의료 영상정보 활용 방법과 예

Oct. 30th, 2018 Young-Gon Kim

Medical Imaging & Intelligent Reality Lab (MI2RL)
Convergence Medicine/Radiology,
University of Ulsan College of Medicine
Asan Medical Center
South Korea





Contents

- Introduction
- Medical Imaging
- CAD(Computer-Aided Diagnosis)
 System
- Deep Learning for Medical Image
- Discussion



Introduction

- 의료 정보
- 익명화
- 임상시험심사위원회



Introduction

- 의료 정보
 - 전사의무기록 EMR (Electrical Medical Record)
 - 표준화되지 못한 어려움
 - 검체 검사 lab data
 - 장비 별 결과 수치 제각각
 - 영상 검사 medical image
 - 처리하기 방대한 데이터



Introduction

• 익명화 관련 규제 [1]

연구·개발 보물창고 의료영상정보, 왜 쓰질 못하나?

활용 무궁무진 하지만, 법적 규제 가로막혀.."개인정보 비식별 조치 방법 모색해야"

[PDF] 의료기기 분야 규제혁신 및 산업육성 방안

policy.nl.go.kr/cmmn/FileDown.do?atchFileId=223513&fileSn=64959 ▼

2018. 7. 19. - 안전한 의료기기'포괄적 네거티브 규제'전환 ····11. III. 산업육성 중점 편의 가 사사자리를 고요하고 현리하는 '투하운영 심사시스템' ... (예) AI 기반 영상진단

뉴스 관련도순 회신순



[이민화의 4차 산업혁명]개인**데이터 익명화** 개방 서둘러야

서울경제 │ 🗃 39면 🚥 │ 2018,09,1 정보규제가 심한 국가로 분류한 이유[관의 클라우드... 의료기록과 납세기록 활용을 위해 개인정보의 **익명화**가...

특히 의료법 제21조에서는 진료기록인 의료영상 정보는 요건을 갖춘 가족, 국민건강보험법, 의료급여법, 형사소송법 등에 근거한 경우를 제외하고는 원칙적으로 제3자 제공이 금지돼 있 다.

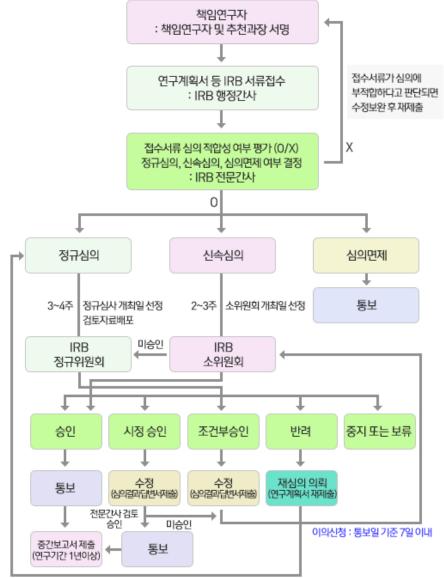
강 연구위원은 이처럼 보수적인 우리나라와 달리 일찍이 의료영상정보에 대한 활용 방법을 마련한 미국과 일본의 사례를 소개했다.

미국은 의료정보보호법(HIPAA; Health Insurance Portability & Accountability Act Privacy Rule)을 통해 비식별화된 개인건강정보는 별도 동의 없이도 수집 또는 이용하도록 했다.

일본은 지난 5월 11일부터 건강·의료에 관한 첨단적 연구 개발 및 신산업 창출을 촉진하기위해 '의료분야의 연구개발에 이바지하기 위한 익명가공 의료정보에 관한 법률'을 시행하고있다.

• 임상시호 Review [

• 임상연구 위하여 ' 리적, 과 는 독립!



안전 • 복지를 -학연구의 윤 승인할 수 있

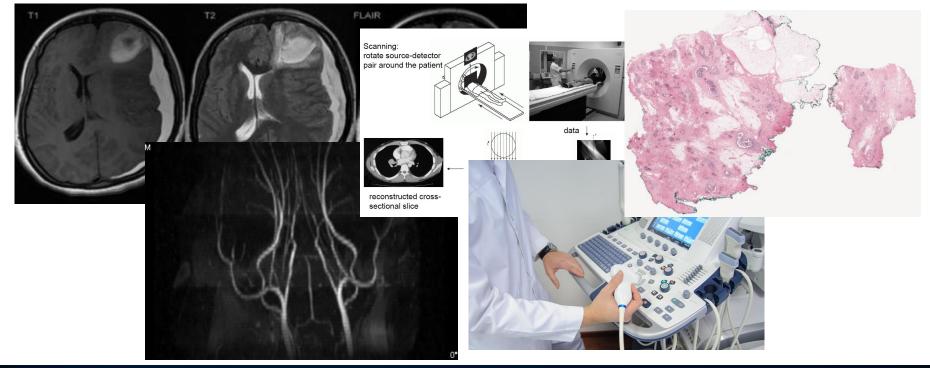
nal

- IRB승인 유효기간: 1년
- IRB 승인 후 1년 이내 연구 시작
- 연구 기간이 1년 이상인 경우 중간보고서 IRB 제출 : 승인유효 만료 2개월 전
- 연구종료 후 종료보고서 및 결과 보고서 제출



Definition

 Medical imaging is the <u>technique and process of creating visual</u> <u>representations of the interior of a body</u> for clinical analysis and medical intervention, as well as visual representation of the function of some organs or tissues (physiology). [3]

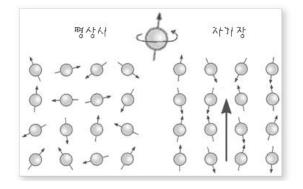




- Image modality
 - MRI (Magnetic Resonance Imaging) [4]

• 물질을 이루는 수소원자의 핵 안에 양성자 (proton)에 에 자기장과 고주파 신호를 주어 방출하는 에너지를

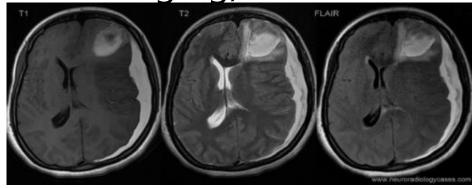
획득하여 영상화



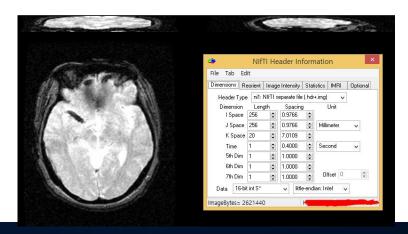
- Sequence
 - T1, T2, DWI, angiography, GRE, etc...
- Image pixel size
 - 256x256x20~512x512x512

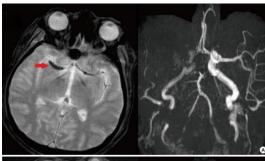


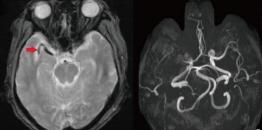
- Image modality
 - MRI (Magnetic Resonance Imging)
 - T1, T2, FLAIR



• GRE, angiography







- Image modality
 - X-ray
 - 방사선의 하나로 자외선보다 파장이 짧은 전자파 투 과력이 매우 크고 의료분야에서는 X선 사진, X선 CT 등으로 응용



X-Rays: MedlinePlus medlineplus.gov



What Are X-Rays? Electromagne...



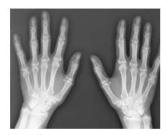
Information Radiation Dose in Medical Imag...



Chest X-Ray for Diagnosis of Lung ... verywellhealth.com



Digital X-Ray - Sand Lake Imagi... sandlakeimaging.com



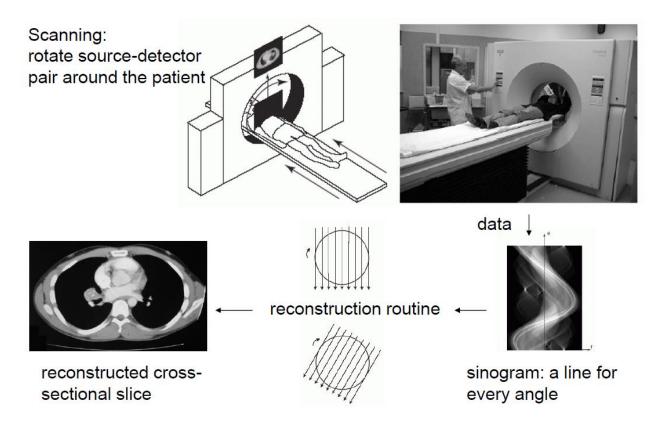
Bone X-ray radiologyinfo.org







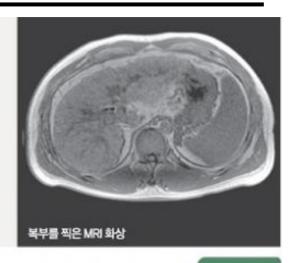
- Image modality
 - CT (Computer Tomography)





- Image modality
 - MRI vs CT [6]





CT		MRI		
X선을 이용해 컴퓨터로 재구성한 영상	검사 원리	자석과 전자기파를 이용해 컴퓨터로 재구성한 영상		
검사 시간 짧음. 3차원 영상도 가능	특징	검사 시간 오래 걸림, X선을 사용하지 않아 비교적 안전		
4만~20만 원	비용	-30만~40만 원(보험 적용 시) -30만~110만 원(보험 적용되지 않을 시)		
평균 15~30초, 전신을 다 찍을 때는 10분	검사시간	30~50분		
각종 폐 질환, 췌장암 담도암 등 소화기관 질환, 뼈 부위	진단 부위	뇌 질환, 척추 질환, 근육 질환, 골관절 질환		
조영제 부작용이 있을 수 있음. X선 노출이 많으므로 단기간 많은 검사는 인체에 해로움	주의사항	폐쇄공포증 환자는 검사에 어려움 겪음. 인공심박동기와 인공내이(內耳)를 이식받은 환자는 촬영 불가능		



- Image modality
 - Ultrasound [7]
 - 우리가 들을 수 있는 소리보다 주파수가 큰 음파를 인 체 내부로 전파시켰을 때 체내 연조직에서 반사된 음 파로 얻어진 반사 영상을 이용한 검사

13

• 인체에 전여 해롭지 않음



Ultrasound - Wikipedia en.wikipedia.org



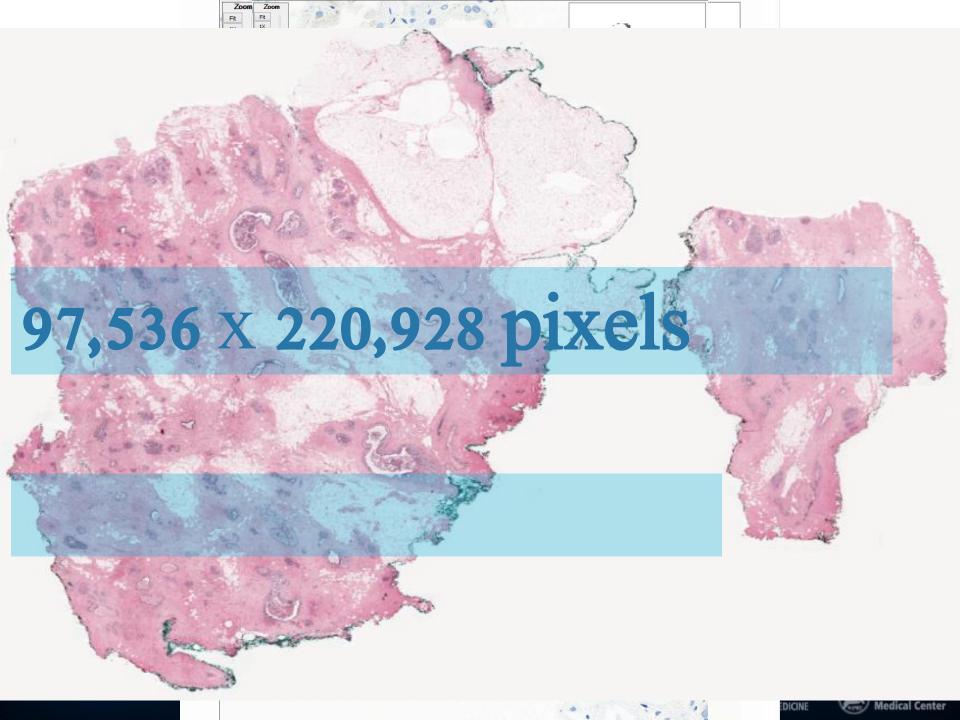
Ultrasound imaging radiologycafe.com



Medical Imaging > Ultrasound Imaging



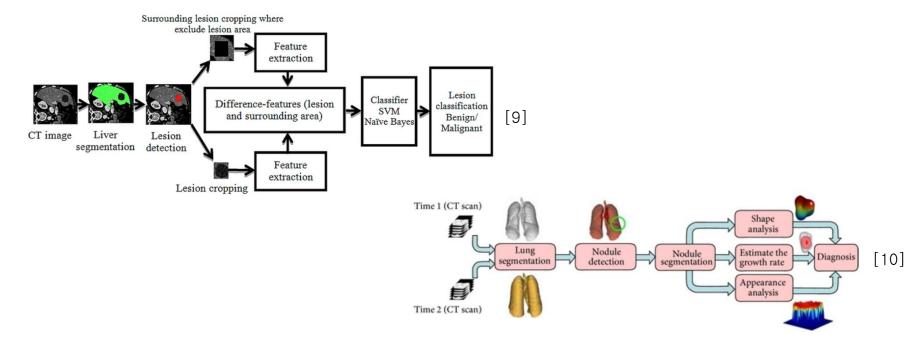
[7] https://www.ausmed.com/articles/medical-imaging-types-and-modalities/



CAD System

Definition [8]

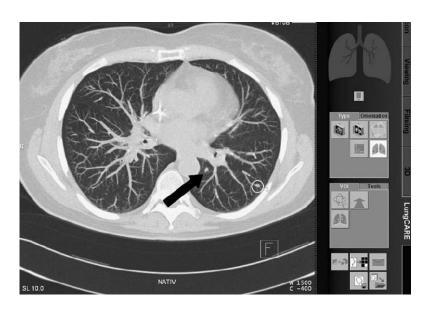
- Computer-aided detection (CADe), also called computer-aided diagnosis (CADx), are systems that assist doctors in the interpretation of medical images.
 - 영상의학과나 다른 의학자들이 분석 및 평가해야만 하는 영상정보들을 전달
 - 질병가능한 부분을 강조하게 함으로써 진단보조에 도움을 줌





CAD System

- Application
 - 폐결절 진단용 [11]



• 뼈나이 보조진단 [12]



CAD System

- Application
 - US Food and Drug Administration (FDA) approved computer-aided detection (CAD) for mammography in 1998... [13]



Original Investigation | LESS IS MORE

Diagnostic Accuracy of Digital Screening Mammography With and Without Computer-Aided Detection

Application

Constance D. Lehman, MD, PhD; Robert D. Wellman, MS; Diana S. M. Buist, PhD; Karla Kerlikowske, MD; Anna N. A. Tosteson, ScD; Diana L. Miglioretti, PhD; for the Breast Cancer Surveillance Consortium

ICE After the US Food and Drug Administration (FDA) approved computer-aided detection (CAD) for mammography in 1998, and the Centers for Medicare and Medicaid Services (CMS) provided increased payment in 2002, CAD technology disseminated rapidly. Despite sparse evidence that CAD improves accuracy of mammographic interpretations and costs over \$400 million a year, CAD is currently used for most screening mammograms in the United States.

Invited Commentary





jama impact fac

OBJECTIVE To measure performance of digital screening mammography with and without

IMPORTANCE After the US Food and Drug Administration (FDA) approved computer-aided detection (CAD) for mammography in 1998, and the Centers for Medicare and Medicaid Services (CMS) provided increased payment in 2002, CAD technology disseminated rapidly. Despite sparse evidence that CAD improves accuracy of mammographic interpretations and costs over \$400 million a year, CAD is currently used for most screening mammograms in the United States.

the category "Me

intraradiologist performance. Sensitivity was significantly decreased for mammograms interpreted with vs without CAD in the subset of radiologists who interpreted both with and without CAD (odds ratio, 0.53: 95% CI, 0.29-0.97).

CONCLUSIONS AND RELEVANCE Computer-aided detection does not improve diagnostic accuracy of mammography. These results suggest that insurers pay more for CAD with no established benefit to women.

Author Affiliations: Department of Radiology, Massachusetts General Hospital, Boston (Lehman); Group Health Research Institute. Seattle Washington (Wellman, Buist, Miglioretti); Departments of Medicine and Epidemiology and Biostatistics, University of California, San Francisco, San Francisco (Kerlikowske) - Norris Cotton Cance



CONCLUSIONS AND RELEVANCE Computer-aided detection does not improve diagnostic accuracy of mammography. These results suggest that insurers pay more for CAD with no established benefit to women.



Journals

- Varun Gulshan, et al., "Development an Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs", *JAMA*, 2016 [15]
- Babak Ehteshami Bejnordi, et al., "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer", *JAMA*, 2017 [16]
- Andre Esteva, et al., "Dermatologist-level classification of skin cancer with deep neural networks", *Nature*, 2017 [17]



Journals

• Varun Gulshan, et al., "Development an Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs", *JAMA*, 2016



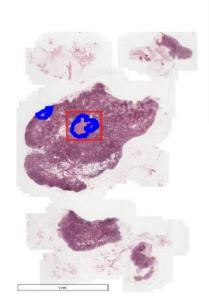
Journals

• Babak Ehteshami Bejnordi, et al., "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer", *JAMA*, 2017

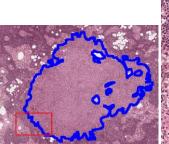


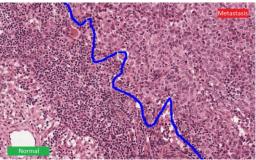
Journals

- Babak Ehteshami Bejnordi, et al., "Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer", *JAMA*, 2017
 - CAMELYON 16
 - https://camelyon16.grand-challenge.org/











Journals

Andre Esteva, et al., "Dermatologist-level classification of skin cancer with deep neural networks", Nature, 2017

LETTER

doi:10.1038/nature21056

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteval*, Brett Kuprell*, Roberto A. Novoa^{2,3}, Justin Ko², Susan M. Swetter^{2,4}, Helen M. Blau⁵ & Sebastian Thrun⁶

neural networks (CNNs)^{4,5} show potential for general and highly variable tasks across many fine-grained object categories⁴⁻¹. Here we demonstrate classification of skin lesions using a single CNN, trained end-to-end from images directly, using only pixels and disease labels as inputs. We train a CNN using a dataset of 129,450 clinical images—two orders of magnitude larger than previous datasets 12—consisting of 2,032 different diseases. We test its performance against 21 board-certified dermatologists on biopsy-proven clinical images with two critical binary classification use cases: keratinocyte carcinomas versus benign seborrheic keratoses; and malignant melanomas versus benign nevi. The first case represents the identification of the most common cancers, the ond represents the identification of the deadliest skin cancer. The CNN achieves performance on par with all tested experts across both tasks, demonstrating an artificial intelligence capable of classifying skin cancer with a level of competence comparable to dermatologists. Outfitted with deep neural networks, mobile devices can potentially extend the reach of dermatologists outside of the clinic. It is projected that 6.3 billion smartphone subscriptions will exist by the year 2021 (ref. 13) and can therefore potentially provide

ow-cost universal access to vital diagnostic care.

There are 5.4 million new cases of skin cancer in the United States² 5% of all skin cancers in the United States, they account for approxifrom over 99% if detected in its earliest stages to about 14% if detected in its latest stages. We developed a computational method which may allow medical practitioners and patients to proactively track skin lesions and detect cancer earlier. By creating a novel disease taxonomy, and a disease-partitioning algorithm that maps individual diseases into training classes, we are able to build a deep learning system for auto-

Previous work in dermatological computer-aided classification 12,14,15 Travision from turnings an tonique state transmission of the generalization capability of medical practitioners (or example, melanoma) we sum the probabilities of their descendants owing to insufficient data and a focus on standardized tasks such as (see Methods and Extended Data Fig. 1 for more details) (see images are acquired via invasive biopsy and microscopy; whereby three-class disease partition—the first-level nodes of the taxonon

images (for example, smartphone images) exhibit variability in factors one camer, the most common natural manageants? , sp primary integes (not example, smartpone mago) examination and diagnosed visually, beginning with an initial clinical screening and followed potentially by dermoscopic analysis, a biopsy and histopathological examination. Automated classification of skin mistopathological examination. Automated dashification of skin mistopathological examination and mistopathological examination. Automated dashification of skin mistopathological examination and mistopathological examination. Automated dashification of skin mistopathological examination and mistopathological examination. Automated dashification of skin mistopathological examination and mistopathological examination variability in the appearance of skin lesions. Deep convolutional techniques require extensive preprocessing, lesion segmentation and extraction of domain-specific visual features before classification. By contrast, our system requires no hand-crafted features; it is trained end-to-end directly from image labels and raw pixels, with a single network for both photographic and dermoscopic images. The existing body of work uses small datasets of typically less than a thousand images of skin lesions.^{46,18,19}, which, as a result, do not generalize well to new images. We demonstrate generalizable classification with a new dermatologist-labelled dataset of 129,450 clinical images, including 3,374 dermoscopy images.

Deep learning algorithms, powered by advances in computation and very large datasets²⁵, have recently been shown to exceed human performance in visual tasks such as playing Atari games26, strategic board games like Go²⁷ and object recognition⁶. In this paper we outline the development of a CNN that matches the performance of dermatologists at three key diagnostic tasks: melanoma classification, melanoma classification using dermoscopy and carcinoma classification. We restrict the comparisons to image-based classification. We utilize a GoogleNet Inception v3 CNN architecture⁹ that was pre-

trained on approximately 1.28 million images (1,000 object categories from the 2014 ImageNet Large Scale Visual Recognition Challenge and train it on our dataset using transfer learning 20. Figure 1 shows the working system. The CNN is trained using 757 disease classes. Our every year. One in five Americans will be diagnosed with a cutaneous malignancy in their lifetime. Although melanomas represent fewer than diseases form the leaf nodes. The images come from 18 different mately 75% of all skin-cancer-related deaths, and are responsible for clinician-curated, open-access online repositories, as well as from ver 10,000 deaths annually in the United States alone. Early detection is critical, as the estimated 5-year survival rate for melanoma drops a subset of the full taxonomy, which has been organized clinically and visually by medical experts. We split our dataset into 127,463 training and validation images and 1,942 biopsy-labelled test images.

To take advantage of fine-grained information contained within the taxonomy structure, we develop an algorithm (Extended Data Table 1) to partition diseases into fine-grained training classes (for example, amelanotic melanoma and acrolentiginous melanoma). During inference, the CNN outputs a probability distribution over these fine classes. To recover the probabilities for coarser-level classes of interest

both modalities yield highly standardized images. Photographic which represent benign lesions, malignant lesions and non-neoplastic

The partment of Electrical Engineering, Stanford University, Stanford, California, USA "Department of Demandings, Stanford, California, USA "Department of Pathology, Stanford University, Stanford, California, USA, "Demandings Service, Veteran Aftein Pair Bull Bull Service System, Palo Alto, California, USA, "State Laboratory for Stam Cell Biology, Depart of Microbiology and Hornically, Institute for Stam Cell Biology and Regenerative Medicine, Stanford California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA," Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University Stanford, California, USA," Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford University, Stanford, California, USA, "Oppartment of Computer Science, Stanford, California, USA, "Oppartment of Computer Science, Stanford, California, USA, "Oppartment of C

2 FERRILARY 2017 | VOL 542 | NATURE | 115

Challenges

- MICCAI (Medical Image Computing & Computer Assisted Intervention)
- ISBI (International Symposium and Biomedical Imaging)
- RSNA (Radiological Society of North America)



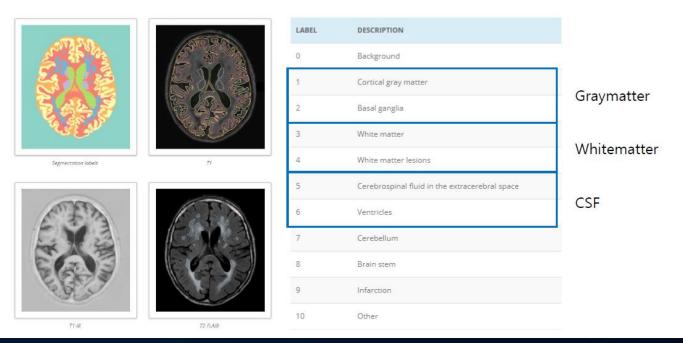
Challenges

• MICCAI (Medical Image Computing & Computer Assisted

Intervention)

ACRONYM	NAME	TIME	DATE	VENUE	MEETING ROOM
EndoVis18	Endoscopic Vision Challenge 2018 + CATARACTS Challenge 2018	FULL DAY	16 SEPTEMBER	Conference Center	Andalucia 2
ISLES	Ischemic Stroke Lesion Segmentation Challenge	FULL DAY	16 SEPTEMBER	Conference Center	Room D
CuRIOUS	MICCAI Challenge 2018 for Correction of Brainshift with Intra-Operative UltraSound	РМ	16 SEPTEMBER	Saray Hotel	Salon Alcazaba Salon 1
СРМ	Computational Precision Medicine Challenge	PM	16 SEPTEMBER	Conference Center	VIP Room
MRBrainS18	MICCAI Grand Challenge on MR Brain Image Segmentation	АМ	16 SEPTEMBER	Saray Hotel	Salon Alcazaba Salon 1
BraTS	MICCAI Multimodal Brain Tumor Segmentation (BraTS) Benchmark: "Survival Prediction"	FULL DAY	16 SEPTEMBER	Conference Center	Room D
IVDM3Seg	Intervertebral Disc Segmentation Challenge 2018	АМ	16 SEPTEMBER	Conference Center	Andalucia 1
ISIC	Challenge on Dermoscopic Skin Lesion Analysis Toward Melanoma Detection 2018(with workshop nr. 41)	FULL DAY	20 SEPTEMBER	Conference Center	Seminar Room 3-4-5
MSD	Medical Segmentation Decathlon	PM	20 SEPTEMBER	Conference Center	Room Albeniz
MoNuSeg	Multi-Organ Histopathology Nucleus Segmentation Challenge for H&E Stained Images 2018	FULL DAY	20 SEPTEMBER	Conference Center	Room C
MUSHAC	Multi-shell diffusion MRI harmonisation and enhancement challenge	РМ	20 SEPTEMBER	Conference Center	Andalucia 2
REFUGE	Retinal Fundus Glaucoma Challenge	РМ	20 SEPTEMBER	Conference Center	Room Machado

- Challenges
 - MICCAI (Medical Image Computing & Computer Assisted Intervention)
 - MRBrainS18
 - Segmentation





Challenges

• MICCAI (Medical Image Computing & Computer Assisted Intervention)

Multimodal Brain Tumor Segmentation Challenge 2018

- BraTS
 - Segmentation
 - Survival prediction



• Scope • Relevance • Tasks • Data • Evaluation • Participation Summary • Data Request • Previous BraTS • People •

Scope

BraTS has always been focusing on the evaluation of state-of-the-art methods for the segmentation of brain tumors in multimodal magnetic resonance imaging (MRI) scans. BraTS 2018 utilizes multi-institutional pre-operative MRI scans and focuses on the segmentation of intrinsically heterogeneous (in appearance, shape, and histology) brain tumors, namely gliomas. Furthemore, to pinpoint the clinical relevance of this segmentation task, BraTS'18 also focuses on the prediction of patient overall survival, via integrative analyses of radiomic features and machine learning algorithms.

IMPORTANT DATES:	
A CONTRACTOR OF THE CONTRACTOR	Release of training datasets. — Request the data here!
30 Apr	
1 Jul	Release of validation datasets. — View the Leaderboard
14 Jul	Submission of short papers, reporting proposed method & preliminary results.
30 Jul-20 Aug	Release of testing datasets for 48hr window (& performance evaluation).
30 Aug	Contacting top performing methods for preparing slides for oral presentation.
16 Sep	Challenge at MICCAI (Granada, Spain) — View the Pre-conference Proceedings
1 Nov	Extended LNCS paper submission deadline.



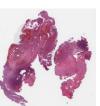
- Challenges
 - MICCAI (Medical Image Computing & Computer Assisted Intervention)
 - CPM
 - Classification





- Challenges
 - MICCAI (Medical Image Computing & Computer Assisted Intervention)
 - CPM Combined Radiology and Pathology Classification
 - (2 class classification)
 - Training Phase
 - » 32 radiology MR images
 - » 32 pathology Whole slice images
 - Test Phase
 - » 20 radiology MR images
 - » 20 pathology Whole slice images

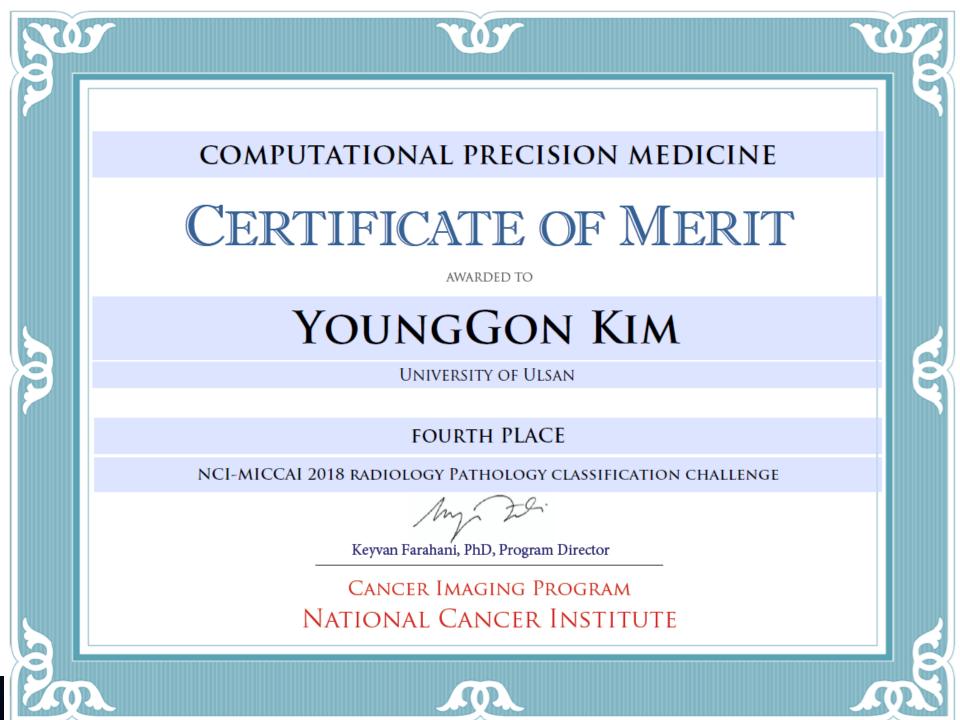




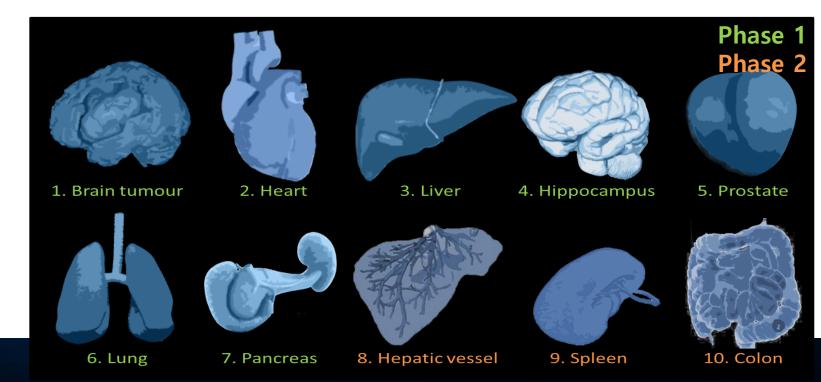




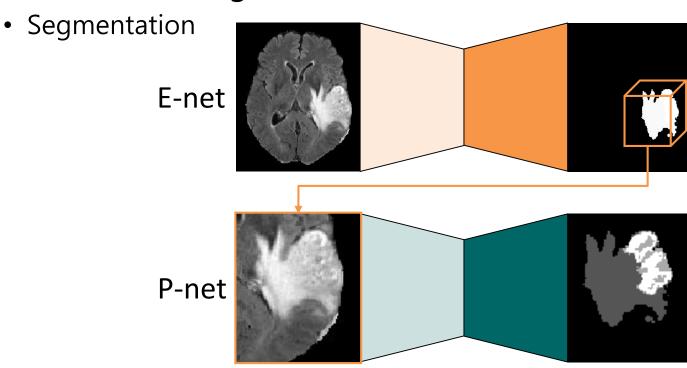




- Challenges
 - MICCAI (Medical Image Computing & Computer Assisted Intervention)
 - MDS (Medical Segmentation Decathlon
 - Segmentation



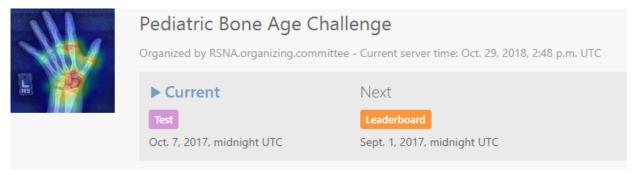
- Challenges
 - MICCAI (Medical Image Computing & Computer Assisted Intervention)
 - MDS (Medical Segmentation Decathlon



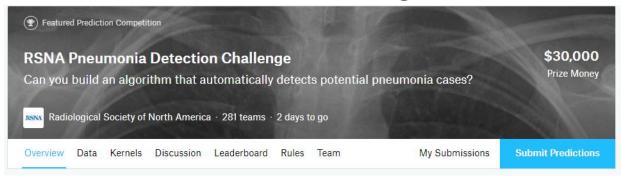
- Challenges
 - ISBI (International Symposium and Biomedical Imaging)
 - CAMELYON 16
 - CAMELYON 17
 - LiTS (Liver Tumor Segmentation Challenge)
 - Diabetic Retinopathy segmentation



- Challenges
 - RSNA (Radiological Society of North America)
 - Pediatric Boneage Challenge



Pneumonia Detection Challenge





- Deep learning based applications in Korea
 - 식약처 허가
 - 뷰노메드 본에이지 (뷰노) [14]





- Deep learning based applications in Korea
 - 식약처 허가
 - 뷰노메드 본에이지 (뷰노) [14]
 - : Xray 손 영상을 통해환자의 뼈 나이를 제시하여 의사가 제 시된 정보 등으로 성조숙증이나 저성장을 진단하는데 도움 을 주는 의료기기
 - 의료 영상분석장치소프트웨어 2등급 허가
 - 판매 불가능

그러나 뷰노메드 본에이지의 성공적인 개발과 식약처의 허가에도 불구하고 뷰노 측은 마음이 급하다고 말했다. 본에이지를 의료기기로 허가 받았지만 여전히 판매는 불가능한 상태이기 때문이다.

현행 국민건강보험법에 따르면 요양급여대상 또는 비급여대상으로 결정되지 않은 요양급여의 행위와 치료재료에 대해서는 요양급여대상여부의 결정을 보건복지부장관에게 신청해야 한다.

즉 의료기기로 허가를 받았으나 이것을 기존기술인지 신의료기술인지로 평가해야지 판매가 가능하다. 기존기술로 판단되면 이를 급여여부만 평가하면 되지만, 신의료기술로 분류되면 시간이 오래 걸린다. 뷰노는 이를 약 10일 전에 신청했다.

김 CSO는 "현재 걱정되는 것은 본에이지를 기존기술로 판단하지 않고, 신의료기술로 평가할 가능성이 높다는 것"이라며 "신의료기술로 평가되면 또 법적검토를 280일간 받아야 한다는 도중에 보완작업을 거치면 결국 9개월을 훌쩍 넘는데, 식약처 인허가를 받고도 1년간 더 기다려야 한다는 것"이라고 말했다.



- Deep learning based applications in Korea
 - 식약처 허가
 - Lunit INSIGHT (루닛)
 - Xray기반 폐결절을 검출하는 검출보조소프트웨어
 - ex) https://insight.lunit.io/#examples
 - JBS-01K (제이엘케이인스펙션)
 - 뇌경색 패턴을 제시해주는 진단보조소프트웨어
 - 셀비 메디보이스 (셀바스AI) [15]
 - AI기반 음성인식 엔진
 - 식약처 임상시험 허가
 - 뷰노메드 체스트엑스레이 (뷰노)
 - Xray기반 폐암, 폐렴 등 5종의 흉부질환 검출하는 검출보조 소프트웨어 (임상시험 돌입)

