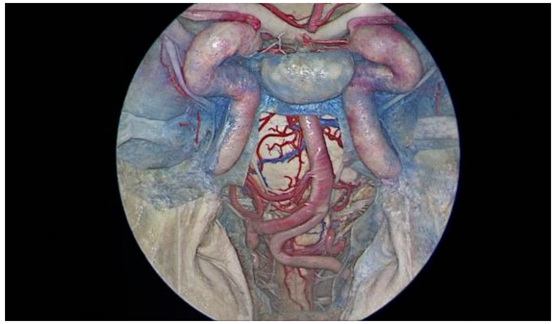


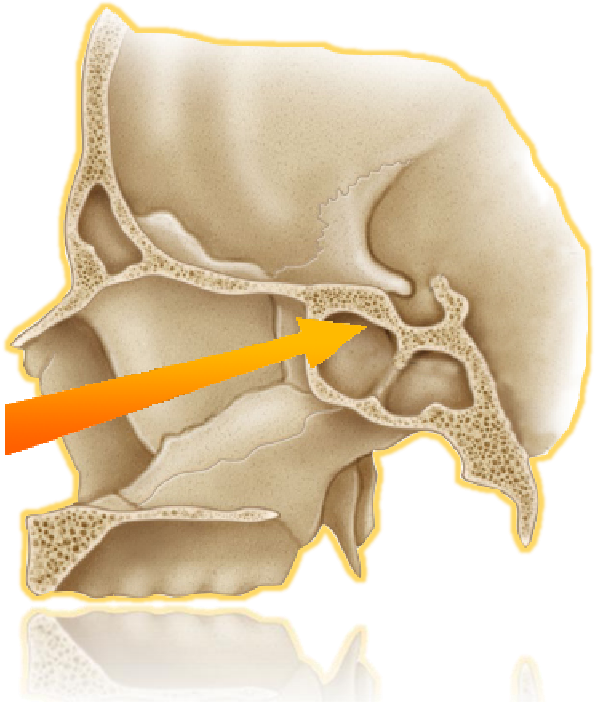


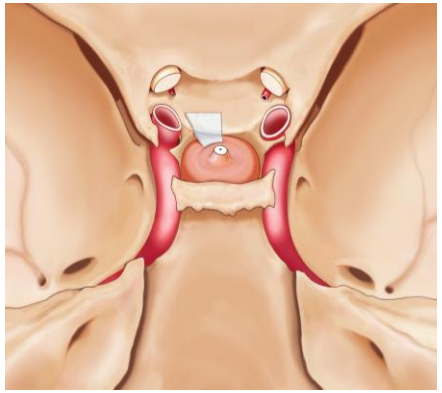


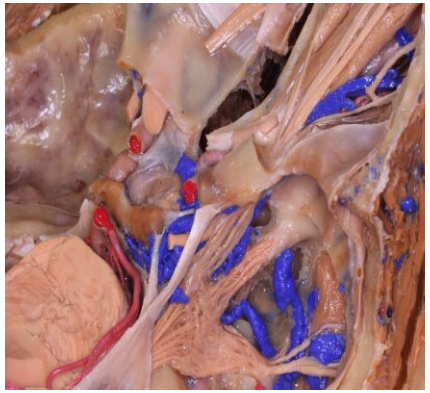
# *BACKGROUND*

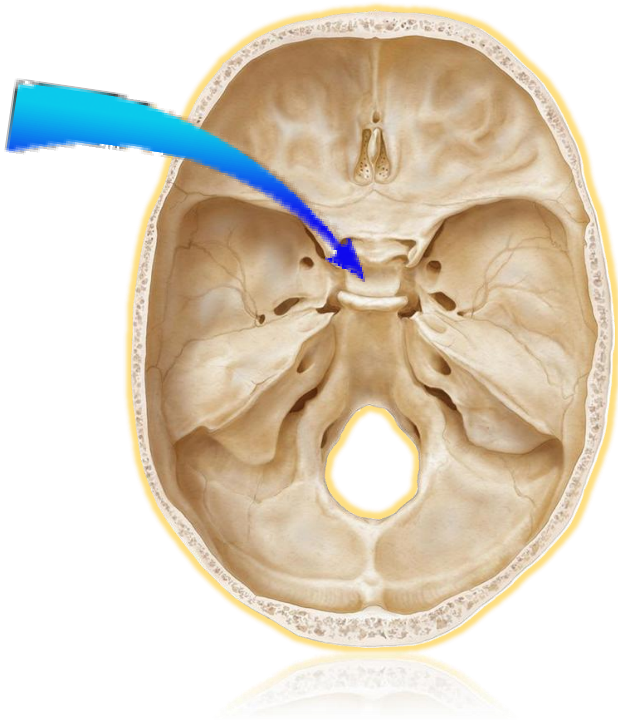
- Firstly MTAs, but now EEAs are commonly used for surgical treatment of PAs











# *BACKGROUND*

- Pre- and intraoperative challenges require technological support and interdisciplinary collaboration
- **AI**, including ML and DL algorithms, is increasingly used in medical imaging to **improve tumor diagnosis** and **treatment**
- Enhance:

- preoperative prediction of lesion features (consistency, relations with surrounding anatomy, histopathological and immunohistochemical patterns)
- intraoperative tumor detection

# *BACKGROUND*

- Apply AI methods, specifically ML and DL algorithms, to enhance the diagnosis, endoscopic surgical treatment outcomes, and prognosis of **patients with PA**
- **Radiomics** → Preoperative assessment of PA features (i.e., consistency)

- Predict tumor relation with surrounding anatomy
- Minimize iatrogenic neurovascular injuries and postoperative CSF leaks

- **Videomics** → Real-time intraoperative detections of PA

- Reduce the risk of postoperative PA remnants
- Minimize iatrogenic neurovascular injuries and postoperative CSF leaks

# PART 1: RADIOMICS FOR PAs

## RADIOMICS FOR PREOPERATIVE ASSESSMENT OF PA CONSISTENCY WITH T2-WEIGHTED MRI: A MULTICENTER STUDY

***Radiomics for Preoperative Assessment of Pituitary Adenoma Consistency with T2-weighted MRI: A Multicenter Study***

# *INTRODUCTION*

- **PA consistency** can impact on surgical (i.e., EEA) outcome: softer tumors, easier to resect
- **MRI** could be a **qualitative** tool (e.g. T2-weigthed and PA consistency prediction) to assess PA consistency

**Prediction of Consistency of Pituitary Adenomas by Magnetic Resonance Imaging**

Kyle A. Smith[1] John D. Leever[2] Roukoz B. Chamoun[1]

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[2] Department of Radiology, University of Kansas Medical Center, Kansas City, Kansas, United States

Address for correspondence Roukoz B. Chamoun, MD, Department of Neurosurgery, University of Kansas Medical Center, 3901 Rainbow Blvd., 3021, Kansas City, KS 66160, United States (e-mail: rchamoun@kumc.edu).

J Neurol Surg B 2015;76:340–343.

**Tumor Consistency of Pituitary Macroadenomas: Predictive Analysis on the Basis of Imaging Features with Contrast-Enhanced 3D FIESTA at 3T**

J. Yamamoto, S. Kakeda, S. Shimajiri, M. Takahashi, K. Watanabe, Y. Kai, J. Moriya, Y. Korogi and S. Nishizawa

*AJNR Am J Neuroradiol* 2014, 35 (2) 297-303

0148-396X/90/2605-0801$02.00/0
NEUROSURGERY
Vol. 26, No. 5, 1990
Printed in U.S.A.


**Is Magnetic Resonance Imaging Useful in Guiding the Operative Approach to Large Pituitary Tumors?**

Robert B. Snow, M.D., Ph.D., Carl E. Johnson, M.D., Susan Morgello, M.D., Michael H. Lavyne, M.D., and Russel H. Patterson, Jr., M.D.

*Divisions of Neurosurgery (RBS, MHL, RHP), Neuroradiology (CEJ), and Neuropathology (SM), The New York Hospital–Cornell Medical Center, New York, New York*

Acta Neurochir (Wien) (1998) 140: 779–786

**MRI Prediction of Fibrous Pituitary Adenomas**

**T. Iuchi, N. Saeki, M. Tanaka, K. Sunami,** and **A. Yamaura**

Department of Neurological Surgery, Chiba University School of Medicine, Chiba, Japan

*British Journal of Neurosurgery*, October 2006; 20(5): 324–326

**To assess the ability of MRI to predict consistency of pituitary macroadenomas**

B. BAHULEYAN, L. RAGHURAM[1], V. RAJSHEKHAR & A. G. CHACKO

*Departments of Neurological Sciences and [1]Radiodiagnosis, Christian Medical College, Vellore, Tamil Nadu, India*

**The Utility of Using Preoperative MRI as a Predictor for Intraoperative Pituitary Adenoma Consistency and Surgical Resection Technique**

Jonathan J. Yun[1] Stephen J. Johans[2] Daniel J. Shepherd[1] Brendan Martin[3] Cara Joyce[3] Ewa Borys[1,4] A. Suresh Reddy[5] Chirag R. Patel[1,5,6] Anand V. Germanwala[1,2,5,6]

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[5] Edward Hines, Jr. VA Hospital, Hines, Illinois, United States
[6] Department of Otolaryngology, Loyola University Medical Center, Maywood, Illinois, United States

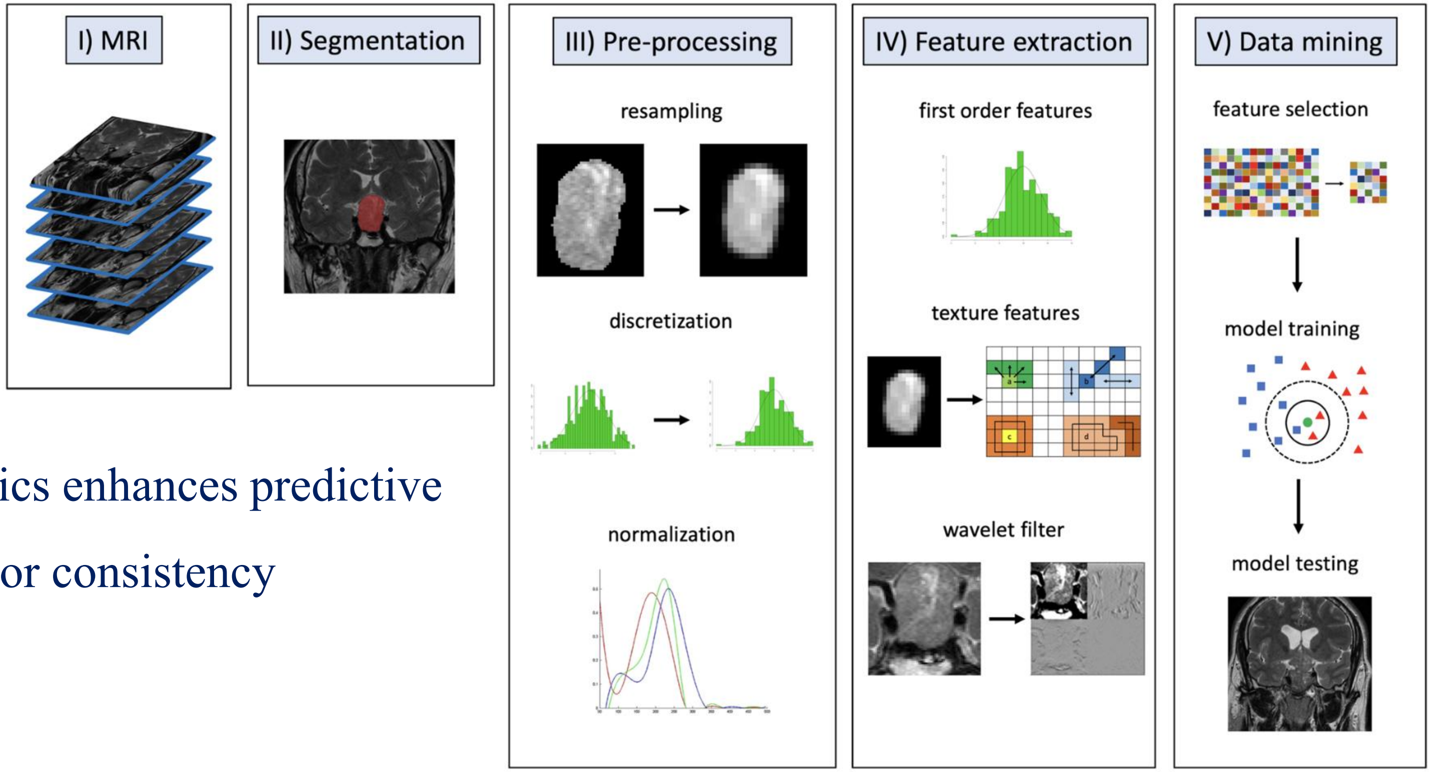
Address for correspondence Anand V. Germanwala, MD, Department of Neurological Surgery, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, United States (e-mail: agermanwala@gmail.com).

J Neurol Surg B 2020;81:651–658.

# *INTRODUCTION*

- **Radiomics**, an advanced imaging technique, transforms medical images into **quantitative data**, revealing tumor heterogeneity through texture analysis

- The integration of **ML algorithms** into radiomics enhances predictive modeling, offering the potential to classify tumor consistency



# *OBJECTIVE*

- To assess the **performance** and **accuracy** of **radiomics-based models** trained with ML algorithms to **predict PA consistency** before endoscopic surgery using texture analysis from **T2-weighted MRI**
- Preoperatively predict **soft and fibrous** PA consistency, enhancing preoperative planning and reducing postoperative complications

# *MATERIALS AND METHODS: Multicenter retrospective registry*

- Ethical approval: Institutional Review Board (**IRB-5924**)
- Patients with **PA** who underwent **preoperative MRI** and **EEA** from January 2012 to December 2023
- Four centers included:

- University of Brescia, Spedali Civili of Brescia
- University of Naples "Federico II," University Hospital Federico II, Naples
- Ca' Foncello Hospital, Treviso
- University of Insubria, Circolo Hospital and Macchi Foundation of Varese

## *MATERIALS AND METHODS: Multicenter retrospective registry*

➢ **Exclusion Criteria**:

- Pediatric patients
- Neoadjuvant RT or CT
- Other simultaneous sellar / parasellar lesions
- Extensive tumor necrosis or hemorrhage
- Significant MRI artifacts

# *MATERIALS AND METHODS: MRI data acquisition*

- **MRI Equipment**: 1.5T or 3T scanners from Philips (Gyroscan Intera) and Siemens (Magnetom Trio)

- **MRI Protocol**: **Coronal T2-weighted Turbo Spin Echo** (T2-w TSE) sequence

T2-w TSE specific acquisition parameters

| | TR | TE | FOV | matrix | thk | ETL | Slice gap | Acquisition time |
|---|---|---|---|---|---|---|---|---|
| **1.5 Tesla** | 2600 ms | 89 ms | 180x180 mm | 288x288 | 3 mm | 17 | no gap | 2 min 17 s |
| **3 Tesla** | 3000 ms | 98 ms | 200x200 mm | 384x384 | 3 mm | 18 | no gap | 3 min 22 s |

- Ensure consistent data for radiomics feature extraction
- Proven best sequence for radiomics prediction of tumor texture and heterogeneity

Neuroradiology
https://doi.org/10.1007/s00234-019-02266-1

**Prediction of high proliferative index in pituitary macroadenomas using MRI-based radiomics and machine learning**

Lorenzo Ugga [1] · Renato Cuocolo [1] · Domenico Solari [2] · Elia Guadagno [3] · Alessandra D'Amico [1] · Teresa Somma [2] · Paolo Cappabianca [2] · Maria Laura del Basso de Caro [3] · Luigi Maria Cavallo [2] · Arturo Brunetti [1]

Neuroradiology (2020) 62:1649–1656
https://doi.org/10.1007/s00234-020-02502-z

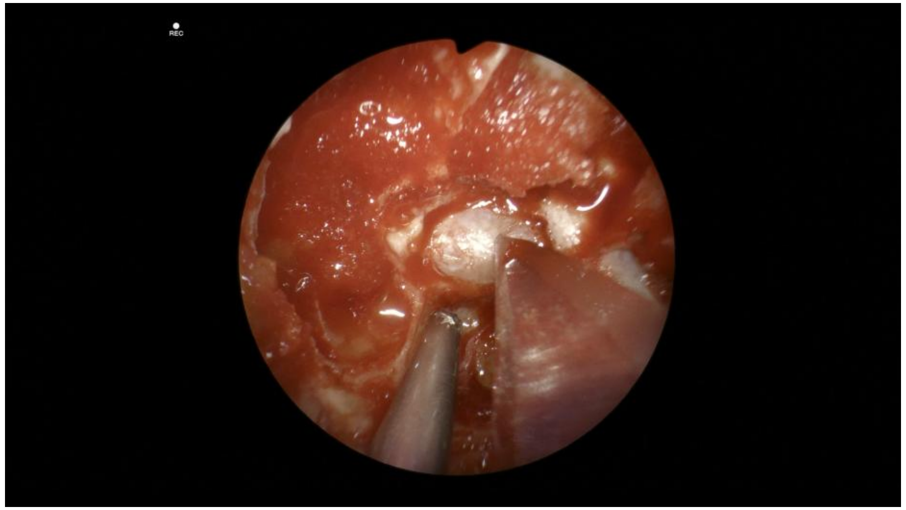
**Prediction of pituitary adenoma surgical consistency: radiomic data mining and machine learning on T2-weighted MRI**

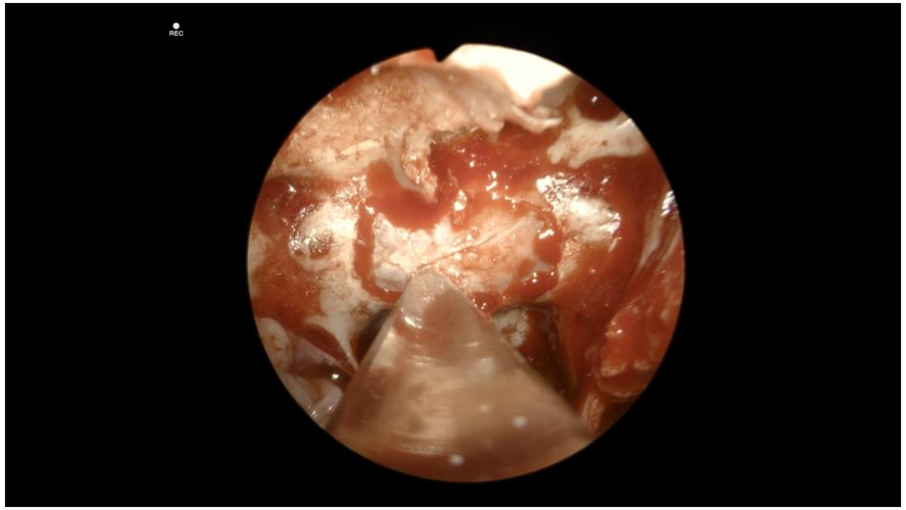
Renato Cuocolo [1] · Lorenzo Ugga [1] · Domenico Solari [2] · Sergio Corvino [2] · Alessandra D'Amico [1] · Daniela Russo [1] · Paolo Cappabianca [2] · Luigi Maria Cavallo [2] · Andrea Elefante [1]

# *MATERIALS AND METHODS: Preoperative consistency assessment*

- Tumor consistency was independently assessed by two neurosurgeons (i.e., **intraoperative report**, **surgical video**)
- The classification was based on intraoperative tumor texture and resistance to manipulation

- **Soft PA**: easily removed with standard surgical instruments like suction and curettage, deforming and fragmenting
- **Fibrous PA**: denser, requiring meticulous extracapsular dissection and microdissectors

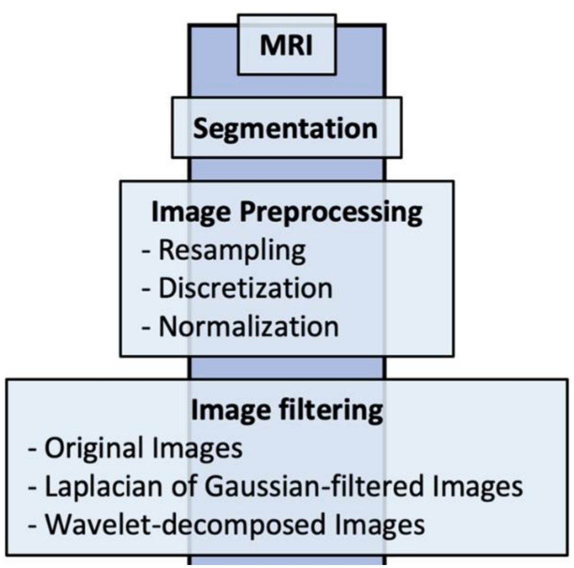




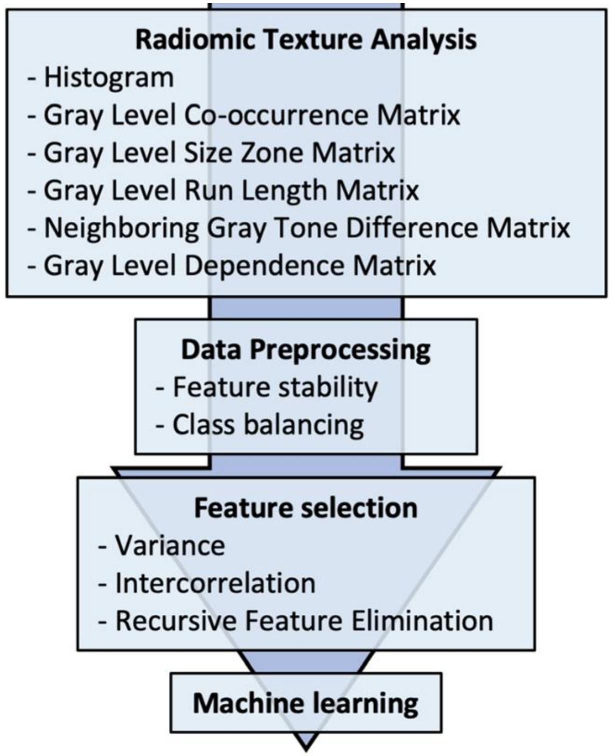
# *MATERIALS AND METHODS: Radiomics analysis*

- Description of the **radiomics workflow pipeline**

1) Image processing

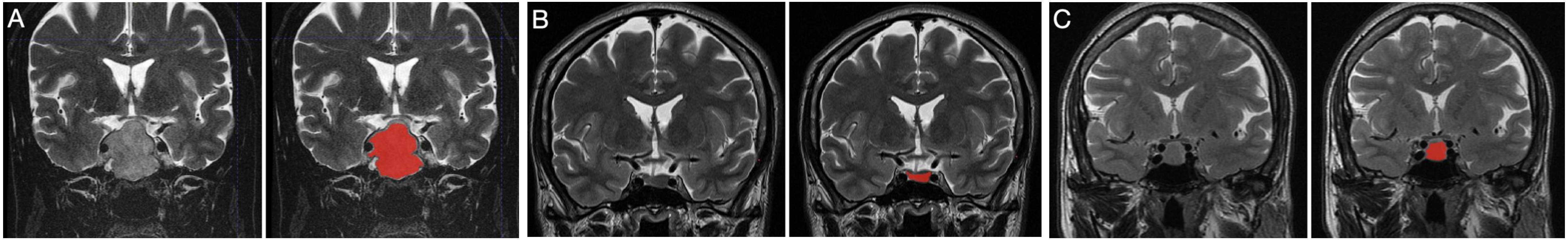



2) Radiomics analysis



# *MATERIALS AND METHODS: Imaging segmentation*

- PA **manual segmentation** using **ITK-SNAP** software by one author
- Two additional authors independently repeated the segmentation to ensure unbiased and reproducible radiomic feature extraction




Case 1: Macro-PA    Case 1: Micro-PA    Case 3: PA

# *MATERIALS AND METHODS: Radiomics analysis and ML algorithms*

- **Pyradiomics → image pre-processing** and **feature extraction**
- **Python → data processing**

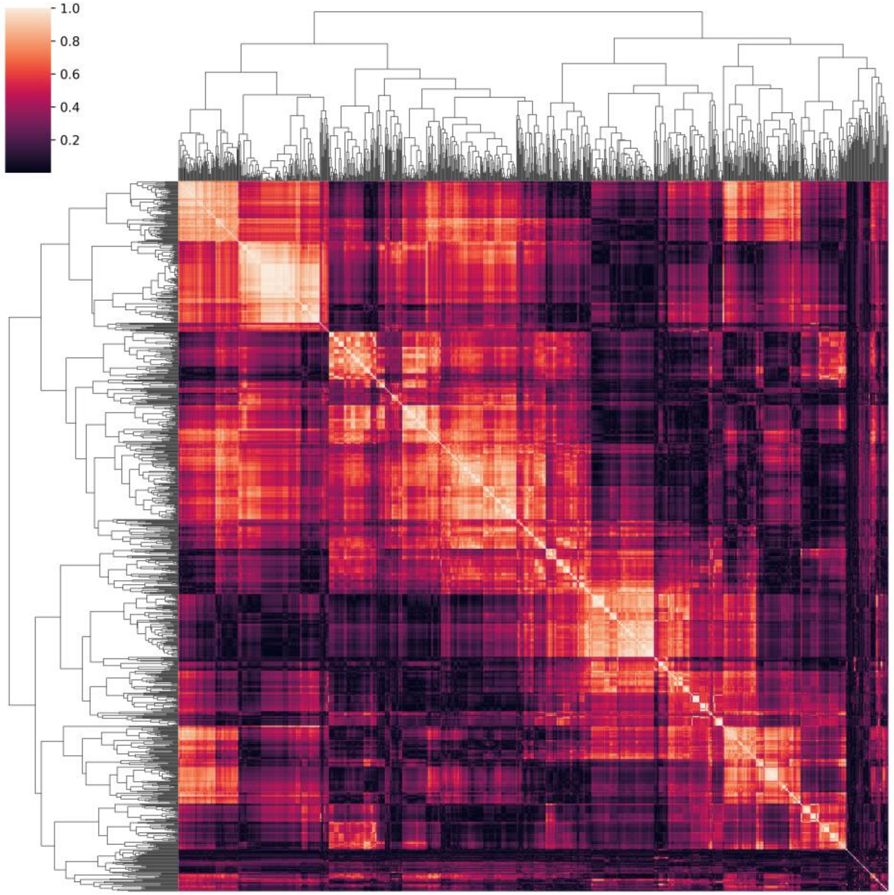
- Intraclass correlation coefficient (**ICC**) → minimize inter-observer variability (threshold of ≥ **1** to confirm the consistency)
- Recursive Feature Elimination (**RFE**) → select the most relevant features

- **SMOTE technique** was applied to reduce **class imbalance** (rarity of fibrous PA)
- Model selected, **Extra Trees (ET) classifier,** was trained, estimating the **AUC-ROC curve** (classifier **performance**) and **confusion matrix** (classifier **accuracy**)

# *RESULTS: Selected features*

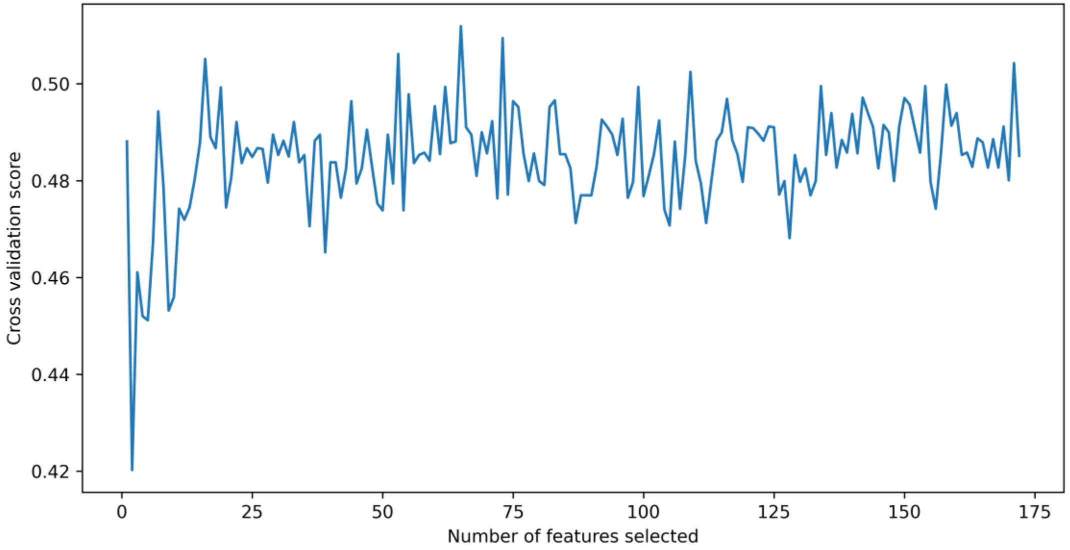
- **394** patients: 311 soft, 83 fibrous
- A total of **1,106** texture features were extracted
- **Features selection**:

- Heatmap of the **correlation matrix** was produce using hierarchical clustering
- **767** features were selected showing **high ICC** (threshold ≥ 1)



# *RESULTS: Selected features*

- Among these, **167** exhibited **low variance**
- **RFE** subsequently identified a refined subset of **65** features as the most predictive

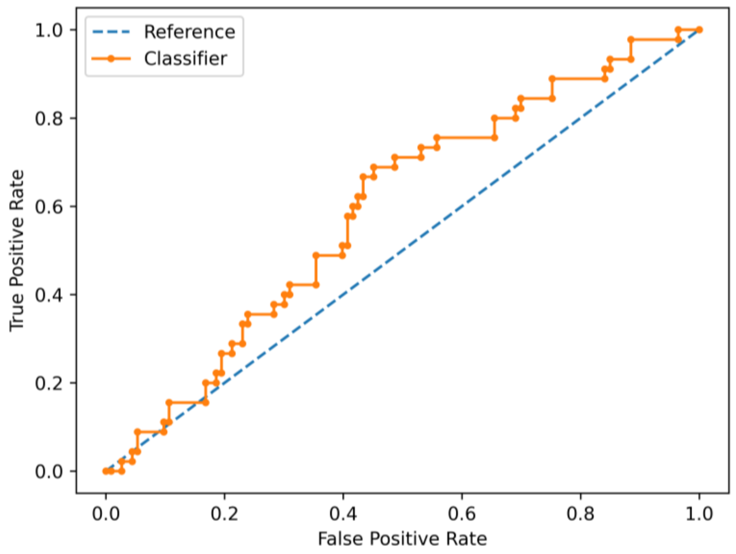



RFE plot: at each iteration, one feature is eliminated from the total number of features (x-axis); average cross-validation score for each feature total is shown on the y-axis

*Radiomics for Preoperative Assessment of Pituitary Adenoma Consistency with T2-weighted MRI: A Multicenter Study*

# *RESULTS: ET classifier*

➢ Model performance (**AUC-ROC curve**) was **0.59** with an **accuracy** of **63%** (± 10%) in the test set




| | | Precision | Recall | *F*-score |
|---|---|---|---|---|
| **Soft** | | 0.74 | 0.74 | 0.74 |
| **Fibrous** | | 0.36 | 0.36 | 0.36 |
| **Accuracy** | Macro Avg | 0.55 | 0.55 | 0.55 |
| | Weighted Avg | 0.63 | 0.63 | 0.63 |

Accuracy metrics for the ET classifier details

➢ Correctly classifying most lesions with a **SE** of **74%** and a **SP** of **74%**

# *CONCLUSION*

- **T2-weighted MRI radiomics** is a valid tool for preoperative **prediction of PA consistency**

- **ET model** provides modest classification performance and accuracy in distinguishing **soft and fibrous PAs** preoperatively

# *CONCLUSION*

➢ **Future perspectives** to improve model accuracy and performance

- Objective methods to assess PA consistency intraoperatively → E.g., elastography
- Further subcategorization of PAs → Fibrous, soft, and mixed
- DL approaches → Improve statistical power
- Automated segmentation methods → Reduce variability in tumor delineation

# PART 2: VIDEOMICS FOR PAs

## DEEP LEARNING FOR AUTOMATIC SEGMENTATION OF PITUITARY ADENOMAS:

## A VIDEOMICS STUDY

***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

## *INTRODUCTION*

- **Videomics** = Integration of AI (i.e., ML and DL algorithms) to video-endoscopy to enhance diagnostic accuracy (e.g. distinction of pathological from healthy tissue) by providing real-time video analysis during surgery
- **First application** of videomics in videoendoscopy:
  - GI lesions (Fig. 1)
  - Laryngeal lesions (Fig. 2)

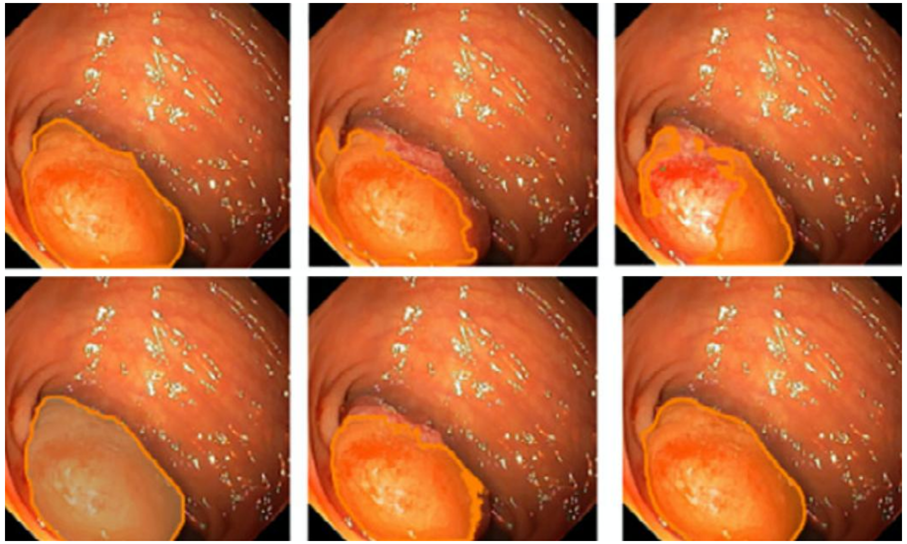


Fig. 1

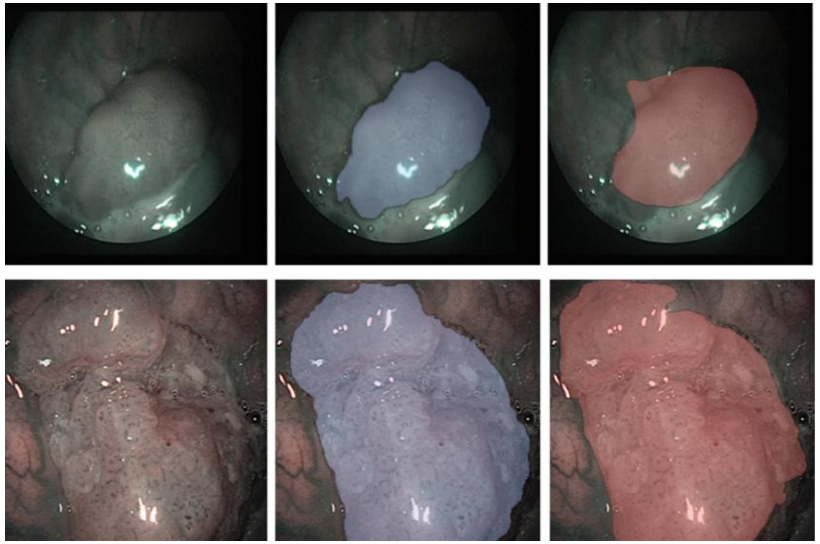


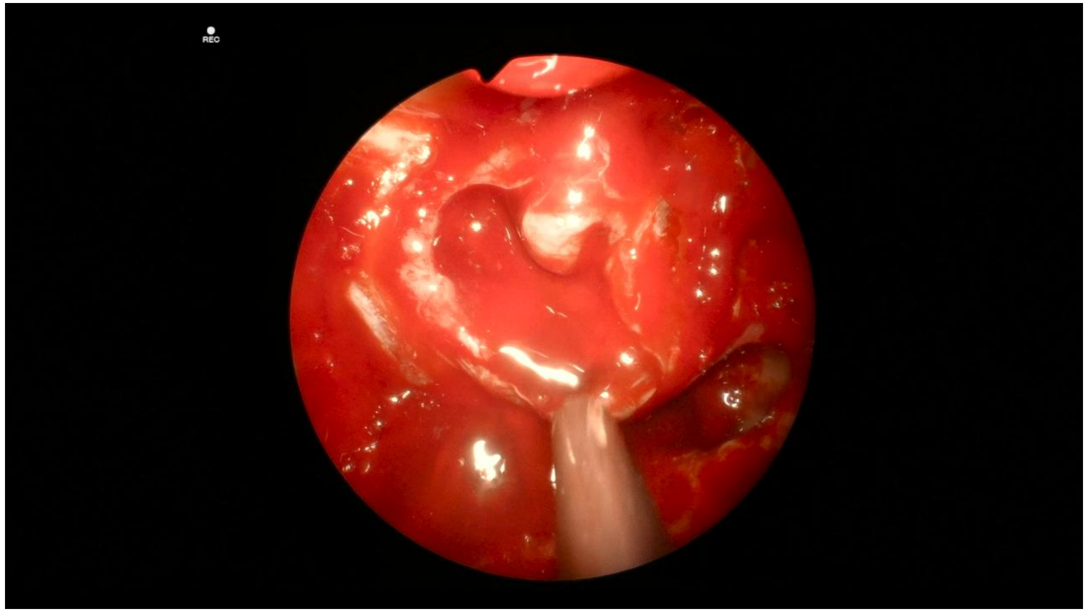
Fig. 2

***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

# *INTRODUCTION*

➢ **PA surgery** (especially in final stages) pose unique **challenges** for accurate identification and differentiation of PA from healthy tissue:

- Technical issues: low contrast, obstructed views, or variable lighting
- Surgical issues: blood, fall of the arachnoid



***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

# *OBJECTIVE*

- Validate videomics techniques to create **models for automatic real-time intraoperative recognition of PA**

- Translation to **clinical applications,** supporting surgeons in:

- Distinction of PA from other tissues
- Reduce the risk of intraoperative iatrogenic injury of neurovascular structures
- Reduce the risk of postoperative tumor remnants
- Enhance patient clinical outcomes

***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

## *MATERIALS AND METHODS*

### *Retrospective registry*

- District Institutional Review Board (**IRB-5925**)
- Data were **retrospectively** collected from medical records of tertiary referring Institution (**Spedali Civili, Brescia**)
- **Inclusion criteria**:
  - Patients with histologically-confirmed PAs after EEA (January 2022 - December 2023)
  - Complete medical records, surgical documentation, and video-endoscopy
- **Exclusion Criteria**:
  - Patients under 18 years of age
  - Patients with a history of previous treatments for sellar or parasellar diseases
  - Patients who had undergone prior treatments for PA or extensive tumor necrosis or hemorrhage

## *MATERIALS AND METHODS*

### *Video-endoscopy data acquisition*

- 0-degree **endoscope** (4 mm, 17.5 cm, Olympus Medical Systems Corporation) with both white light and NBI

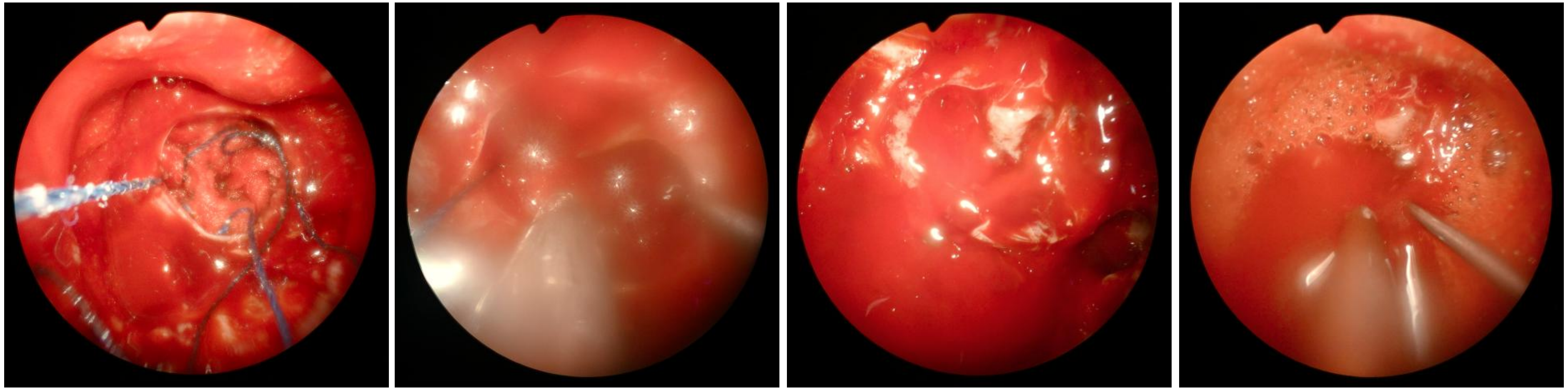
- The endoscope was paired with CH-S400_XZ-EB **camera** connected to an VISERA 4K UHD CLV-S400 **light source** (Olympus Medical Systems Corporation)


***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

## *MATERIALS AND METHODS*

### *Video-frames selection*

- NBI video-frames were **manually selected** from PA video-endoscopies
- Video-frames **dataset**: 20 video-endoscopies → 35 video-frames per video → **700** video-frames
- Video-frames **exclusion criteria**: Out of focus, too dark, major bleeding, major interposition of cottonoids or other synthetic materials



## *MATERIALS AND METHODS*

### *Video-frames categorization*

➢ Video-frames were randomly distributed into **3 subsets**:

- 80% for training
- 10% for validation
- 10% for testing

➢ **Random distribution →** Reduce selection bias

***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

# *MATERIALS AND METHODS*

## *Video-frames elaboration*

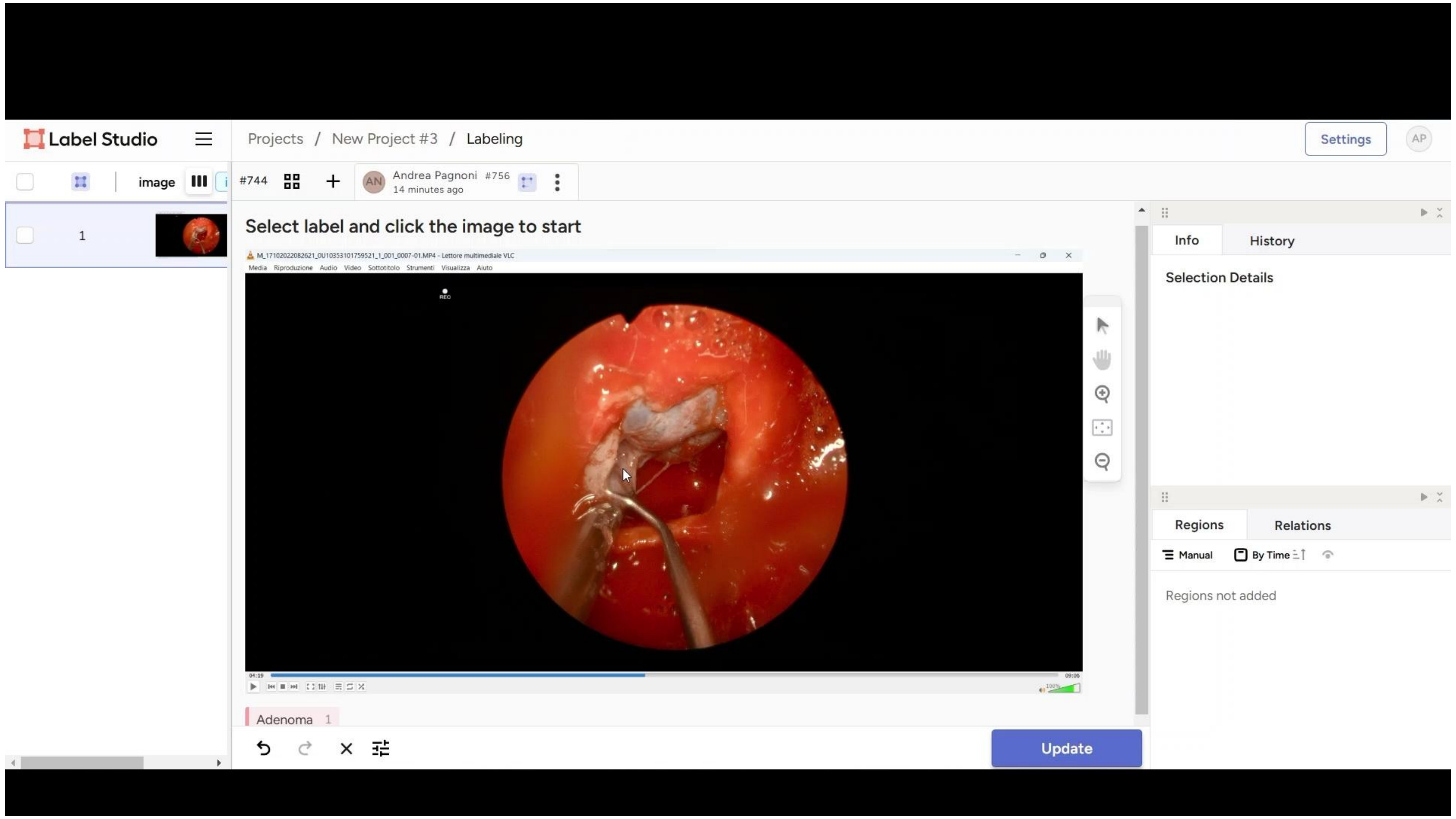
- **Preprocessing** and **augmentation** techniques were applied to the selected video-frames to increase the effective dataset size

- Preprocessing: Images were resized using a fill method, incorporating a center crop to standardize dimensions to 640x640 pixels.
- Augmentation: Each image in the training set was augmented to generate five variants using the following transformations:
  - Flip: Horizontal and vertical flipping
  - Crop: 0% minimum zoom, 20% maximum zoom
  - Rotation: Between -15° and +15°
  - Hue: Between -20° and +20°
  - Saturation: Between -25% and +25%
  - Brightness: Between -15% and +15%
  - Exposure: Between -10% and +10%
  - Noise: Up to 1.68% of pixels

# *MATERIALS AND METHODS*

## *PA segmentation on video-frames*

- Video-frames were uploaded in **Label Studio** for semantic segmentation

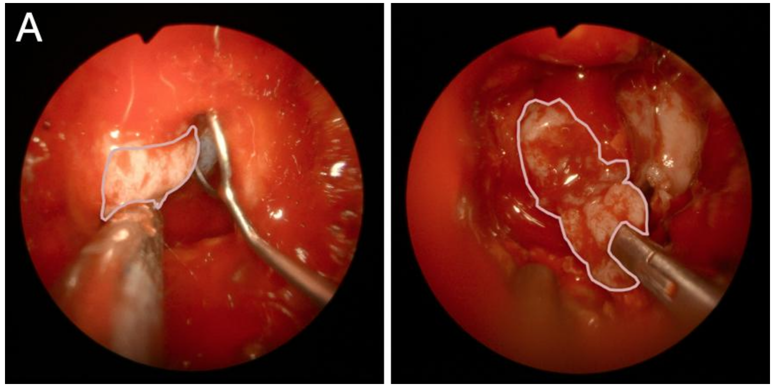


*Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective*

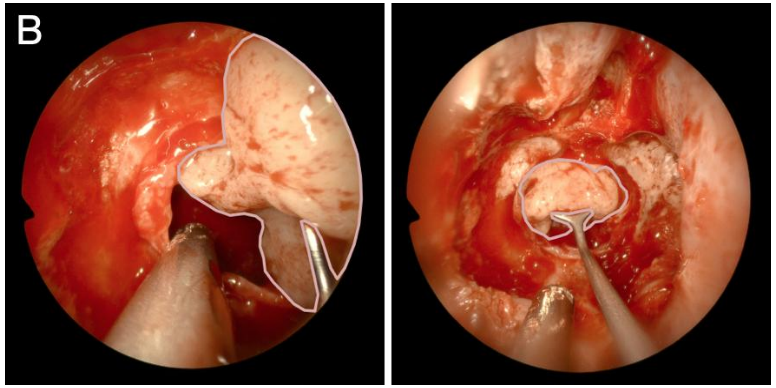
## *MATERIALS AND METHODS*

### *PA segmentation on video-frames*

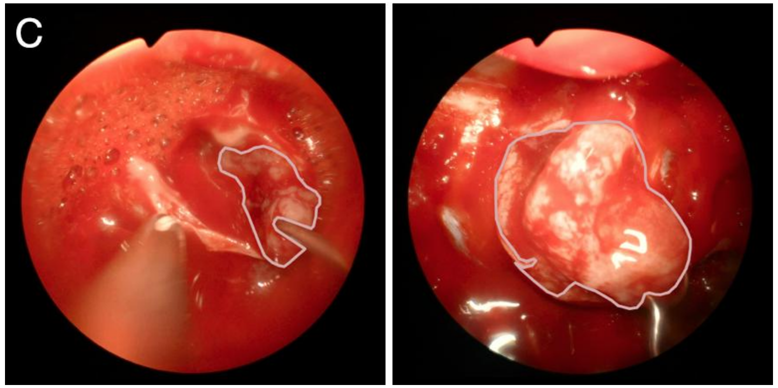
- The corresponding **masks** of the PA segmented were stored in **.json** format and used to train Fully Convolutional Neural Networks (FCNNs) for automatic segmentation (i.e., models for automatic segmentation)



Case 1



Case 2

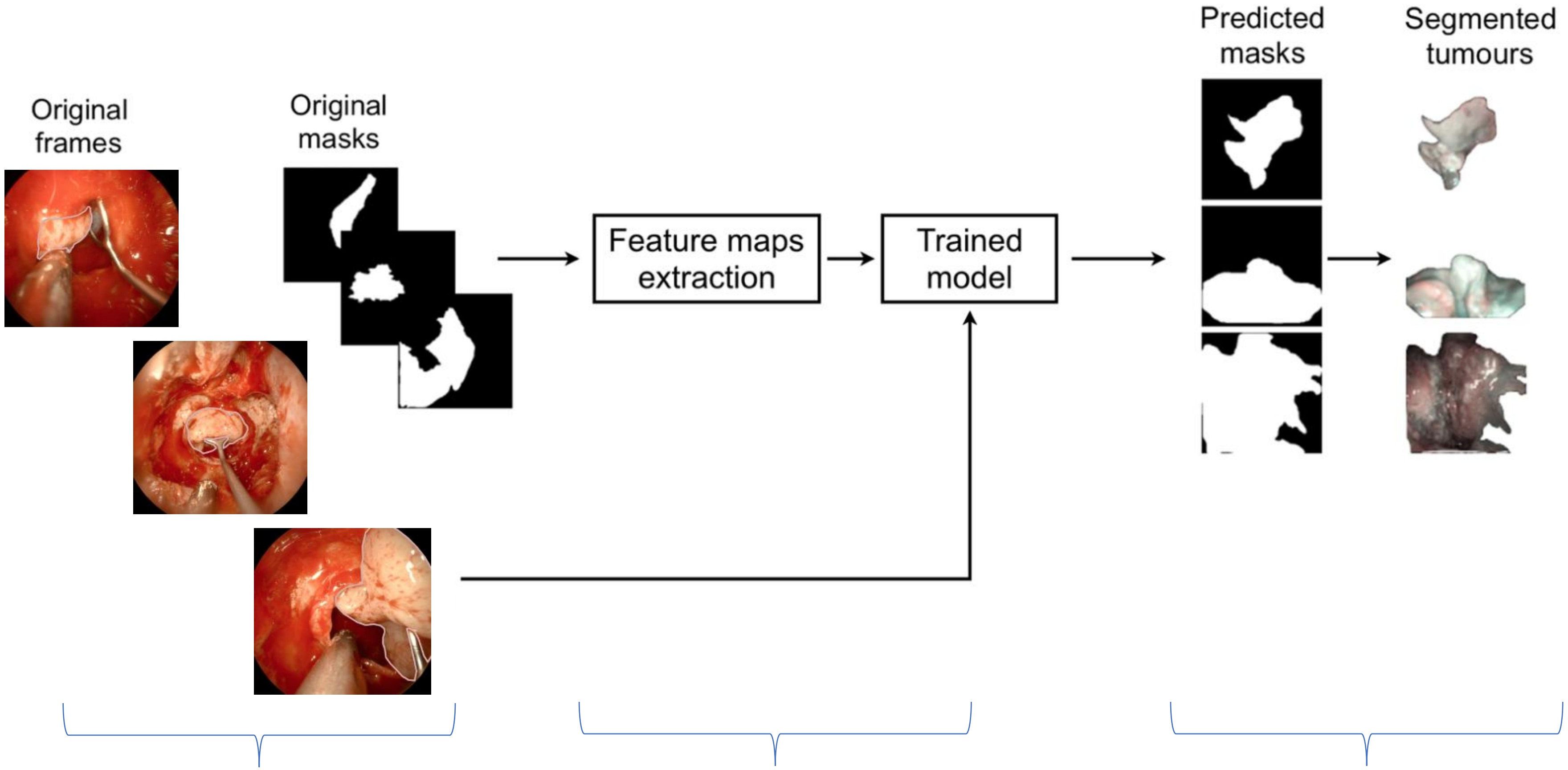


Case 3

## *Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective*

# *MATERIALS AND METHODS*

## *Workflow from manual to automatic segmentation models*




Manual segmentation

Model training
- ML / DL analysis

Automatic segmentation by model trained

***Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective***

## *MATERIALS AND METHODS*

### *Automatic segmentation models selection*

➢ Two DL frameworks were trained for image automatic segmentation:

1) **YOLO models** → 6 models, including:

- YOLOv8x-seg
- YOLOv8n-seg
- YOLOv9c-seg
- YOLOv9e-seg
- YOLOv11x-seg
- YOLOv11n-seg

2) **MMDetection models** → 3 models, including:

- Cascade Mask R-CNN 50
- Cascade Mask R-CNN 101
- Swin Transformer

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# *MATERIALS AND METHODS*

## *ML and DL analysis: Training set*

- All models were trained on an **NVIDIA RTX 3090 Ti GPU** software with:
- Adam optimizer protocol for YOLO models
- Stochastic Gradient Descent protocol for MMDetection models
- **Model performance** was assessed using the **mean Average Precision (mAP)** metric, calculated at an Intersection over Union (IoU) threshold of 0.5, as well as a weighted mAP across IoU values from 0.50 to 0.95
- Each model were trained for **100 epochs**
- Epoch = complete pass through the entire training dataset

*Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective*

## *MATERIALS AND METHODS*

### *ML analysis: Validation set and Test set*

- **Validation set** (70 video-frames) → Monitor model **overfitting**
  - Model performance was monitored across validation set, with **MMDetection** models showing overfitting beyond the **30th epoch**, indicated by increasing validation loss despite reduced training loss.
  - To prevent overfitting, MMDetection models were truncated at 30 epochs
  - While **YOLO** models had a more gradual training progression, their performance at 30 epochs was slightly lower than MMDetection models (truncated at **45 epochs**)
- **Test set** (70 video-frames) → Evaluate final model **generalization**, ensuring consistency and robustness

*Deep learning for automatic segmentation of pituitary adenomas using Narrow Band Imaging: Preliminary experience in a clinical perspective*

# *MATERIALS AND METHODS*

## *Statistical analysis*

- **Models performance** was evaluated against manual segmentation, using TP, TN, FP, and FN to calculate metrics like accuracy (Acc), recall (Rec), precision (Prec), and Dice Similarity Coefficient (DSC) to assess segmentation quality
  - The **DSC** measured the **overlap between manual and automatic segmentations**, with values ranging from 0 (no overlap) to 1 (full overlap).
  - The **mAP** was calculated as the average **area under the Recall-Precision curve**, and processing time for each frame was measured to assess tumor detection final performance.
- **Statistical analyses**, including the Kruskal-Wallis H-test, Mann-Whitney U test, ANOVA, and pairwise t-tests, were performed using **Jupiter Notebooks** to compare segmentation outcomes and identify significant differences between metrics at a significance level of 0.05

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# *RESULTS*

- **YOLOv8x-seg** (62 million parameters), was the top performer among YOLO models, with a validation box mAP[0.50] of 0.546, test segmentation mAP[0.50] of 0.921 and test mAP[0.50:0.95] of 0.509
- **Cascade mask R-CNN 101** (135 million parameters), was the top performer among Cascade mask models, with a validation box mAP[0.50] of 0.610, test segmentation mAP[0.50] of 0.827 and test mAP[0.50:0.95] of 0.480
- **Swin Transformer** (70 million parameters), was the overall **top performer model**, with a validation box mAP[0.50] of 0.663, test segmentation mAP[0.50] of 0.911 and test mAP[0.50:0.95] of 0.601

| Model | N. params | Val box mAP | Val mAP[0.50] | Val mAP | Test mAP |
|---|---|---|---|---|---|
| YOLOv8x-seg | 62M | 0.546 | 0.921 | 0.579 | 0.509 |
| YOLOv8n-seg | 3M | 0.536 | 0.827 | 0.466 | 0.452 |
| YOLOv9c-seg | 24M | 0.629 | 0.919 | 0.554 | 0.483 |
| YOLOv9e-seg | 56M | 0.116 | 0.216 | 0.070 | 0.000 |
| YOLOv11x-seg | 62M | NC | NC | NC | NC |
| YOLOv11n-seg | 3M | 0.600 | 0.882 | 0.513 | 0.480 |
| C Mask R-CNN 50 | 77M | 0.591 | 0.808 | 0.521 | 0.479 |
| C Mask R-CNN 101 | 135M | 0.610 | 0.827 | 0.550 | 0.480 |
| Swin Transformer | 70M | 0.663 | 0.911 | 0.620 | 0.601 |

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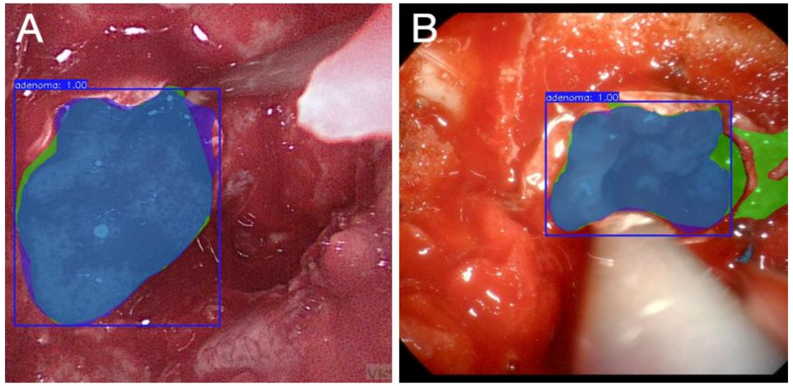
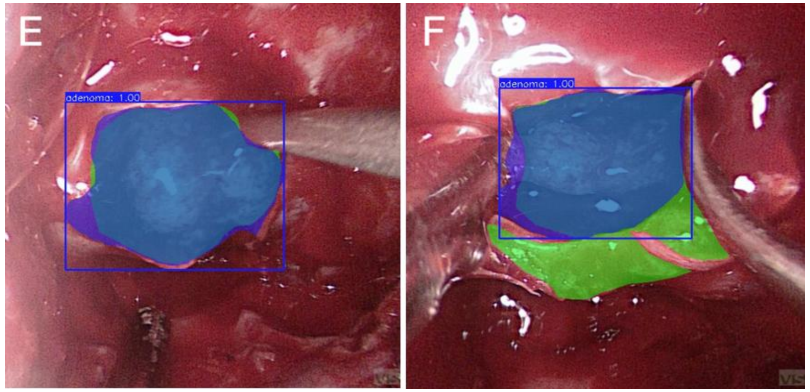
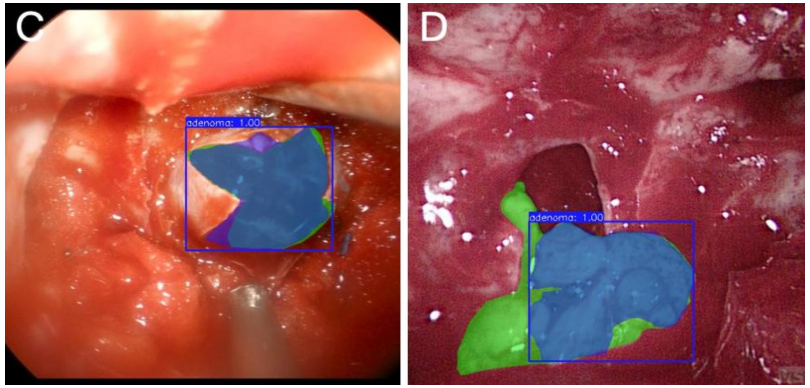
# *RESULTS*

- The Swin Transformer model demonstrated strong **generalization capabilities** in recognizing a specific target, indicating the effectiveness of transformer-based models for automatic segmentation tasks
- Examples of **six PA cases** in which Swin Transformer model predicts PA localization in the surgical field:



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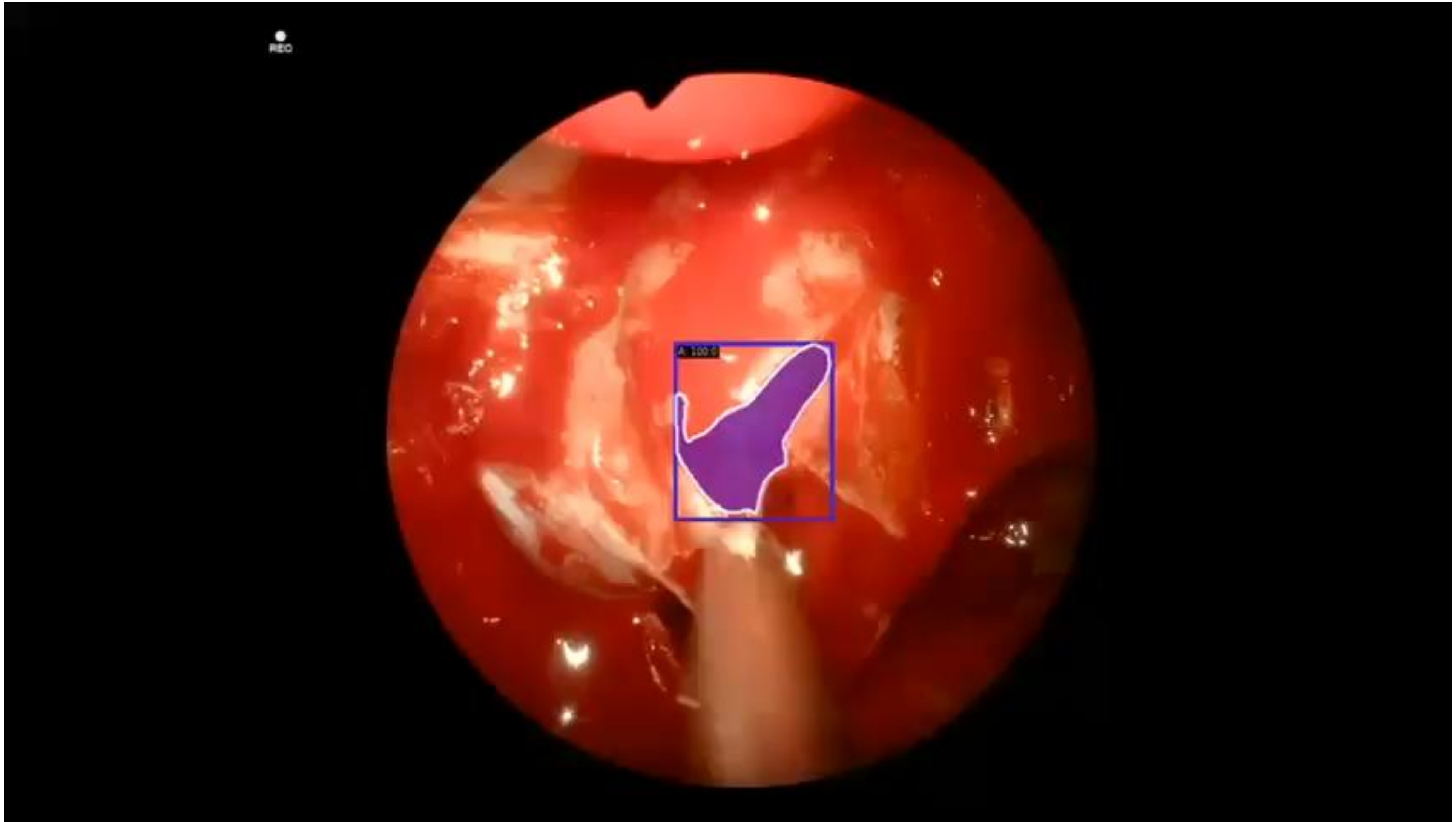
# *RESULTS*



## *CONCLUSION*

- This study demonstrated the **effectiveness** of a transformer-based model - **Swin Transformer** - for automatic segmentation of PAs, achieving the highest test mAP scores compared to YOLO and Mask R-CNN models

- This model, with its advanced self-attention capabilities, allows for precise **automatic segmentation and real-time detection** of complex anatomical and pathological structures

- Ideal candidate for **clinical applications** in endoscopic endonasal PA surgery

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# *Optimizing Preoperative Diagnosis and Treatment of Pituitary Adenomas Using Machine Learning and Deep Learning Algorithms: A Radiomics and Videomics Approach*

**Deep Learning for Automatic Segmentation of Pituitary Adenomas: A Videomics Study**

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**Radiomics for preoperative assessment of pituitary adenoma consistency with T2-weighted MRI: A multicenter study**

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# Thank you

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