설명가능 인공지능의 의료응용

2020/11/20

xaic eXplainable Artificial Intelligence Center 설명가능인공지능연구센터

연구책임자: 최재식

세부연구책임자: 김광준

http://www.openXAI.org/

■ 주관연구기관 : 울산과학기술원

■ 참여연구기관 : KAIST 한국과학기술원 | 고려대학교 | 연세대학교 의료원 YONSEI UNIVERSITY HEALTH SYSTEM | AItrics

■ 해외협력기관 : Technische Universität Berlin | Microsoft Research | IBM Watson | Penn | MICHIGAN STATE UNIVERSITY | UC DAVIS | JOHNS HOPKINS UNIVERSITY | THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL | 中國科學院 CHINESE ACADEMY OF SCIENCES

■ 미국 XAI 프로젝트 참여 협력기관 : Massachusetts Institute of Technology | UCLA | Carnegie Mellon University | SRI International

Machine learning for medical Application

Kwang Joon Kim, M.D.

Assistant Professor, Division of Geriatrics, Department of Internal Medicine, Yonsei University College of Medicine.

Vice Director, Executive Health Promotion Center, Severance Hospital.

- 대장용종
- 췌장암 및 담낭용종
- 현재 진행중인 연구와 추가 연구 계획

- 소수의 데이터 : 의료데이터
- 학습방법의 학습 : 소수의 데이터를 재학습
- 해석가능: 의료진의 판단을 돕기 위한 보조도구

대장내시경 검사시 **실시간으로** 암이 의심되는 용종을 판별하는 기술

Gastroenterology: colorectal cancer research

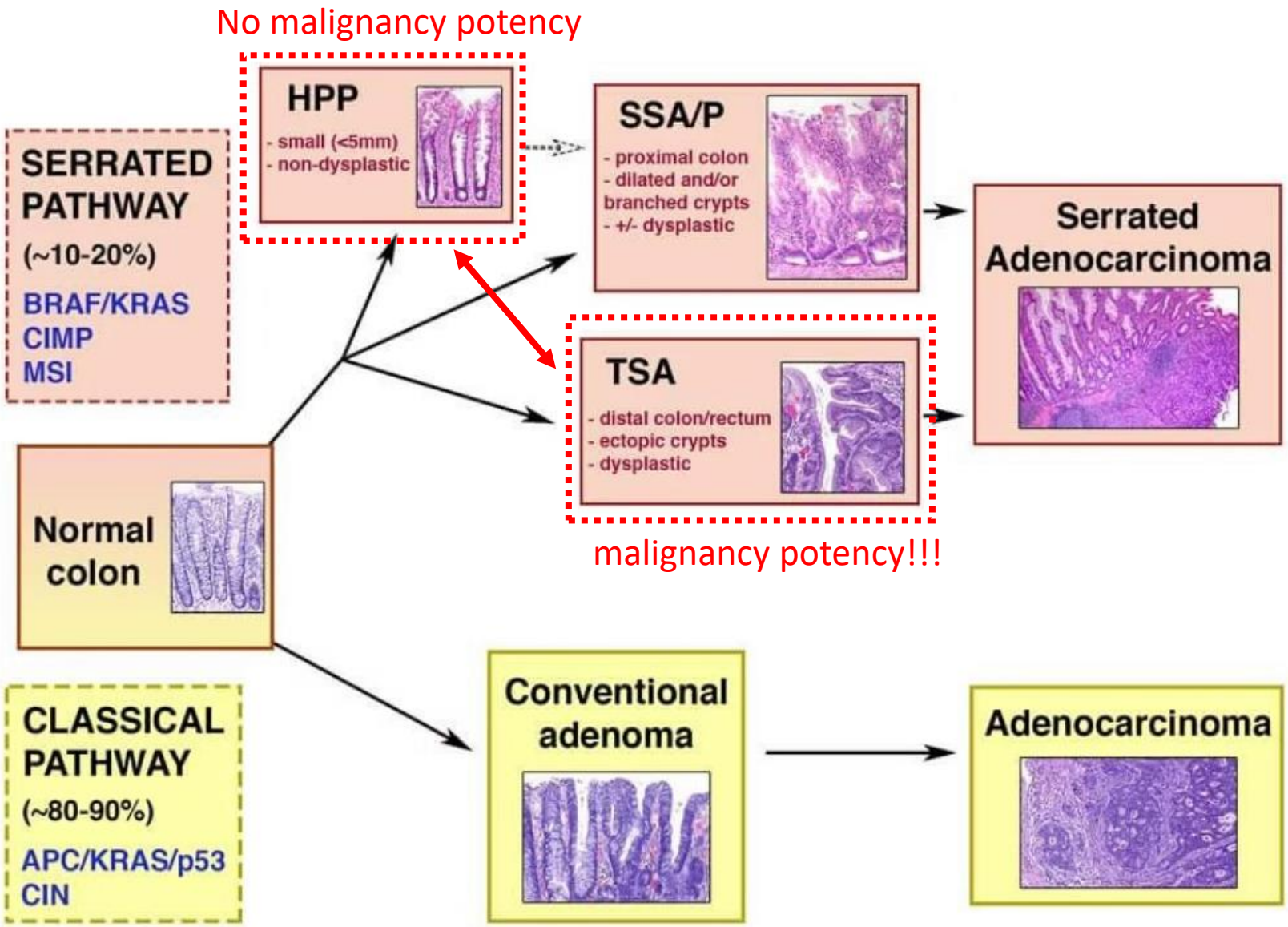
- TOPIC: "**Real-time differentiation** of hyperplastic colorectal polyps and traditional serrated adenoma during standard colonoscopy using Transfer Learning based Deep Neural Network"
  - Gastroenterology. 2020 May 1;158(6):S-17 (lecture presentation DDW 2020)
  - Submitted to The American journal of gastroenterology 2020 (under review)

Associated publication list

- Kim, S., Kwon, S., Markey, M.K., Bovik, A.C., Kim, K.J., Park, S.J., Kim, T.I., Cheon, J.H. & Park, Y.. The Long-term Risks Of Low-risk Adenoma, High-risk Adenoma, And Colorectal Cancer Following Adenoma Removal. Gastroenterology. 2020, May; 158(6): S-1173. Pub Status: Published.
- Kim, S., Kwon, S., Markey, M.K., Bovik, A.C., Kim, K.J., Kim, T.I., Cheon, J.H., Park, S.J. & Park, Y.. Towards Computer-aided diagnosis (CAD) for colonoscopy: Real-time differentiation of diminutive hyperplastic colorectal polyps and diminutive traditional serrated adenomas using a transfer learning based deep neural network. Gastroenterology. 2020, May; 158(6): S-17. Pub Status: Published.

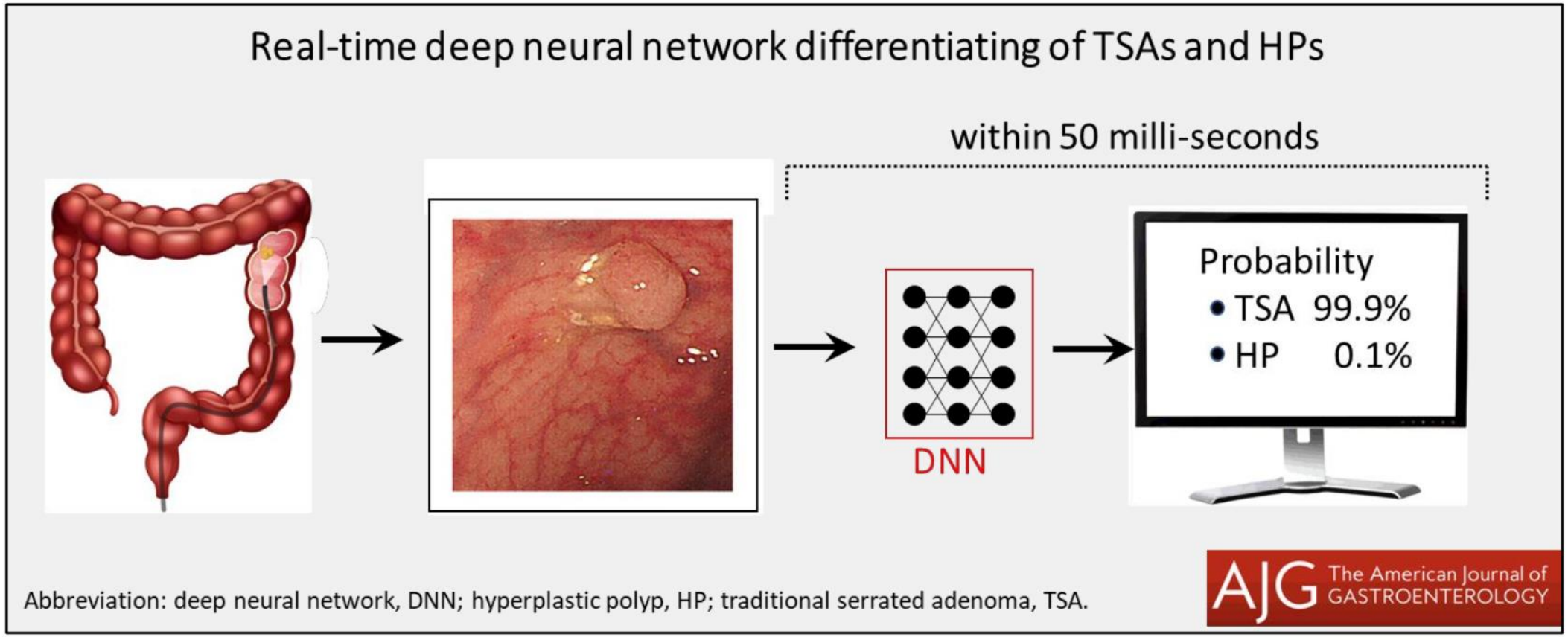
본 주제로 2개의 논문 발표

background | **Study design** | **result** | **Conclusion**

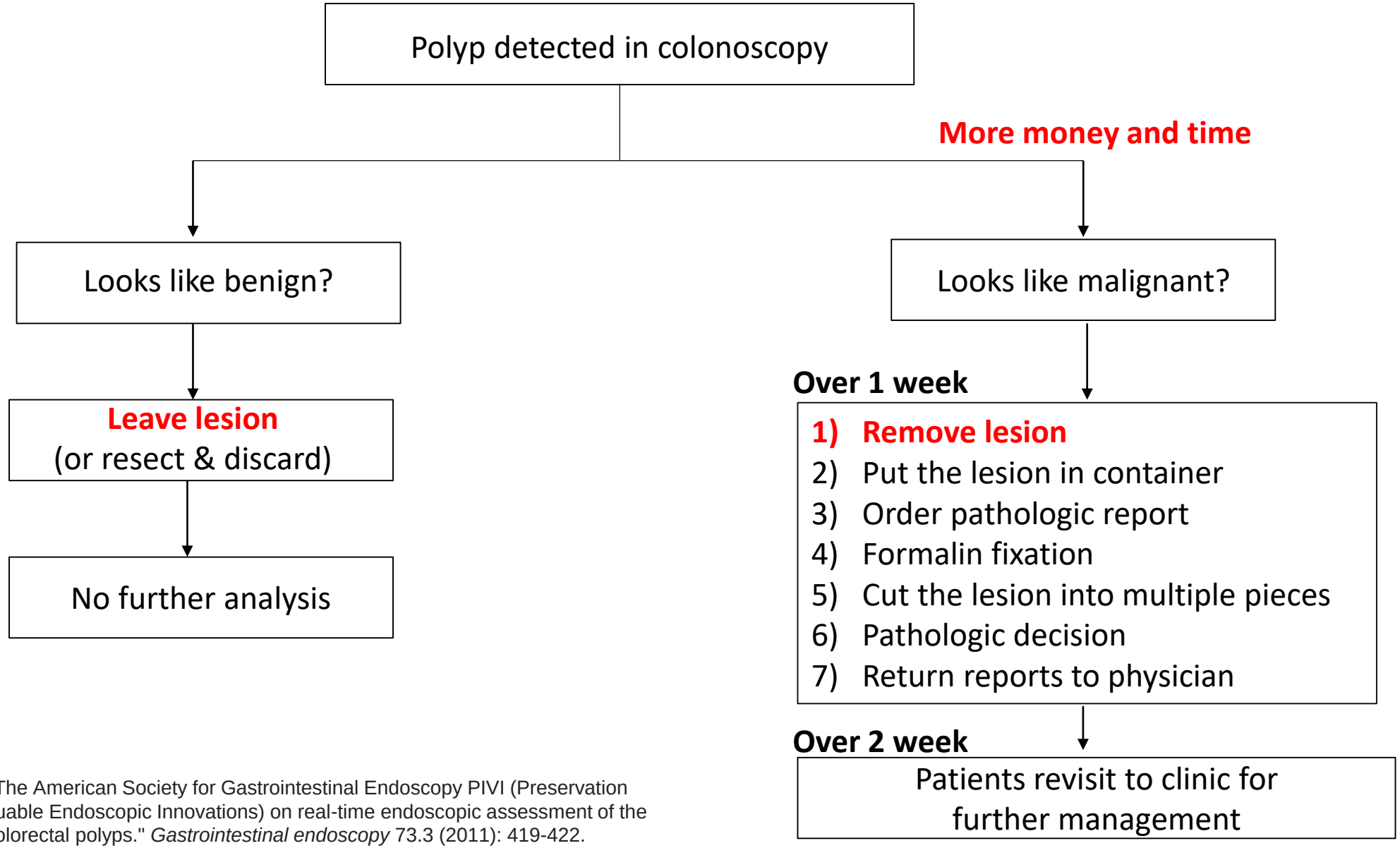


Ambiguity!

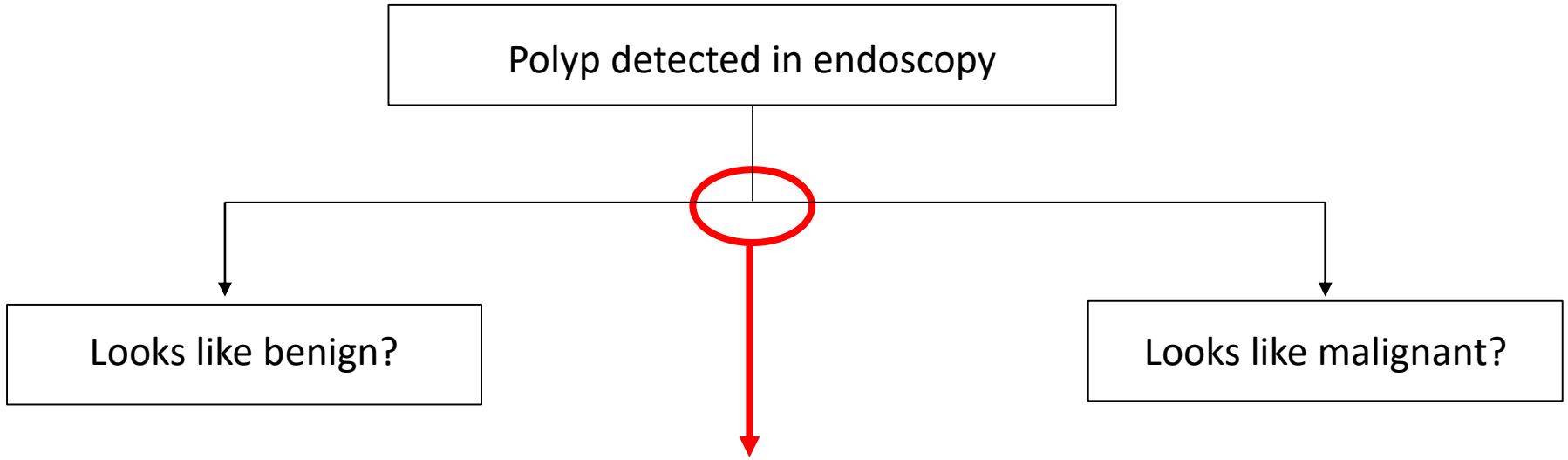
Serrated Polyposis Is an Underdiagnosed and Unclear Syndrome: The Surgical Pathologist has a Role in Improving Detection. Crowder CD, Sweet K, Lehman A, Frankel WL. Am J Surg Pathol. 2012 Aug;36(8):1178-85. PMID: 22790859


Real-time deep neural network differentiating of TSAs and HPs
within 50 milli-seconds
DNN
Probability
TSA 99.9%
HP 0.1%
Abbreviation: deep neural network, DNN; hyperplastic polyp, HP; traditional serrated adenoma, TSA.
AJG The American Journal of GASTROENTEROLOGY

background | **Study design** | **result** | **Conclusion**



Rex, Douglas K., et al. "The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps." *Gastrointestinal endoscopy* 73.3 (2011): 419-422.



Then, who & how to decide “benign-like” vs “malignant-like”?

Clinical judgement can be used deciding whether the histology of a given polyp can be assessed accurately using an endoscopic technology

Rex, Douglas K., 73.3 (2011): 419-422.

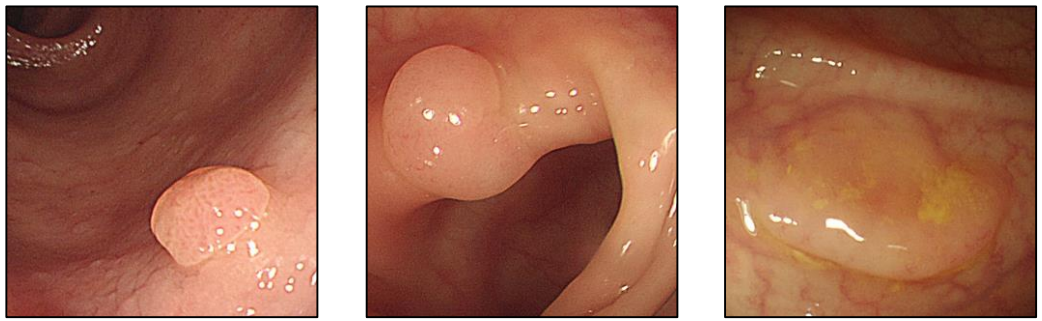
의료진간의 차이!

It means that physician will decide it by his own clinical knowledge.

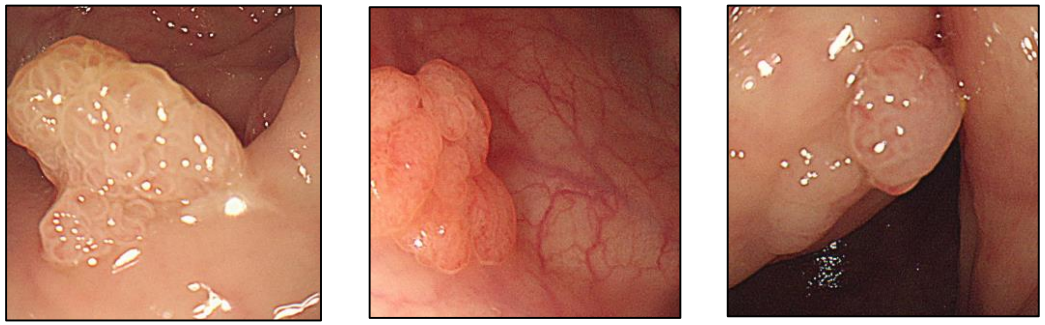
→ the variability of performance is well-known problem .

Severance Hospital Polyp dataset
(confirmed by pathology after a resection)

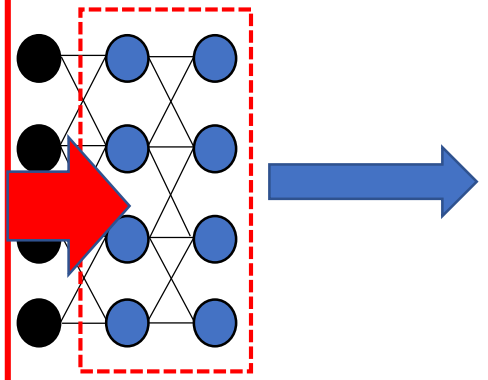
HP



TSA



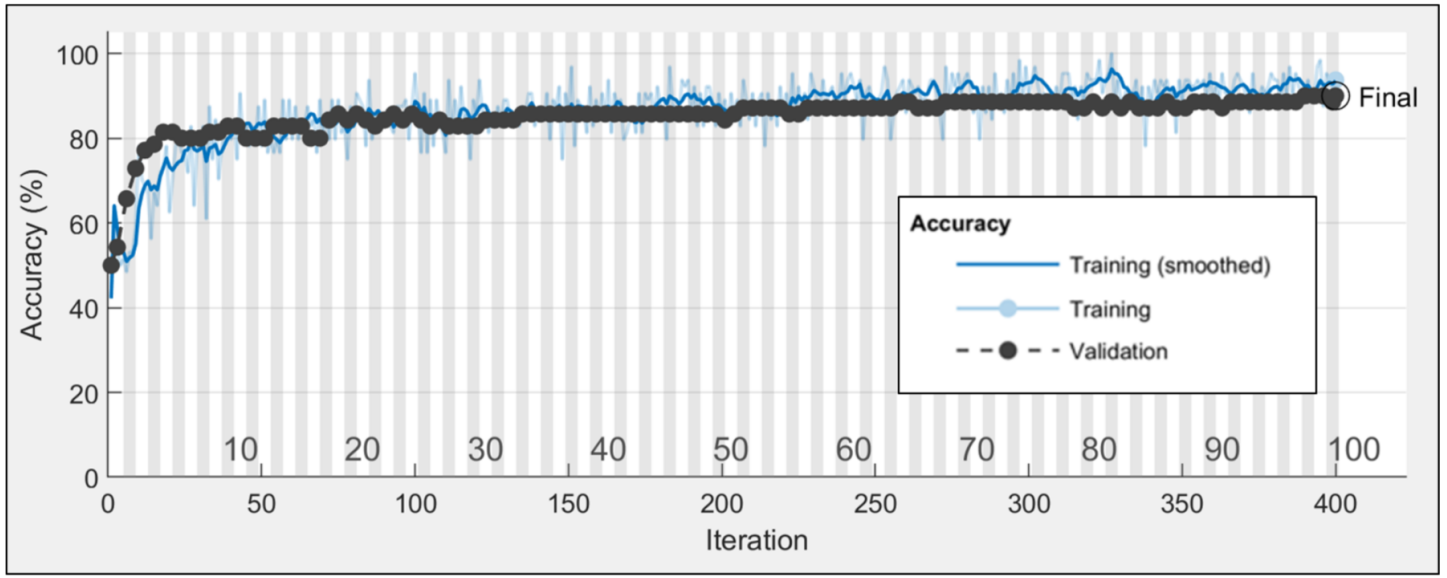
tuning last layers with
a transfer learning



a

A network for
Classification between
HP vs. TSA

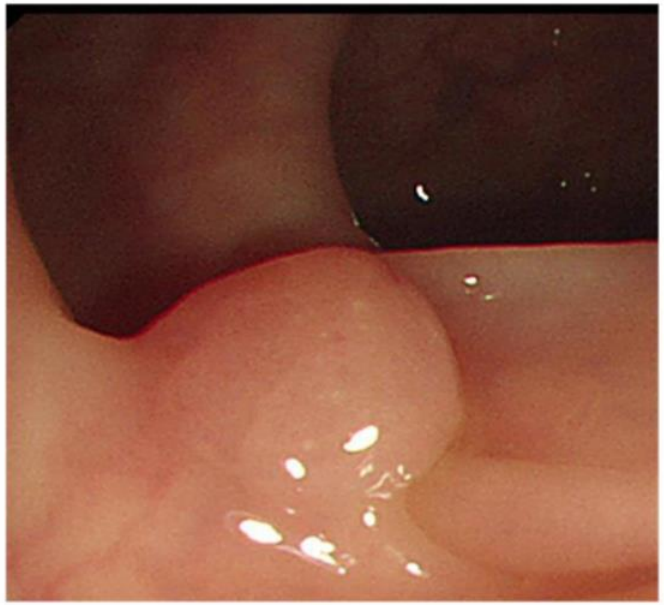
	Hyperplastic polyp	Traditional serrated polyp
No. of participants (lesions)	92	84
No. of colonoscopy images	111	116
Age, year	53 (43-62)	58 (49-66)
Female, %	20 (50%)	6 (66%)
Size, mm	4.7 (2.3-6.4)	7.2 (3.3-12.4)
Location		
proximal	12 (26%)	3 (30%)
distal	38 (74%)	7 (70%)
Body mass index, kg/m2	23 (23-23)	23 (23-23)
Year of endoscopy, %		
Before 2011	12 (26%)	3 (30%)
2011-2015	38 (74%)	7 (70%)
After 2005	12 (26%)	3 (30%)
Reason for first endoscopy, %		
Routine screening	8 (6%)	3 (3%)
Symptom	6 (4%)	7 (7%)
Disease	12 (16%)	15 (15%)
Evaluation	3 (3%)	3 (3%)
others	63 (67%)	52 (61%)
Bowel preparation		
clean	72 (70%)	67 (64%)
dirty	16 (17%)	7 (10%)
unknown	21 (26%)	10 (30%)



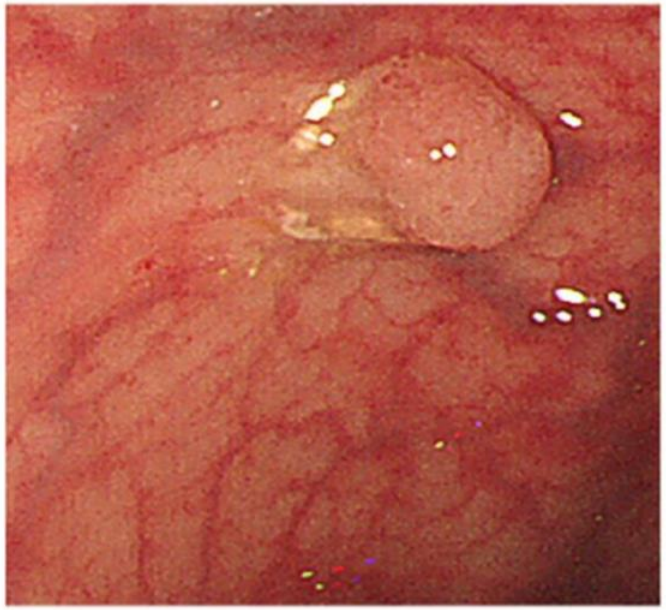
Abbreviation: Deep Neural Network, DNN.

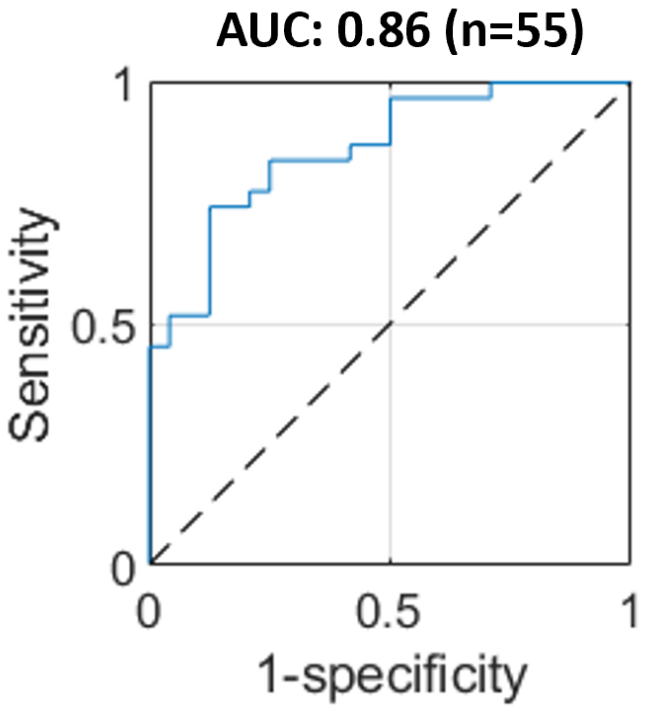
소수의 데이터를 학습 하여 암이 의심되는 용종을 판별하는 기술

Probability of HP: 99.2%
Probability of TSA: 0.8%
Ground truth: HP

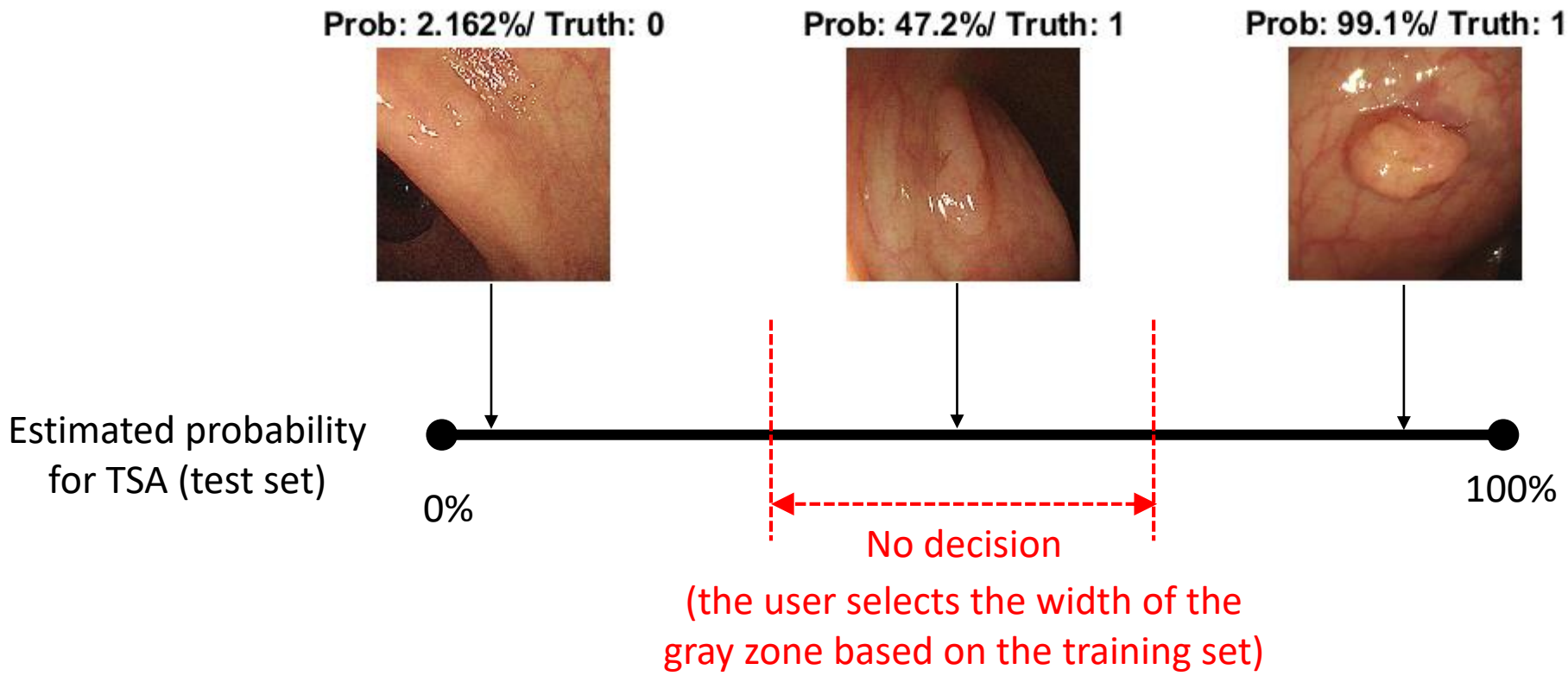


Probability of HP: 0.1%
Probability of TSA: 99.9%
Ground truth: TSA

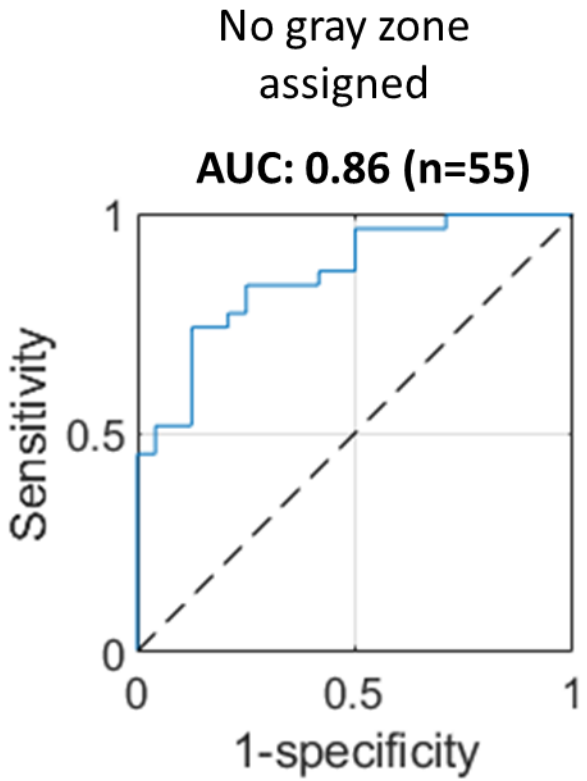




암이 걱정되는 TSA 와 암이 아닐 것이라고 판단되는 HP 를 86% 의 정확도로 구별!



해석가능한 결과값을 얻기 위해 의료진이 grey zone 을 지정하여 학습결과를 해석


No gray zone
assigned
AUC: 0.86 (n=55)
Sensitivity
1
0.5
0
0
0.5
1
1-specificity

- Our machine may provide clinical utility to classify
  - hyperplastic polyp from traditional serrated adenoma
  - Achieving high accuracy
  - Using real-time decision with standard colonoscopy.

- This approach has been applied to a variety of research.
  - Includes Pancreatic cancer, gall bladder polyps, cardiology

- Has potential for further research in various types of cancer and image modality.

소수의 검사 (단 두가지) 결과를 가지고 췌장암의 **진단 정확도를 높이는** 기술

Gastroenterology: Pancreatic cancer research

- Kwon, S., Kim, S., Hidalgo, M., Giovannucci, E.L., Markey, M.K., Bovik, A.C., Kwon, M.J., Kim, K.J., Im, H., Park, J.Y., Bang, S., Park, S.W., Song, S.Y., & Chung, M.J.. Combined use of Lewis antigen phenotype and carbohydrate antigen 19-9 concentration for prediction of survival in patients with pancreatic cancer. Pancreas. 2020, Sep; Pub Status: Published.

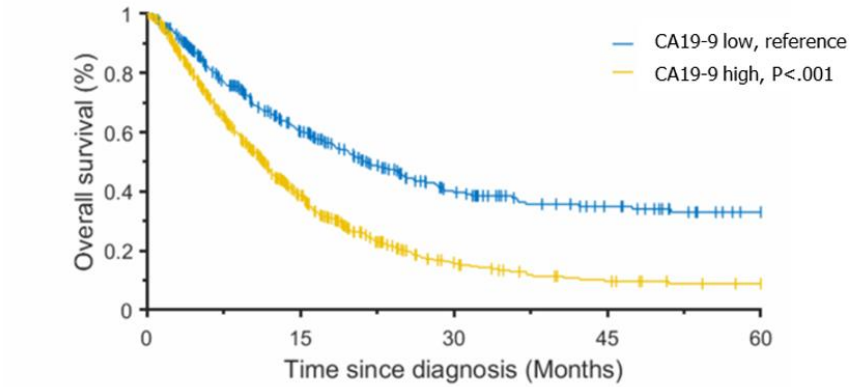
Lewis antigen phenotype and survival of patients with pancreatic cancer

- Study population: a hospital cohort study of 1187 patients diagnosed with Pancreatic ductal adenocarcinoma (PDAC)
- Objective: To examine the association Lewis antigen phenotype and survival of PDAC patients
- Measures: Comparison between machine learning vs Cox proportional Hazards regression models to calculate HRs and CIs

Pancreas. 2020 Nov/Dec;49(10):1348-1354. doi: 10.1097/MPA.0000000000001687. PMID: 33122524.

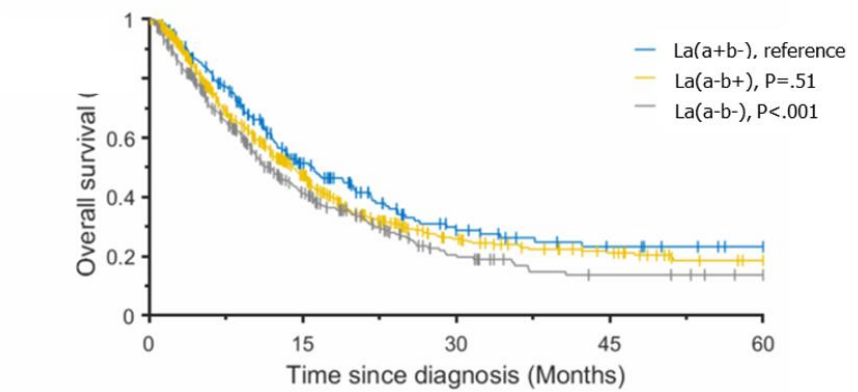
Survival rate of patients with PDAC by Lewis antigen phenotype and CA 19-9 concentration

(a) CA 19-9 (low vs. high)



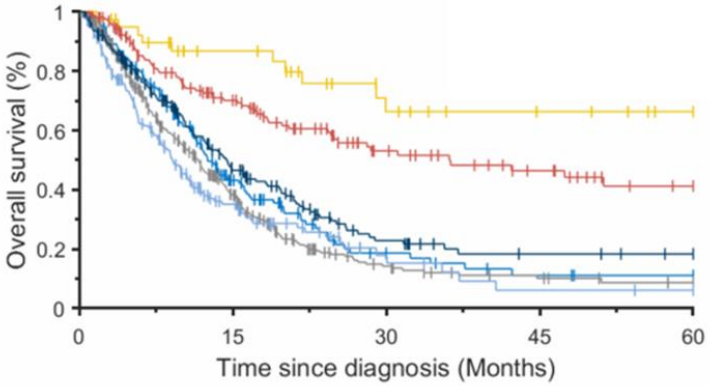
CA19-9 low	408	174	71	42	24
CA19-9 high	779	193	40	17	9

(b) Lewis antigen



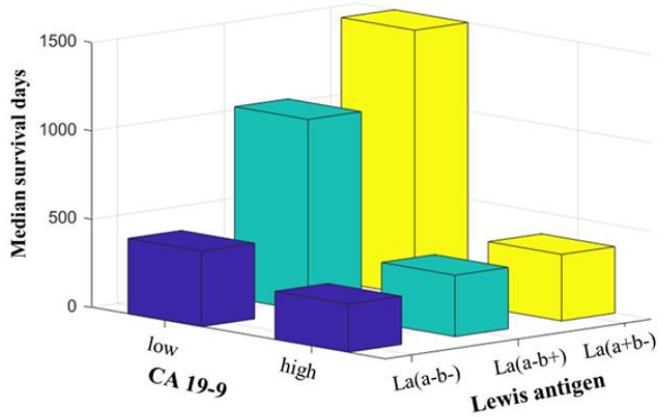
Le(a+b-)	220	74	26	14	8
Le(a-b+)	592	192	58	33	17
Le(a-b-)	375	101	27	12	8

(c) CA 19-9 and Lewis antigen



La(a+b-) & CA19-9 low*	180	48	12	5	3
La(a-b+) & CA19-9 low*	40	26	14	9	5
La(a-b-) & CA19-9 low*	427	110	21	10	5
La(a+b-) & CA19-9 high*	165	82	37	23	12
La(a-b+) & CA19-9 high*	172	35	7	2	1
La(a-b-) & CA19-9 high*	203	66	20	10	7

(d) Median survival rate classified by CA 19-9 and Lewis antigen



Cox proportional hazards regression model for mortality

Unadjusted survival model[a]	HR (95% CI)	P value
Lewis antigen		
Lewis antigen A positive	1 (reference)	
Lewis antigen B positive	1.16 (0.95-1.43)	.13
Lewis antigen negative	1.38 (1.12-1.72)	.003
Adjusted survival model[b]	**HR (95% CI)**	**P value**
Lewis antigen		
Lewis antigen A positive	1 (reference)	
Lewis antigen B positive	1.27 (1.03-1.57)	.02
Lewis antigen negative	1.65 (1.31-2.09)	<.001

Abbreviations: HR, hazard ratio; CI, confident interval.

[a] Cox proportional hazards regression model was applied for HR and 95% CI for Lewis antigen phenotype (Lewis antigen A positive, Lewis antigen B positive, or Lewis antigen negative).

[b] Cox proportional hazards regression model was applied for multivariable-adjusted HR, 95% CI, and p-value after adjusting for serum Lewis antigen phenotype (Lewis antigen A positive, Lewis antigen B positive, or Lewis antigen negative), serum CA 19-9 concentration (U/mL; log-scale), age (years), Body Mass Index (Kg/m^2), sex (male or female), origin of cancer (head vs. non-head), AJCC with liver metastasis (I, II, III, IV without liver metastasis, or IV with liver metastasis), smoking history (smoker or non-smoker), and drinking history (drinker or non-drinker).

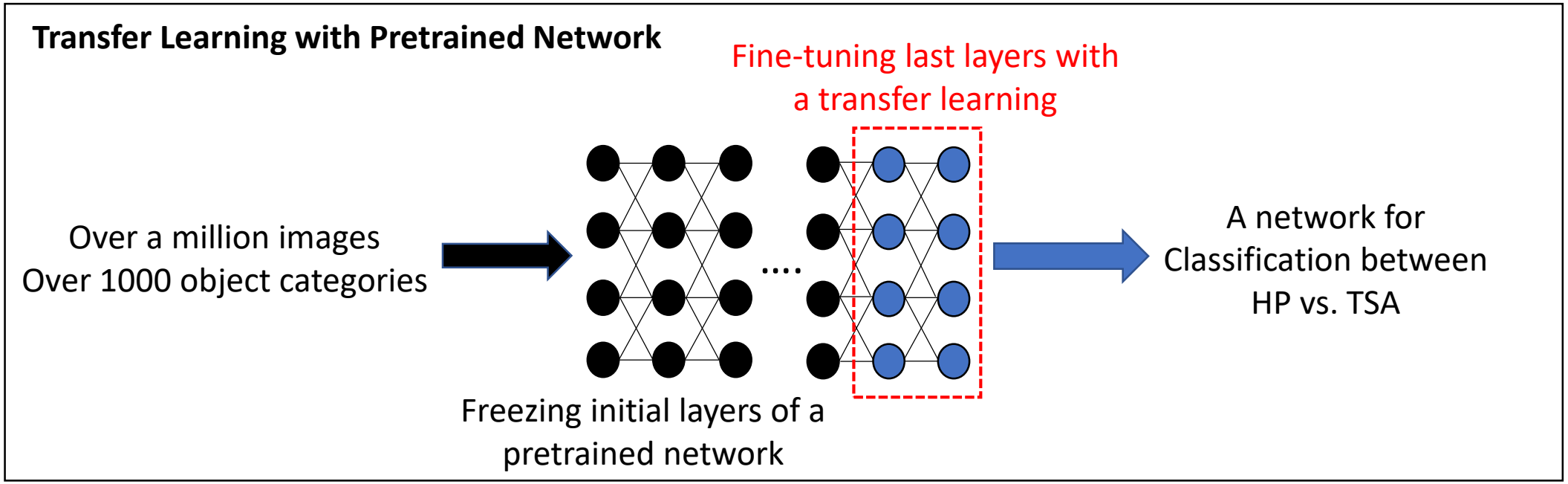
담남용종의 진단 정확도를 높이는 기술

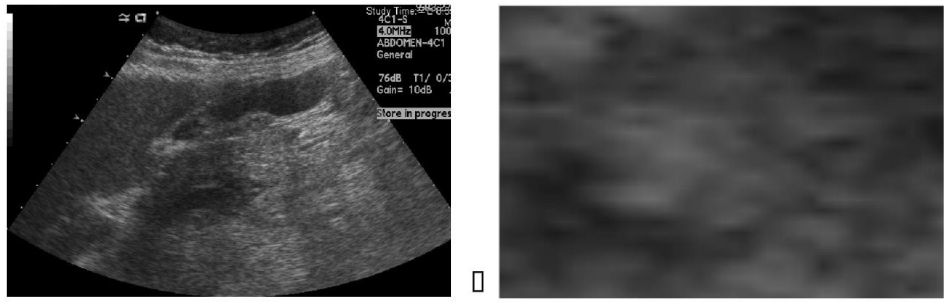
GB polyp classification

- On-going project
  - Classification of gall bladder polyp into adenoma vs polyp
  - Pre-malignant lesion detection

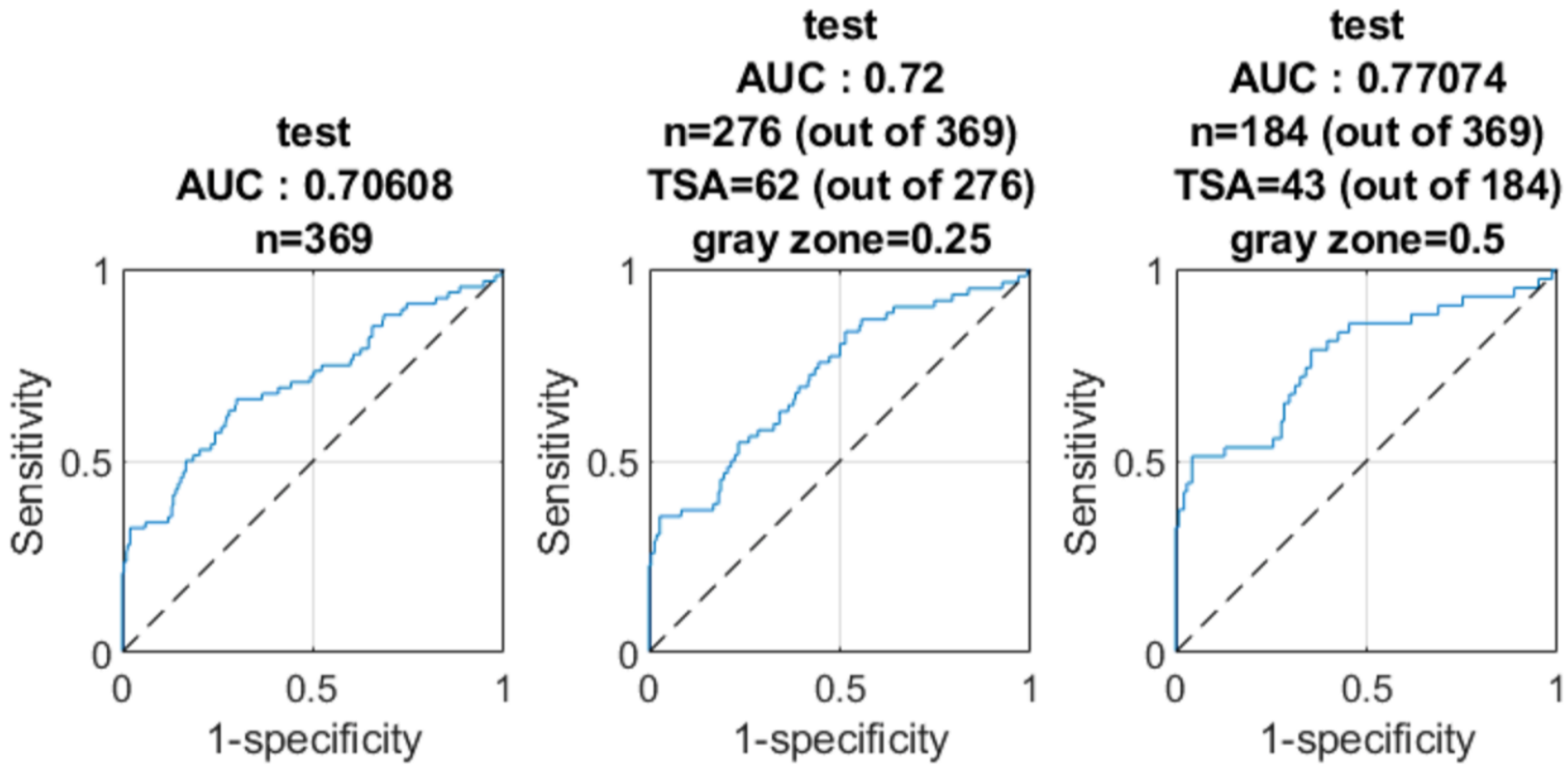
극히 제한된 소수의 검사결과를 가지고 담낭용종의 **진단 정확도를 높이는** 기술

System design

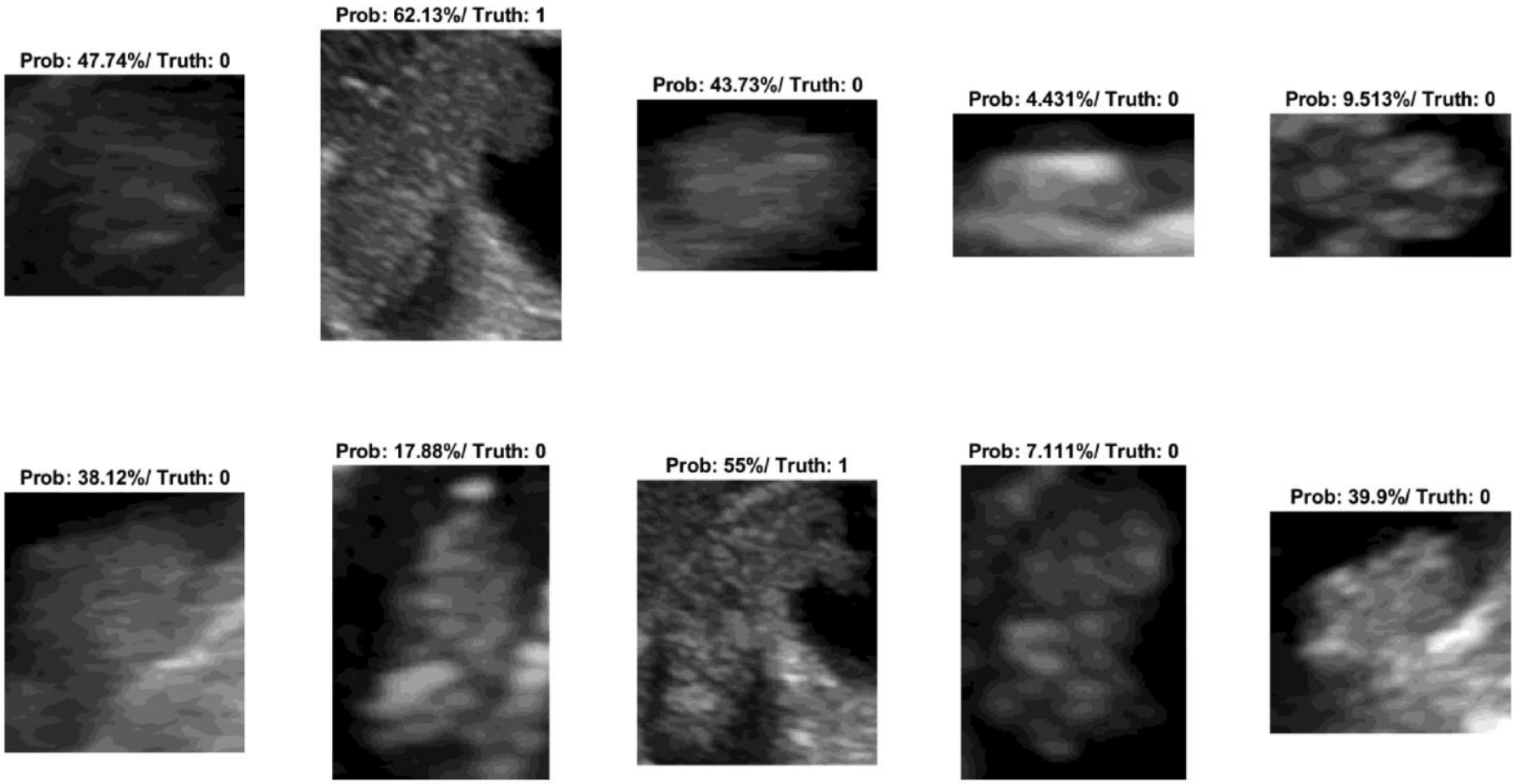




ROC performance



Estimated probability



Future work

Phase 1

Training Set

Yonsei dataset

- Study Design
- Build model
- Analyze result

Phase 2

Test Set

Validation hospital dataset

- Performance check
- Refine model

On going research

- Prediction of incidence of pancreatic cancer in type 2 DM pateints using National insurance dataset

Thank you for your attention.