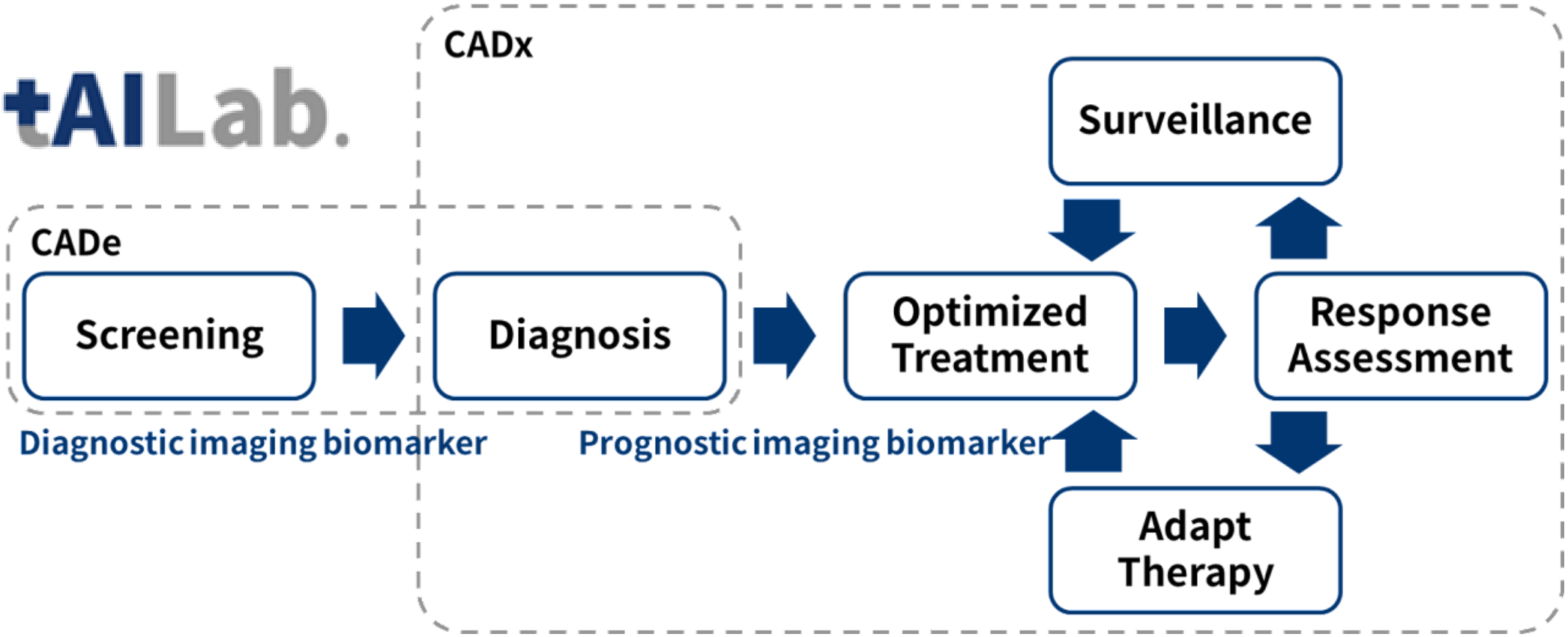
240228 AIRIS2024

AI-based Clinical Decision Support System (CDSS) and its Clinical Validation

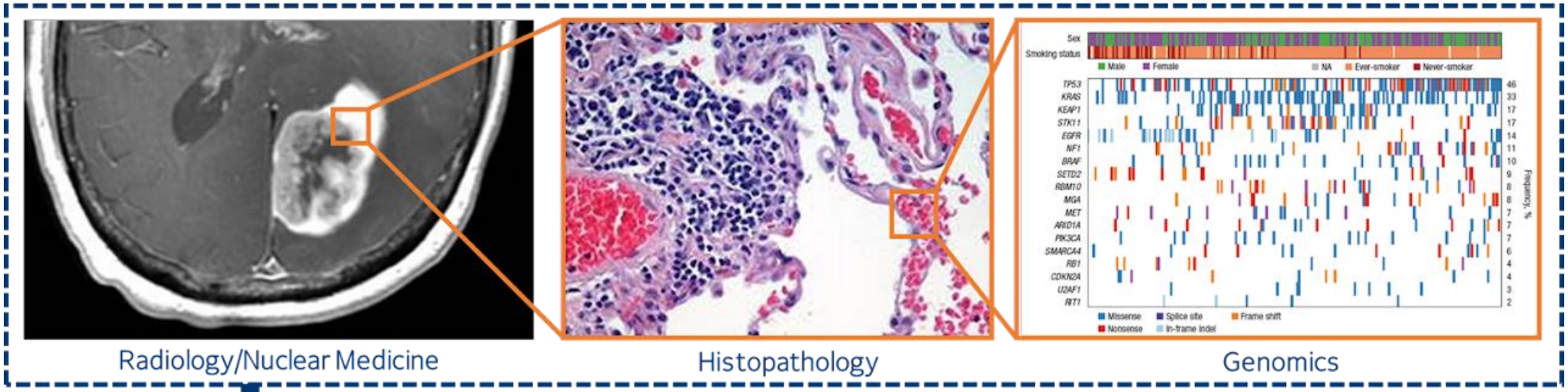
Hwiyoung Kim, Ph.D.
Dept. of Biomedical Systems Informatics,
Translational Artificial Intelligence Laboratory (TAILab),
Yonsei University College of Medicine

Research Group for AI & Machine Learning in Medicine

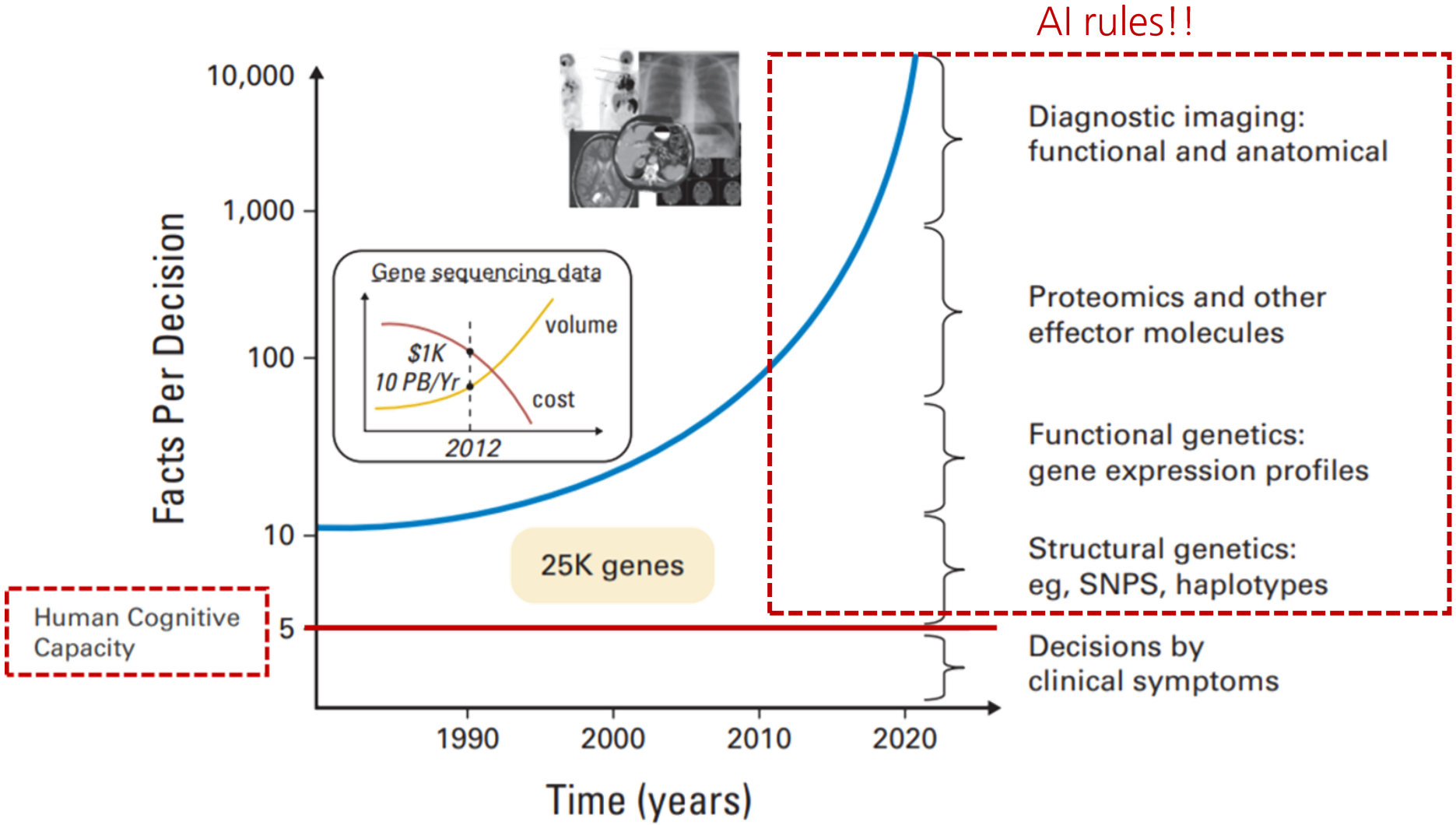
- We established **Translational AI Laboratory (in Korean, 의료인공지능연구실)** to quickly meet the clinical unmet needs using artificial intelligence technology and to improve the standard of care.



Aim 1: Finding Integrated Biomarker for Cancer & various Diseases

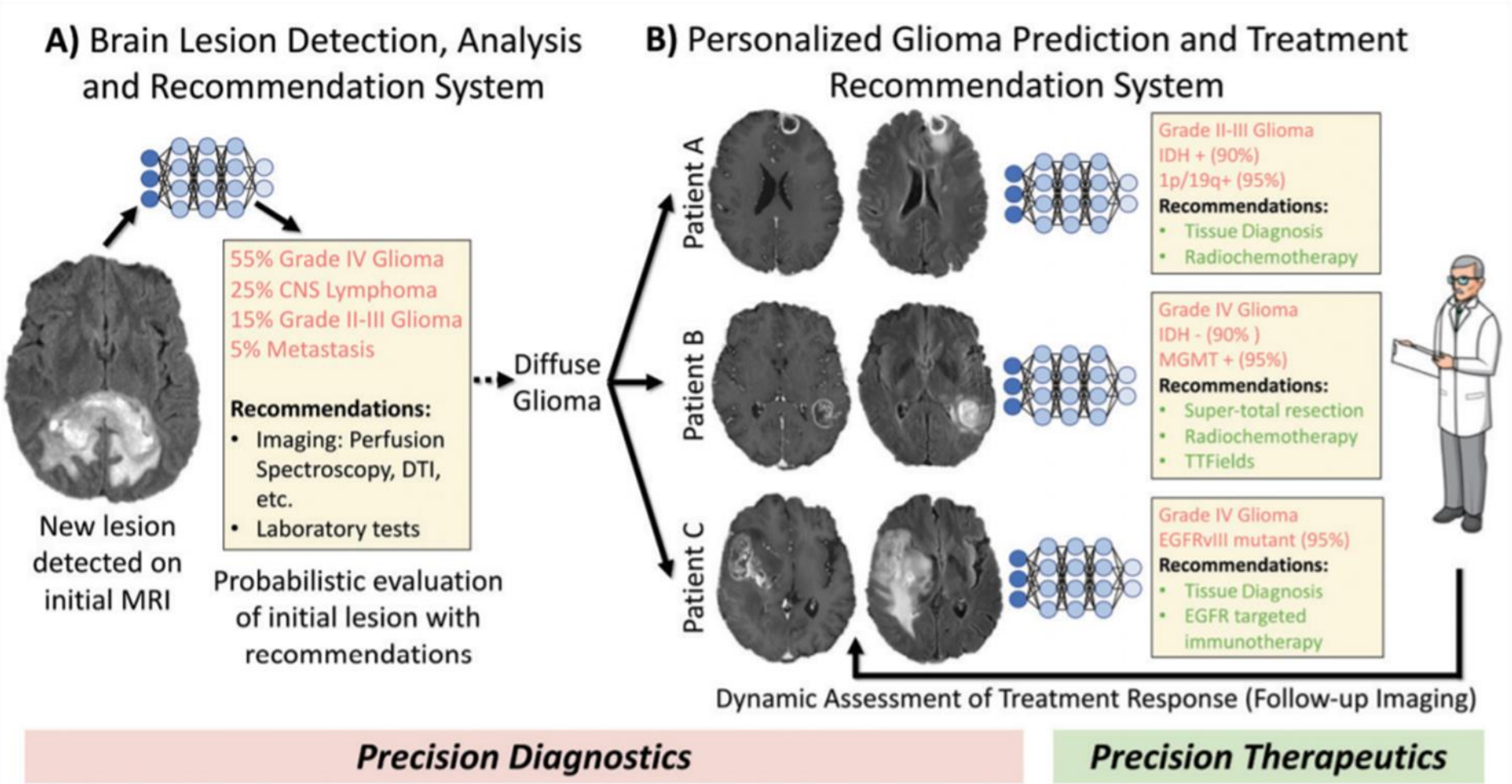


Increase in data required for medical decision making relative to human cognitive capacity



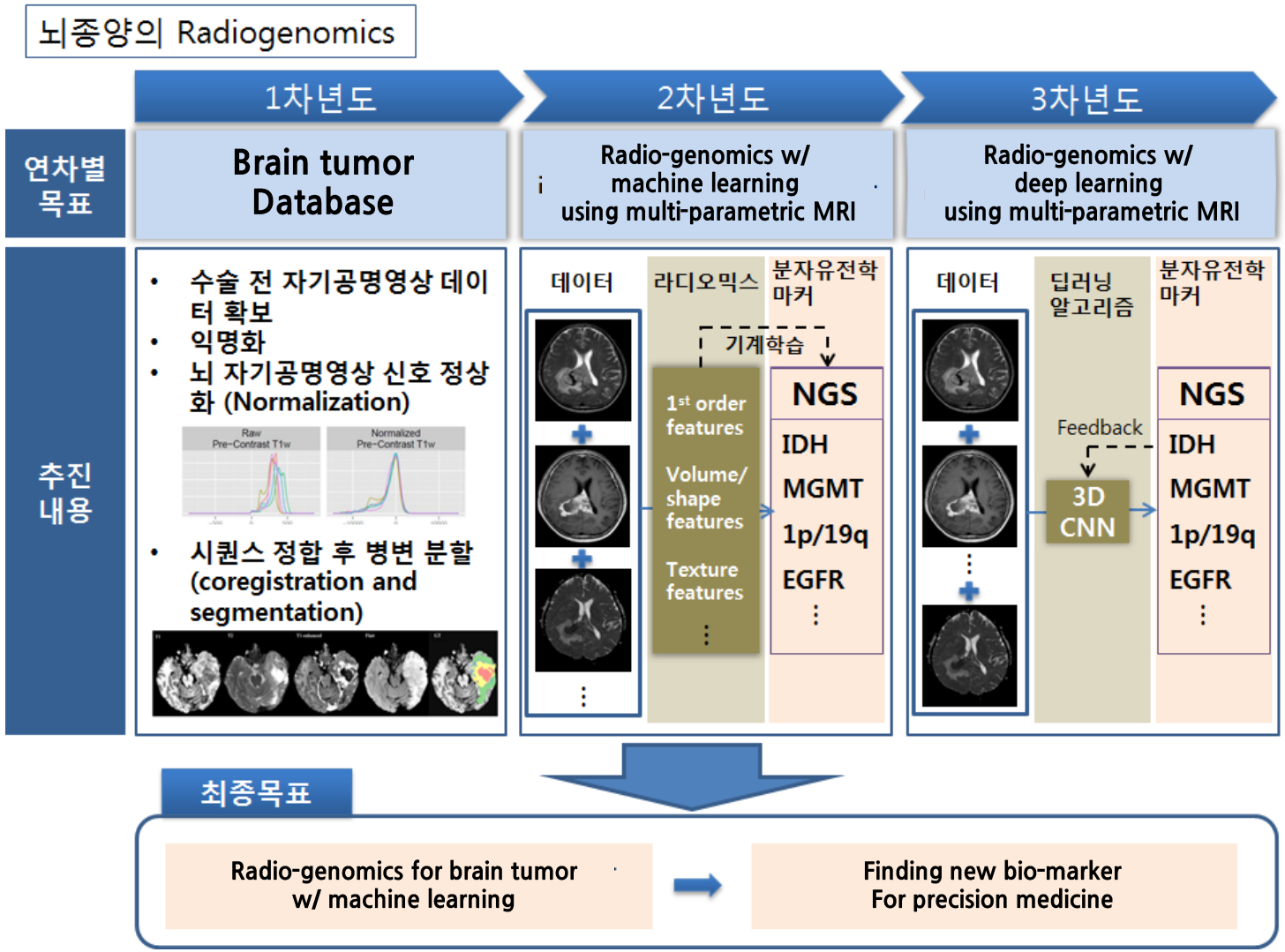
Abernethy, Amy P., et al. "Rapid-learning system for cancer care." *Journal of Clinical Oncology* 28.27 (2010): 4268.

Future AI-based Neuro-oncologic Imaging and Clinical Management Workflow



Rudie, J. D., Rauschecker, A. M., Bryan, R. N., Davatzikos, C., & Mohan, S. (2019). Emerging Applications of Artificial Intelligence in Neuro-Oncology. Radiology, 181928.

Brain Tumor Classification



European Radiology IF=7.03 | AJNR American Journal of Neuroradiology IF=4.97 | Scientific Reports IF=4.99

Ilah Shin*, Hwiyoung Kim* *et al.*, "Development and validation of a deep learning-based model to distinguish glioblastoma from single brain metastasis in conventional magnetic resonance images.", *American Journal of Neuroradiology* (2020)

Chaejung Park *et al.*, "MRI features may predict molecular features of glioblastoma in isocitrate dehydrogenase wild-type lower-grade gliomas", *American Journal of Neuroradiology* (2020)

Yae Won Park *et al.*, "Radiomics Features of Hippocampal Regions in Conventional and Diffusion Tensor Imagings can Differentiate Temporal Lobe Epilepsy Patients from Healthy Controls", *Scientific Reports* (2020)

Chaejung Park, *et al.*, "Radiomics risk score may be a potential imaging biomarker for predicting survival in isocitrate dehydrogenase wild-type lower-grade gliomas" *European Radiology* (2020)

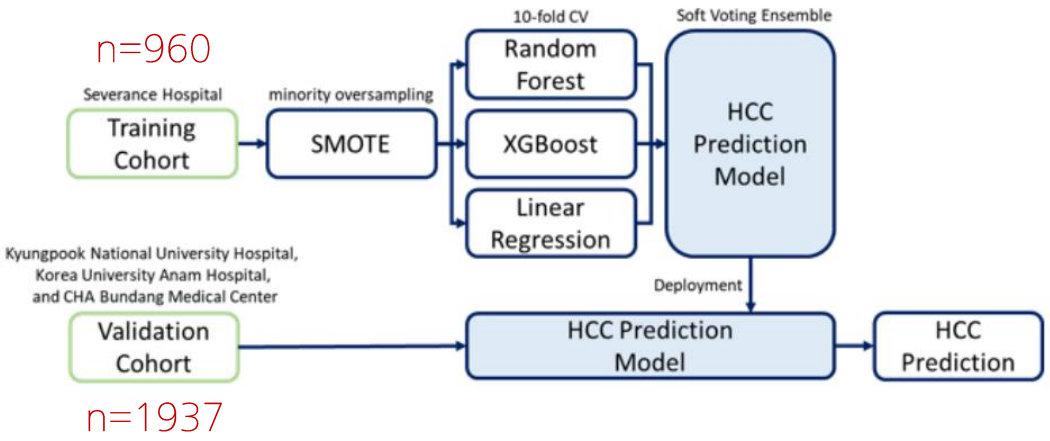
Yae Won Park *et al.*, "Diffusion Tensor and Conventional Imaging Radiomics Features to Differentiate the Epidermal Growth Factor Receptor Mutation Status of Brain Metastases from Non-Small Cell Lung Cancer", *Neuroradiology* (2020)

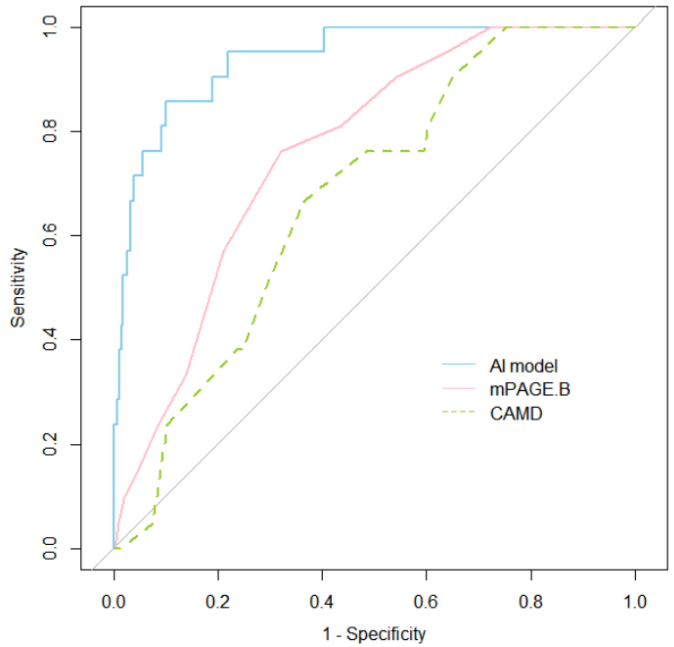
Sohi Bae *et al.*, "Robust performance of deep learning for distinguishing glioblastoma from single brain metastasis using radiomic features: Model development and validation", *Scientific Reports* (2020)

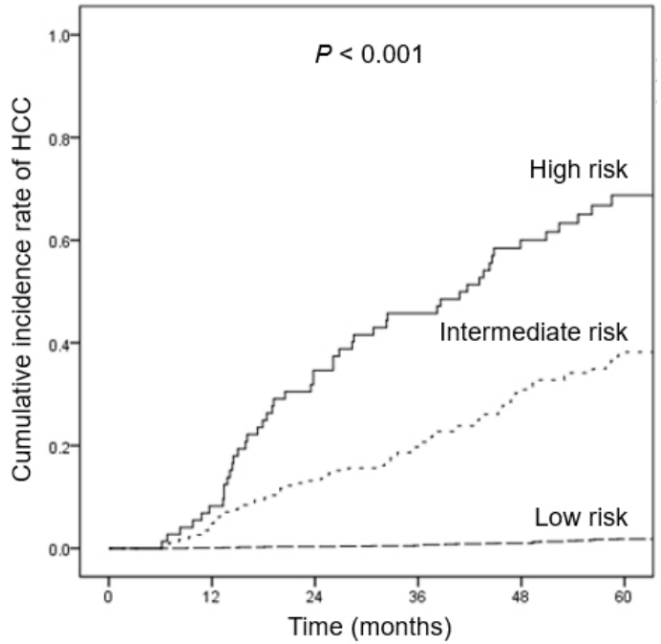
박예원, 배소희, 신일아, 박채정, 최동민, 김상욱, 한경화, 김휘영*, 안성수*

AI-assisted risk stratificaion of patients (chronic hepatitis B)

- established and validated an ML-based HCC predictive model optimized for patients with chronic hepatitis B (CHB) infections receiving antiviral therapy (AVT)
- Our new ML model performed better than models in terms of predicting the risk of HCC development in CHB patients receiving AVT.







Liver INTERNATIONAL IF=8.75

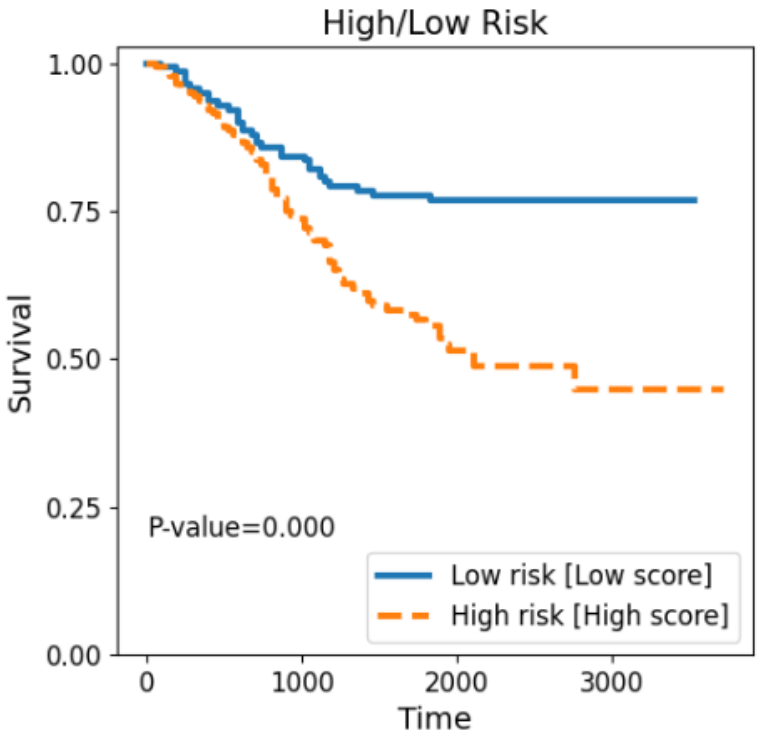
이혜원*, 김휘영*, 이재승, 박준용, 김도영, 안상훈, 김범경*, 김승업*

Image-based biomarker for clinical decision support (gastric cancer)

THE LANCET Digital Health IF=36.62, under review

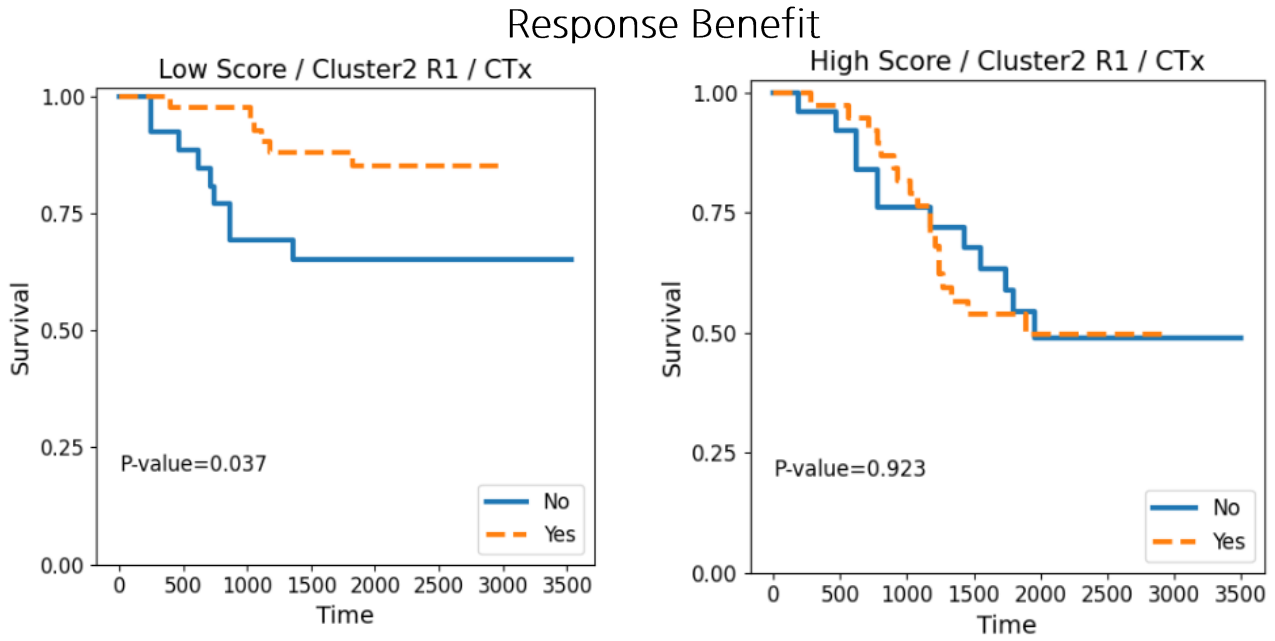
Risk stratification

- In both training and validation cohorts, high-risk patients showed significantly lower mortality rate than low-risk patients.



Added value of Radiomics features

surgery only and surgery+adjuvant chemotherapy group in risk group

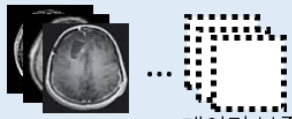


김민규, 조상욱, 황태현(Cleveland Clinic), 임준석, 김휘영, 정재호

Aim2: Generative AI Model for Medicine

AS-IS

희귀 난치성 뇌종양 정밀 진단 어려움



데이터 부족

뇌교종의 분자아형, 뇌전이암의 원발암 별 데이터 수 부족

별도의 검증용 데이터셋 구성 어려움

희귀 난치성 뇌종양 원데이터 공유 어려움

환자 프라이버시 보호 어려움

기관별 상이한 영상 프로토콜

TO-BE

희귀 난치성 뇌종양 정밀 진단 실현

AI 기반 진단보조 모델의 학습 및 검증을 위한 효율적 의료데이터 확보

희귀 난치성 뇌종양 정밀 진단 실현

AI 기반 진단보조모델 임상적유효성 검증

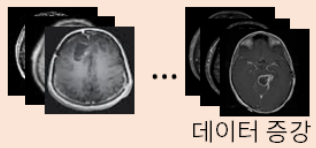
희귀 난치성 뇌종양 데이터 공유 활성화

희귀 난치성 뇌종양 데이터베이스 공개

다기관 데이터 공유 안정성 확보

다기관 데이터 공유 유효성 확보

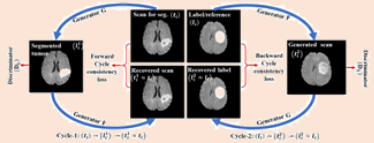
희귀 난치성 뇌종양 합성데이터 생성



데이터 증강

뇌교종의 분자아형, 뇌전이암의 원발암 별 충분한 데이터 확보

별도의 검증용 합성 데이터셋 확보



익명화 된 공개 가능한 데이터 생성

기관별 상이한 영상 품질 최소화

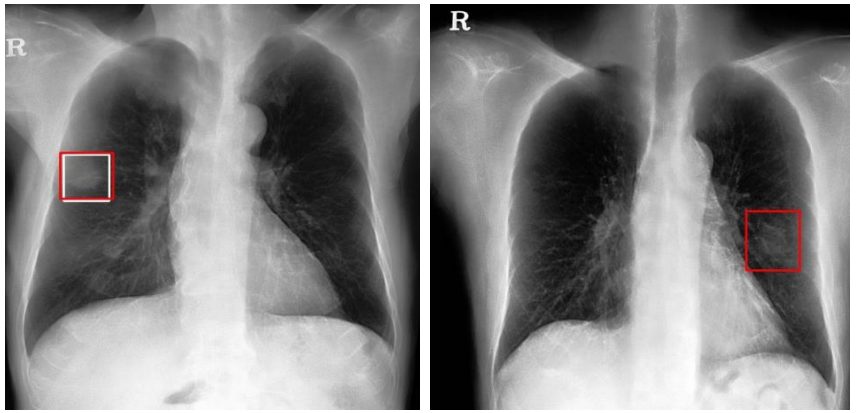
보건산업진흥원
의료데이터 보호·활용 기술개발 사업
(3년 총 12억)

세브란스병원 영상의학과
안성수 부교수

서울아산병원 영상의학과
박지은 조교수

울산과학기술원 원자력공학과
이지민 조교수

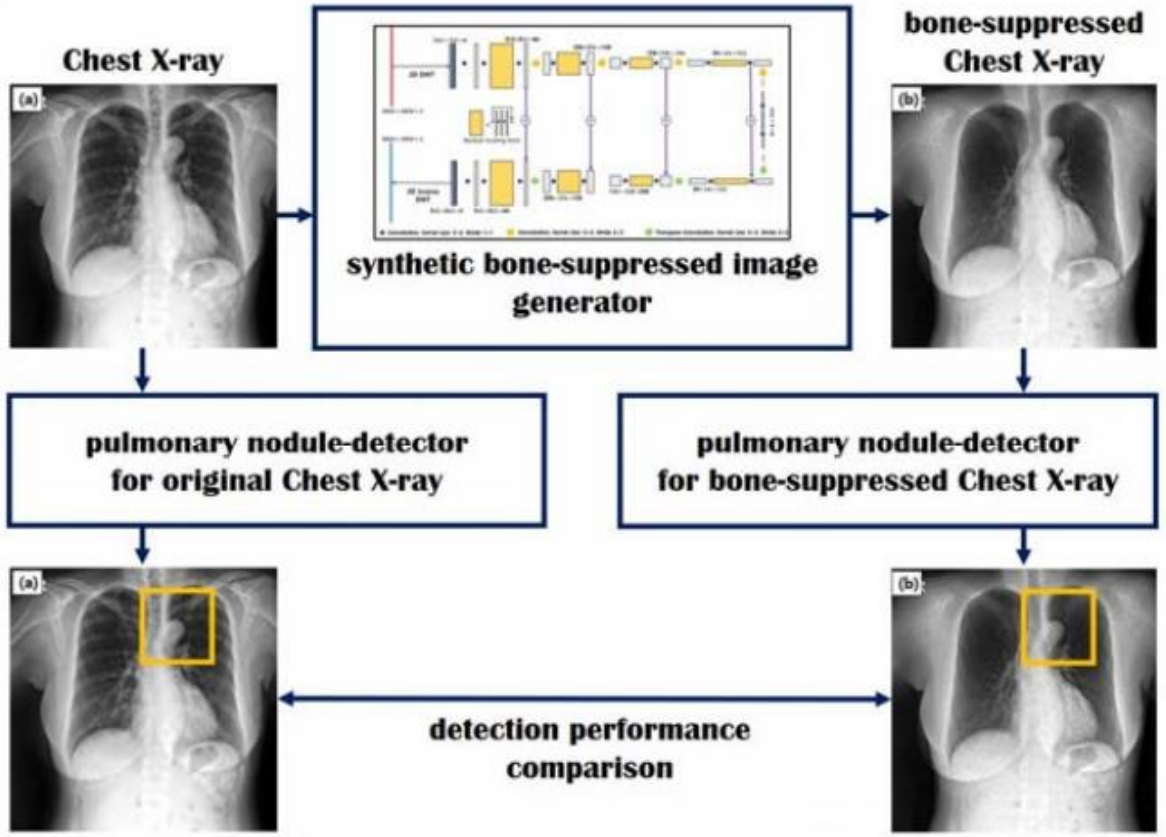
AI-based image synthesis for better reading of medical imaging



subsystem A:
synthetic bone-suppressed image generation

subsystem B:
pulmonary nodule detection

Observer	Sensitivity (%)			FPPI		
	Observer only	Observer + DLBS	*P*-value	Observer only	Observer + DLBS	*P*-value
Observer 1	80.4 (74/92) [72.3–88.5]	92.4 (85/92) [87.1–97.8]	.001	0.143 (30/205) [0.098, 0.208]	0.059 (12/205) [0.034–0.101]	< .001
Observer 2	76.1 (70/92) [66.4–83.8]	91.4 (85/92) [85.7–97.1]	<.001	0.165 (35/205) [0.116, 0.235]	0.087(18/205) [0.051–0.148]	.001
Observer 3	77.2 (71/92) [68.6–85.8]	91.4 (85/92) [85.7–97.1]	<.001	0.154 (33/205) [0.109, 0.218]	0.063(13/205) [0.051–0.148]	<.001
Average	77.5 [69.9–85.2]	92.1 [86.3–97.3]	<.001	0.151 [0.111, 0.210]	0.071 [0.041–0.111]	<.001

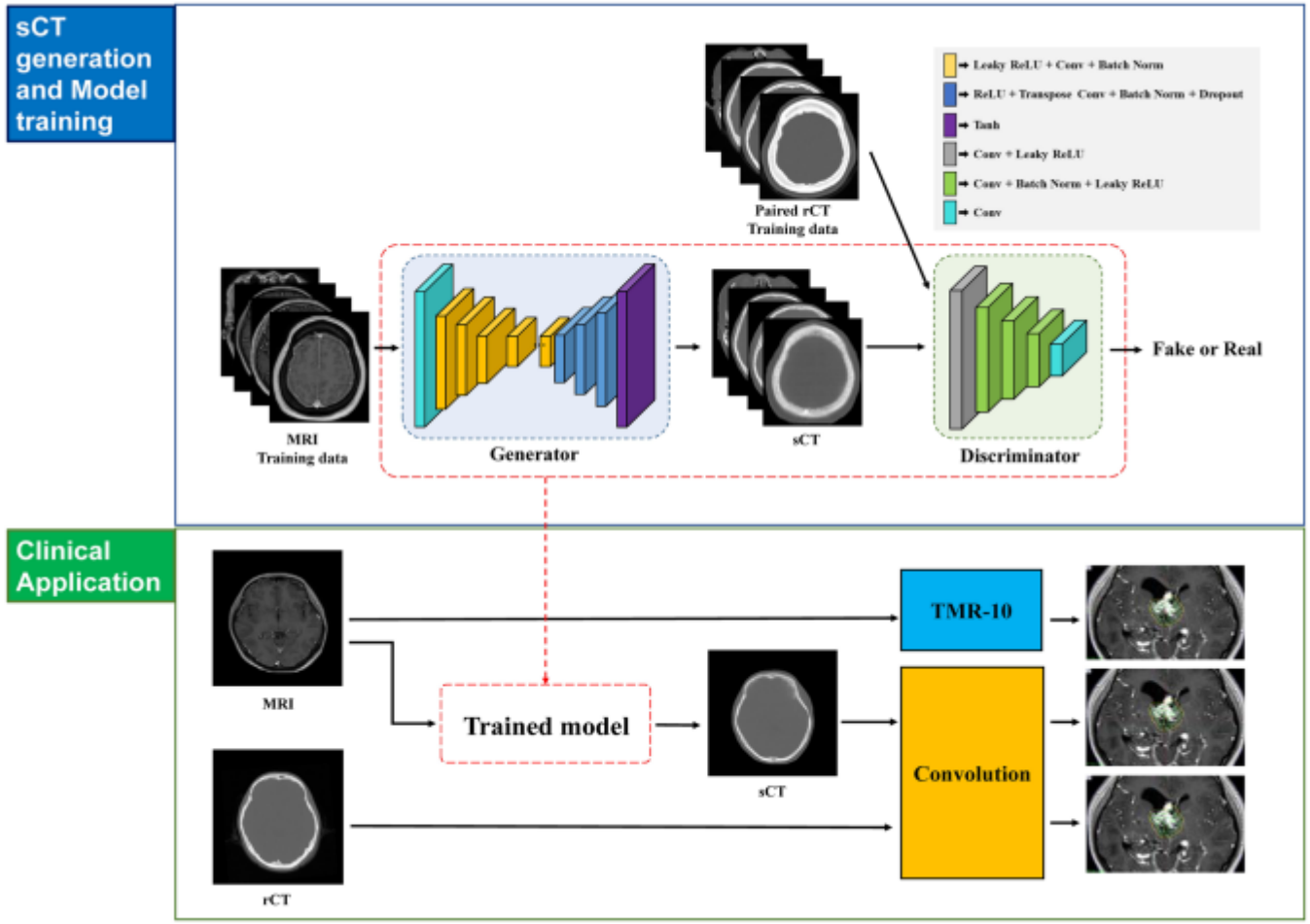


Lee, Donghoon, et al. *Physics in Medicine & Biology* 64.11 (2019)

김휘영, 이계호, 한경화, 이지원, 김진영, 임동진, 홍유진, 최병욱, 허진

JAMA Network Open IF=13.35

AI-based image translation to improve GK treatment planning accuracy



연세의료원, 감마나이프 치료계획용 영상 생성 기술 이전

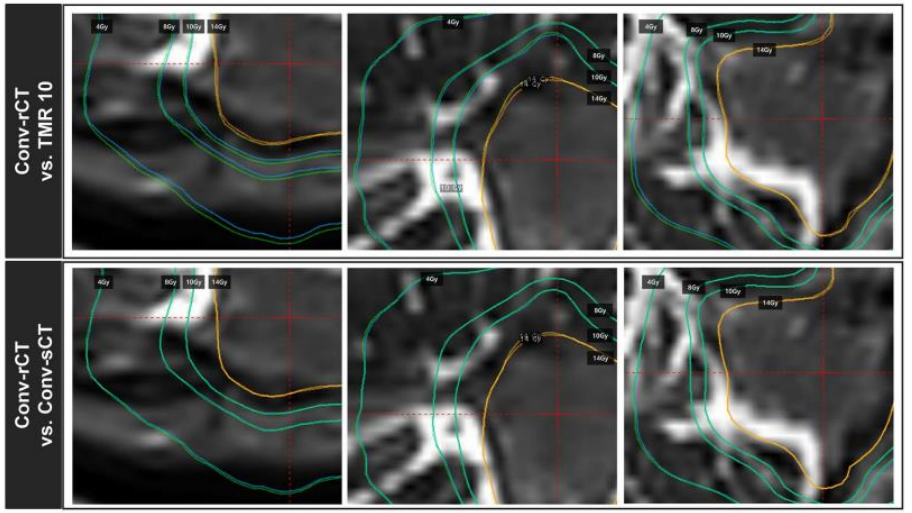
인공지능 기반으로 기존 MRI 기반 치료계획 한계 보완
정확한 치료계획 수립으로 비침습적 뇌 수술 정확도 향상


▲ 장 원 석 교수


▲ 김 휘 영 교수

세브란스병원 장원석 교수(신경외과학교실), 연세의대 김휘영 교수(의생명시스템정보학교실) 연구팀은 인공지능 기반의 기술 개발을 통해 환자 맞춤형 감마나이프 치료계획을 수립이 가능하게 됐다.

감마나이프 치료는 '무혈·무통'의 뇌수술법으로 두개골을 절개하지 않고 병변에 감마선을 조사해 뇌종양 등 뇌수술을 진행할 수 있기 때문이다. 또한 환자가 느끼는 통증이 적어 수술 당일 퇴원도 가능하다.

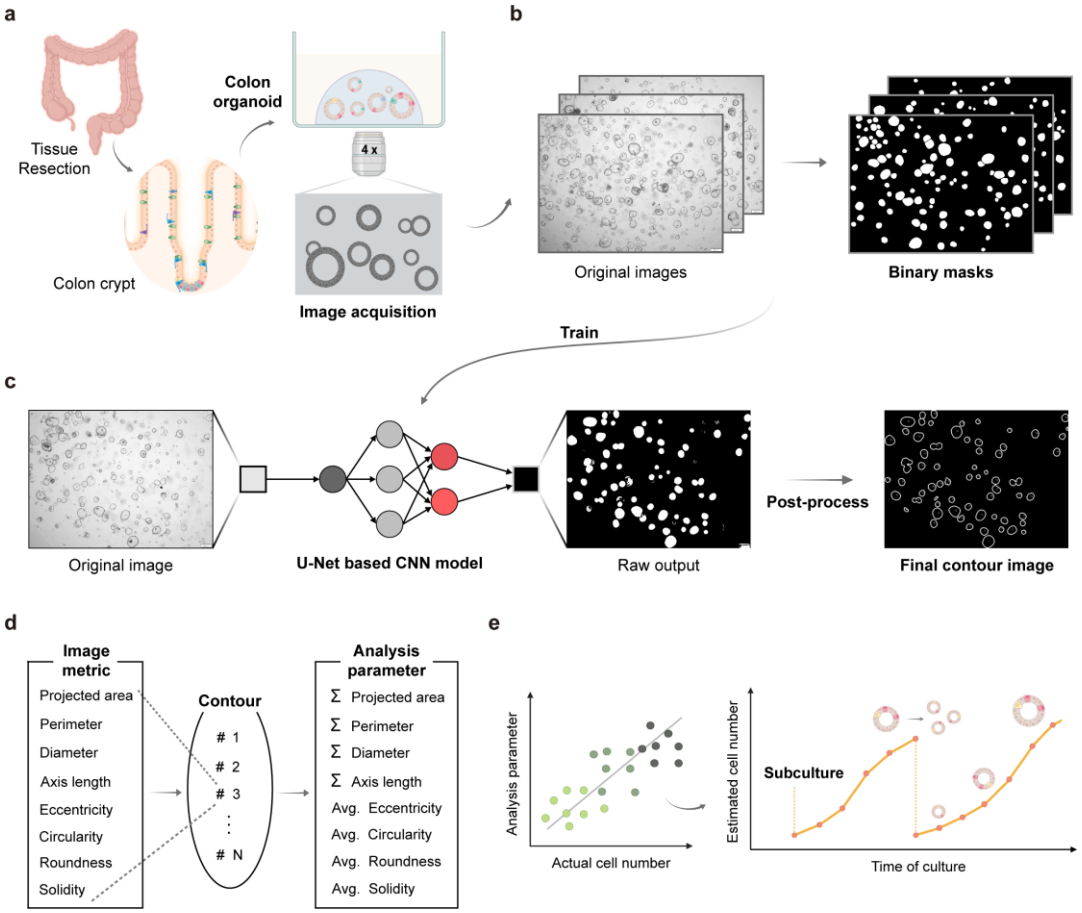


박소희. 최동민, 김휘영, 장원석(세브란스병원 신경외과)

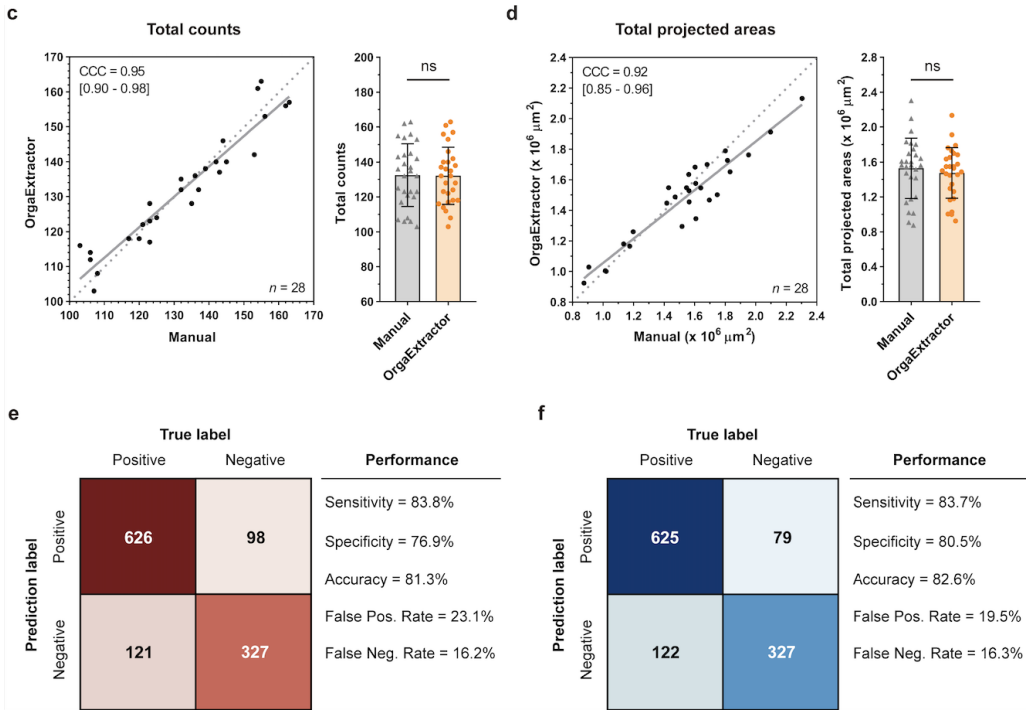
Biomedical Engineering Letters IF=3.920

Aim 3: AI-based tool for Biomedical Research

OrgaExtractor: An easy-to-use deep learning-based image processing tool for organoid image analysis



Manual vs OrgaExtractor

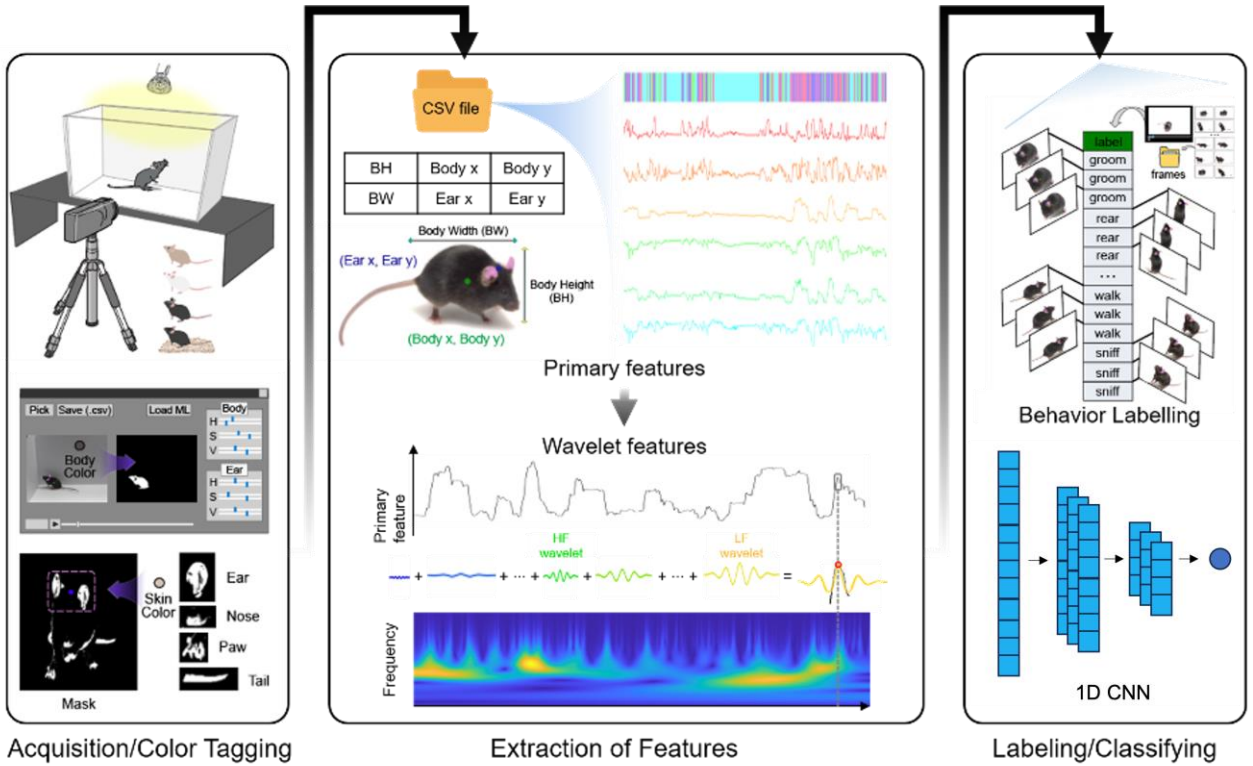


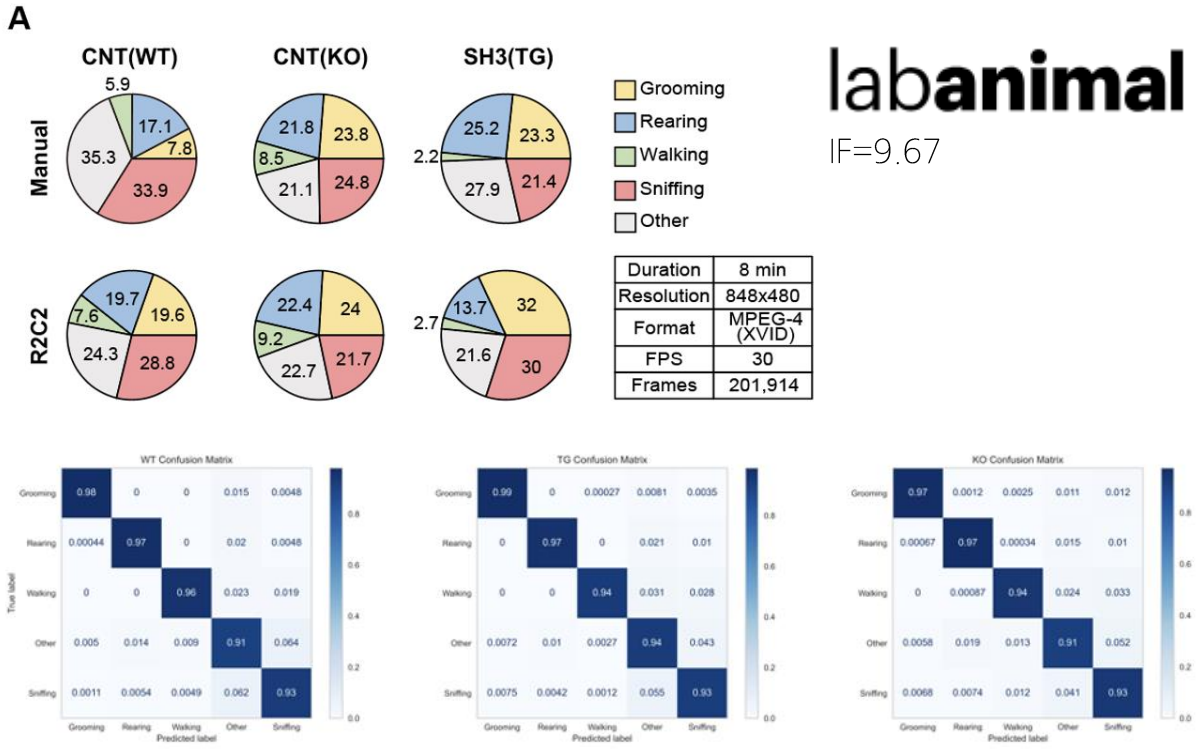
- An End-to-End algorithm to analyze organoid image
- Recognizes over >85% colon organoids
- Provides 8 pre-defined parameters per organoids.

Exosome Cancer Metastasis Lab 박태윤, 김태율, 한윤대, 김경아, 김휘영, 김한상

SCIENTIFIC REPORTS IF=4.60

R2C2: Real-time Rodent Behavior Classifier Using Color-based Body Segmentation





labanimal
IF=9.67

Duration	8 min
Resolution	848x480
Format	MPEG-4 (XVID)
FPS	30
Frames	201,914

- An End-to-End Rodent Behavior Classifier algorithm
- Achieves AUC of 0.97 in behavior classification
- Shows expert-level human performance in distinguishing subtle behaviors associated with Autism Spectrum Disorder.
- GUI helps easy and fast automatic labeling of fine actions

NEUROIC LAB Brain Science Institute Korea Institute of Science and Technology
Korea Institute of Science and Technology THE KIST,Making New History
조정아, 박근홍, 황수현, 박태윤, 민지환, 이선우, 송민호, 광지현, 김휘영, 이창혁, 김정진

Aim 4: Standardization of AI-MD and Biomedical Big Data

AI-based Medical Device

LYDUS
(Leave Your Data to US)

AS-IS

비정형 의료 데이터
(생체신호, 자유기술문, 의료영상)
정제, 가공 기술 부재

형태적 품질만
평가가능

(생체신호, 자유기술문, 의료영상)
정형, 비정형 의료데이터

자동 정제, 가공 기술개발
품질평가 기술개발

다기관 교차검증

임상적 의미 반영
완전성, 신뢰성, 일관성, 익명성

TO-BE

비정형 의료데이터의
신뢰도 확보로
다양한 활용 증대

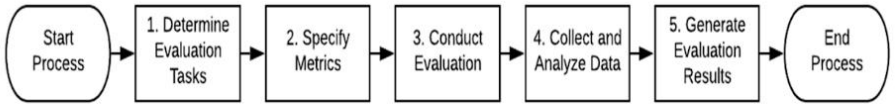
의미적 품질 평가

다기관 검증으로
일반화 가능

연세대학교 의과대학 YONSEI UNIVERSITY COLLEGE OF MEDICINE
SNUH 서울대학교병원
SAMSUNG 삼성서울병원
세브란스병원 SEVERANCE HOSPITAL

Clinical utility	clinical efficacy, beyond the approval
Clinical validity	real-world performance clinical intended use
Scientific validity	robustness justification of using ML/DL technique (in terms of prediction performance)
Technical validity	proof-of-concept, feasibility

Three Pillars



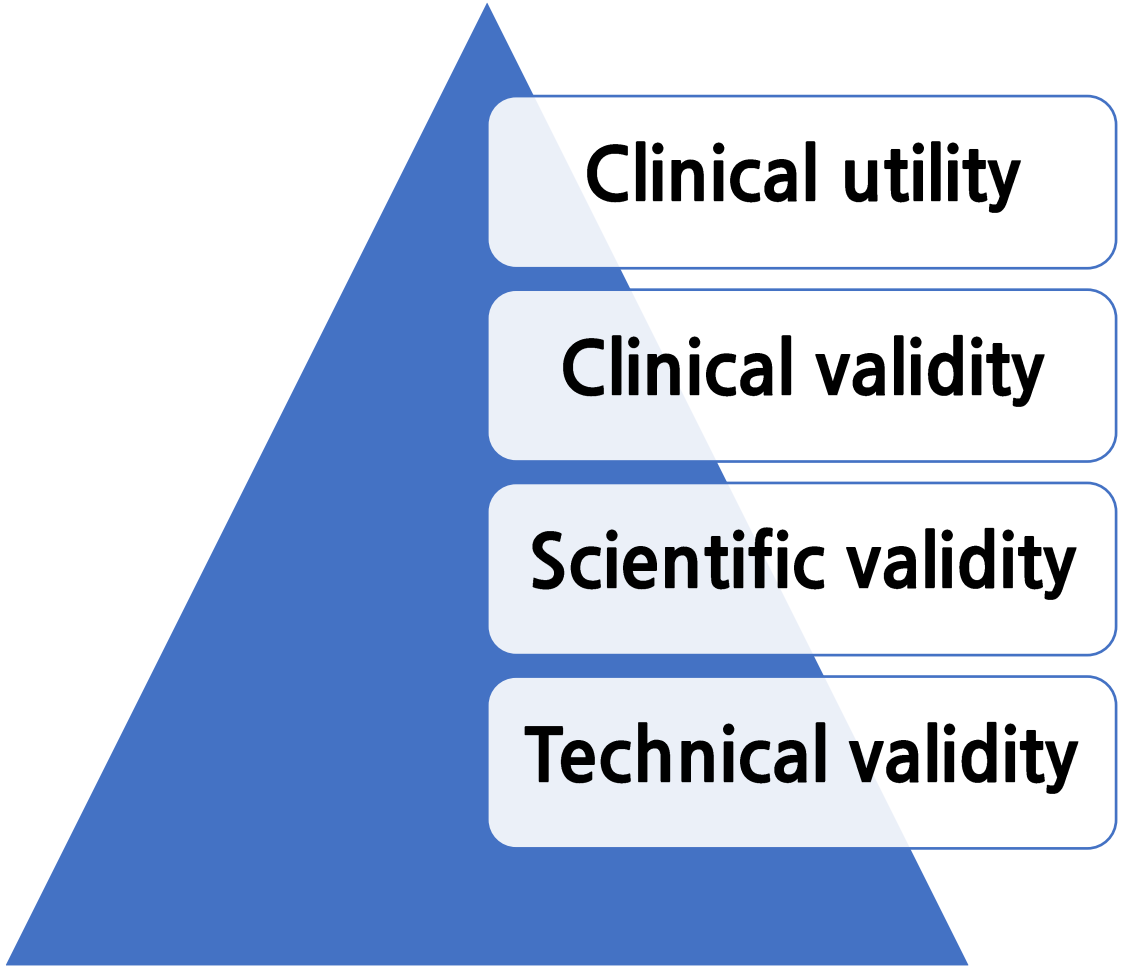
Step 1: Determine Evaluation Tasks
분류/검출/정량화(분할) 문제 등 해당 task 정의

Step 2: Specify Metrics
해당 task와 적응증에 적합한 평가 metric을 구체화하고 명시

Step 3: Conduct Evaluation
평가용 시스템 및 평가용 표준 데이터 셋의 spec. 정의
평가를 위한 데이터 수집
임상시험 수행, 분석 일정/절차 정의

- Step 4: Collect and Analyse Data
  - 성능평가용 표준 데이터 취합 및 curation. Annotation 시행, 시험결과 분석
- Step 5: Generate Evaluation Results
  - 평가 보고서 작성, 관련 structed report 정의

Hierarchy of AI-MD Performance Evaluation



clinical efficacy, beyond the approval

real-world performance
clinical intended use

robustness
justification of using ML/DL technique
(in terms of prediction performance)

proof-of-concept, feasibility

Three Pillars

England et al. *AJR* (2019); 212:513-519

Park, Seong Ho, and Kyunghwa Han. "Methodologic guide for evaluating clinical performance and effect of artificial intelligence technology for medical diagnosis and prediction." *Radiology* 286.3 (2018): 800-809.

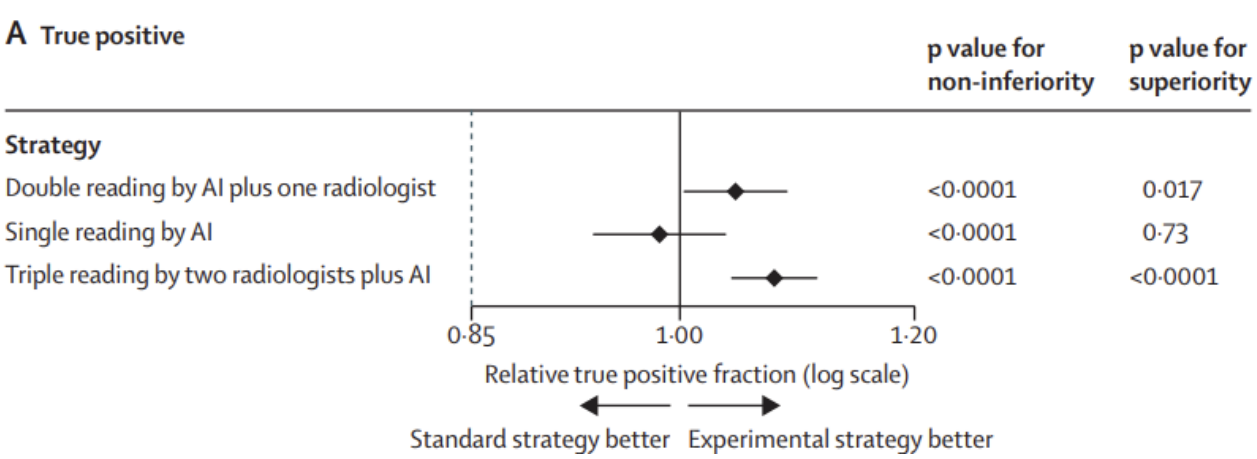
활용근거를 임상적으로 확보하는 노력

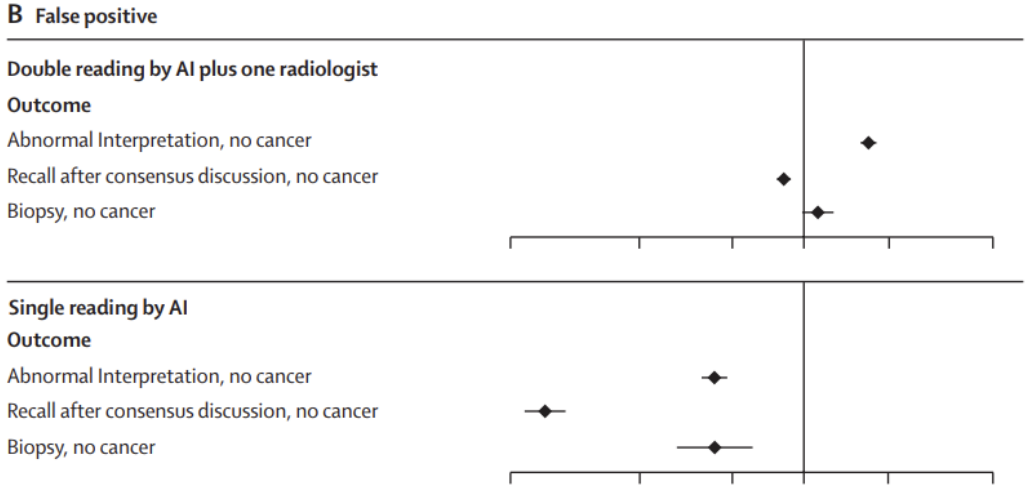
THE LANCET Digital Health

Artificial intelligence for breast cancer detection in screening mammography in Sweden: a prospective, population-based, paired-reader, non-inferiority study

*Karin Dembrower, Alessio Crippa, Eugenia Colón, Martin Eklund, Fredrik Strand, and the ScreenTrustCAD Trial Consortium**

- 유방암 검진시 영상의학과 전문의 2명 double reading
- AI가 전문의 1명을 대체할 경우 향상된 cancer detection rate
  - 동시에, 환자가 병원을 방문해 재검사를 하는 recall rate를 낮출 수 있음을 보임.





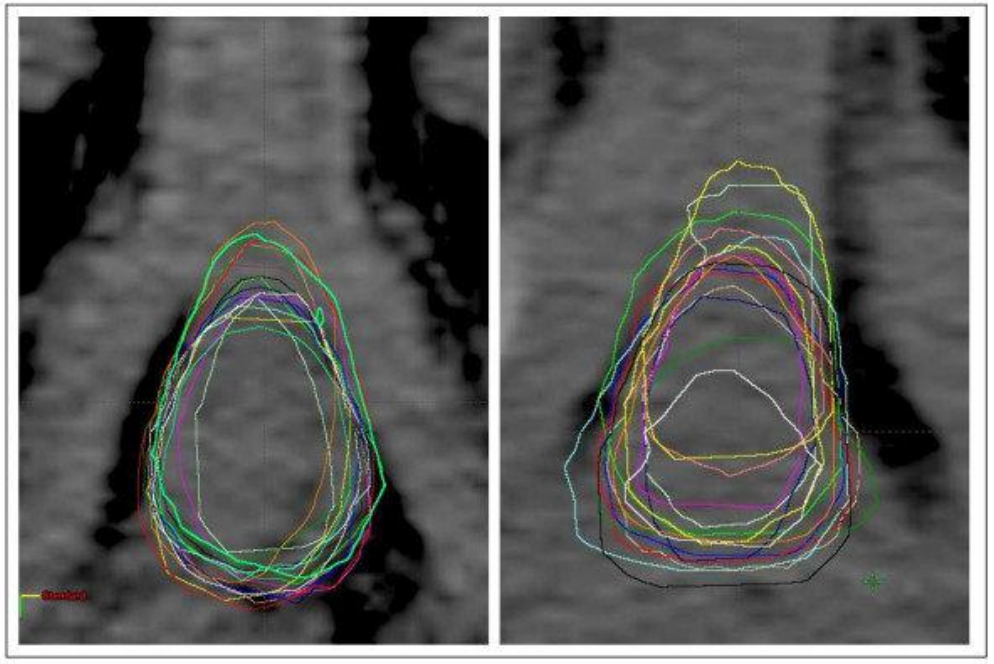
활용근거를 임상적으로 확보하는 노력 (2)

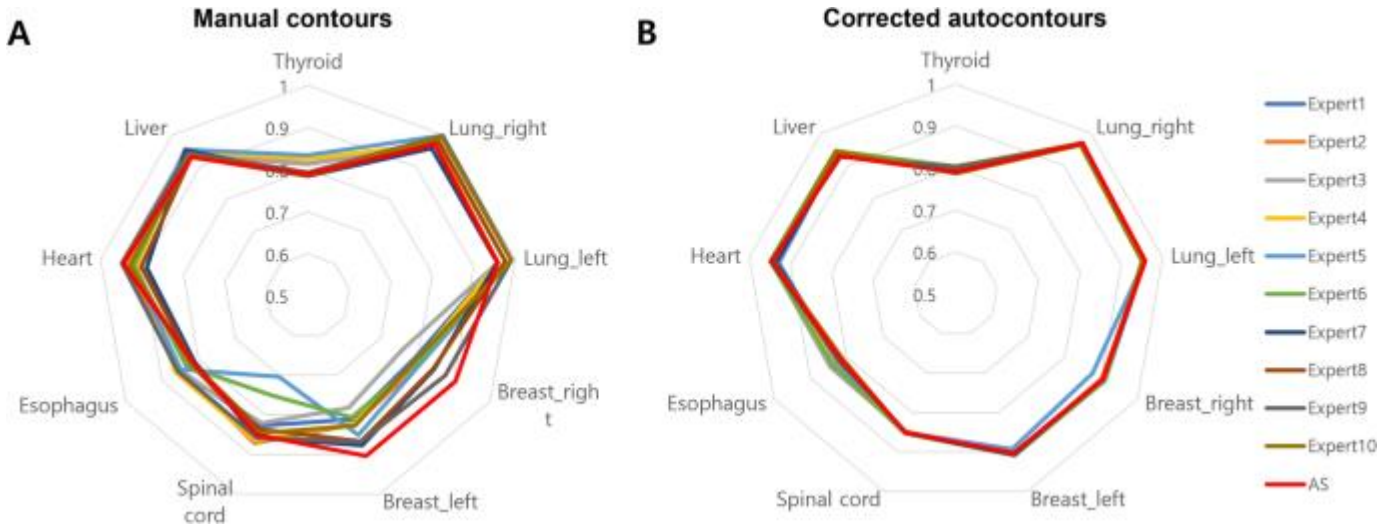
THE LANCET Oncology

NEWS | VOLUME 24, ISSUE 9, E363, SEPTEMBER 2023 Download Full Issue

NICE approval of AI technology for radiotherapy contour planning

Emma Wilkinson



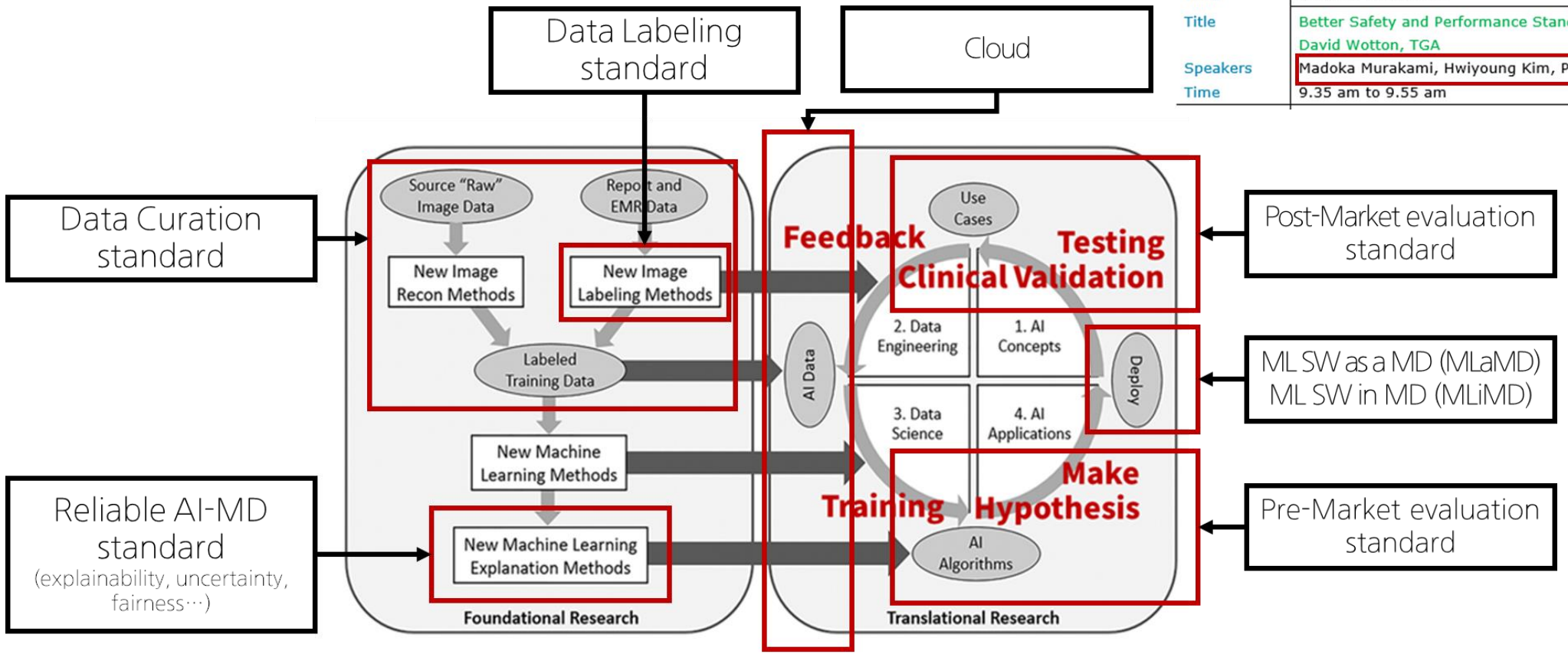


Comprehensive standard for AI-MD

- A comprehensive standard to deal with a total life-cycle of AI-MD is need

IMDRF/DITTA Joint Workshop Agenda
Standards for Health Software
Improving Quality for Regulatory Use
12 September 2022

Session	Safety and Performance - Developing "THE" Comprehensive Standard
Title	Needs and Challenges - Regulator's Perspective
Speaker	Madoka Murakami, Ph.D. (MHLW, Japan)
Time	9.15 am to 9.25 am
Title	Needs and Challenges – Academic Perspective
Speakers	Hwiyoung Kim (Yonsei University, DITTA), Pat Baird (Philips, GMTA)
Time	9.25 am to 9.35 am
Title	Better Safety and Performance Standard(s) - Panel Discussion, Moderator: David Wotton, TGA
Speakers	Madoka Murakami, Hwiyoung Kim, Pat Baird, Scott Colburn (US FDA)
Time	9.35 am to 9.55 am



AI기반 의료기기 국제 표준 개발 활동

범부처전주기의료기기연구개발사업
의료기기 표준화 사업
(3년 총 8억)

- IEC TC62 SNAIG-AG
  - 인공지능 기반 의료기기 관련 국제표준 자문그룹
- ISO JTC1/WG12
  - 의료영상 기반 3D 프린팅 모델링 국제표준개발
- IMDRF

IMDRF/DITTA Joint Workshop Agenda
Standards for Health Software
Improving Quality for Regulatory Use
12 September 2022

Session	Safety and Performance - Developing "THE" Comprehensive Standard
Title	Needs and Challenges - Regulator's Perspective
Speaker	Madoka Murakami, Ph.D. (MHLW, Japan)
Time	9.15 am to 9.25 am
Title	Needs and Challenges – Academic Perspective
Speakers	Hwiyoung Kim (Yonsei University, DITTA), Pat Baird (Philips, GMTA)
Time	9.25 am to 9.35 am
Title	Better Safety and Performance Standard(s) - Panel Discussion, Moderator: David Wotton, TGA
Speakers	Madoka Murakami, Hwiyoung Kim, Pat Baird, Scott Colburn (US FDA)
Time	9.35 am to 9.55 am

ISO Global Directory
Modification of user's data
Notification to member users

Dear Dr Hwiyoung Kim,

You are informed of the following modifications.

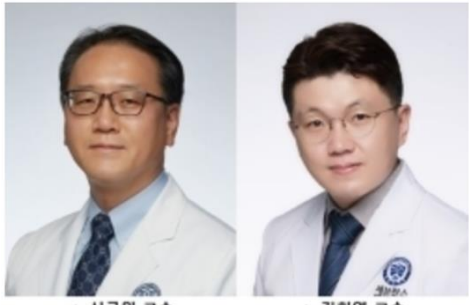
User	Event	Role/Property	Content
Kim, Hwiyoung Dr	Added	Project leader	ISO/IEC AWI 8801

연세의대, 의료용 3D 프린팅 모델링 국제표준 선도

2022-07-08 10:40:10

심규원 교수팀 '의료 영상 기반 의료 3D 프린팅 모델링' 국제 표준화 제안 승인‥ 김휘영 교수는 표준운영절차 수립

세계적으로 의료용 3D 프린팅 개발이 한창인 가운데 연세대학교 의과대학이 의료용 3D 프린팅 모델링 국제표준을 선도하고 있다.



▲ 심규원 교수 ▲ 김휘영 교수

IMDRF: 국제의료기기규제당국자포럼

- 국가 간 협력체계 강화와 국제 의료기기 규제 선도

Session	Safety and Performance - Developing "THE" Comprehensive Standard
Title	Needs and Challenges - Regulator's Perspective
Speaker	Madoka Murakami, Ph.D. (MHLW, Japan)
Time	9.15 am to 9.25 am
Title	Needs and Challenges - Industry Perspective
Speakers	Hwiyoung Kim (Yonsei University, DITTA), Pat Baird (Philips, GMTA)
Time	9.25 am to 9.35 am
Title	Better Safety and Performance Standard(s) - Panel Discussion, Moderator: David Wotton, TGA
Speakers	Madoka Murakami, Hwiyoung Kim, Pat Baird, Scott Colburn (US FDA)
Time	9.35 am to 9.55 am

IMDRF: 국제의료기기규제당국자포럼 (2)

Ministry of Food and Drug Safety

☐ 국제의료기기규제당국자포럼(IMDRF) AI/ML WG 활동 참여('23.9~)

— 우수기계학습기준(Good Machine Learning Practice, GMLP) 개발

— 생성형AI의 특성을 고려한 우수기계학습기준 개발

These guiding principles may be used to:

- Adopt good practices that have been proven in other sectors;
- Tailor practices from other sectors so they are applicable to medical technology and the health care sector; and
- Create new practices specific for medical technology and the health care sector.

Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended Population	Training Data Sets are Independent of Test Sets
Selected Reference Datasets are Based Upon Best Available Methods	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions
Users are Provided Clear, Essential Information	Deployed Models are Monitored for Performance and Re-training Risks are Managed

Hwiyoung Kim, PhD
Dept. of Biomedical Systems Informatics,
Translational Artificial Intelligence Laboratory (TAILab),
Yonsei University College of Medicine

hykim82@yuhs.ac

YONSEI UNIVERSITY
COLLEGE OF MEDICINE