NAGOYA UNIVERSITY

Medical procedure assistance based on machine learning – Current status and future direction

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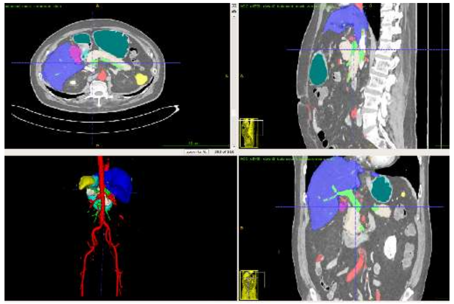
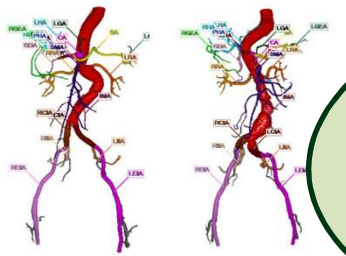
Nagoya University

科研費 KAKENHI

Research topics at Mori Laboratory, Nagoya University

Anatomical structure analysis





Surgical simulation / planning/ navigation

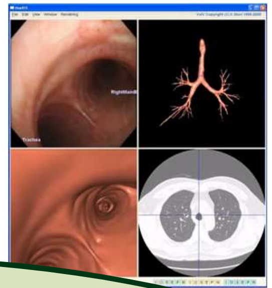
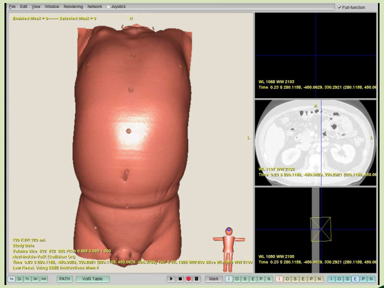


Image analysis

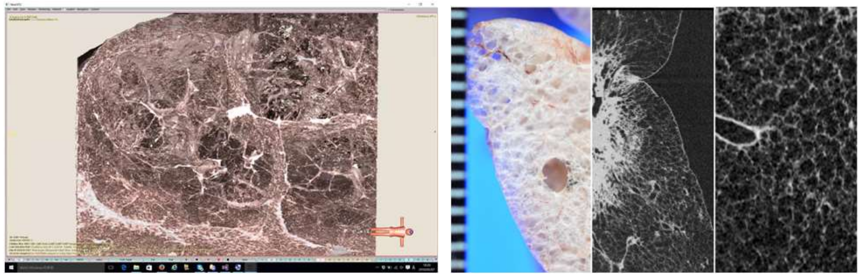
- Image Processing
- Machine learning
- Visualization and VR/AR
- Sensor fusion



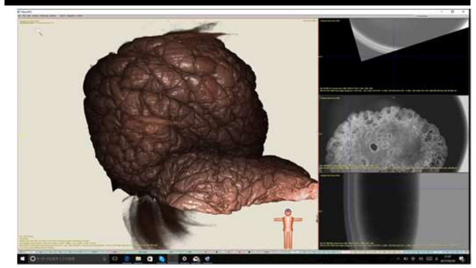
3D Printing

EC-CAD

Micro-structure analysis



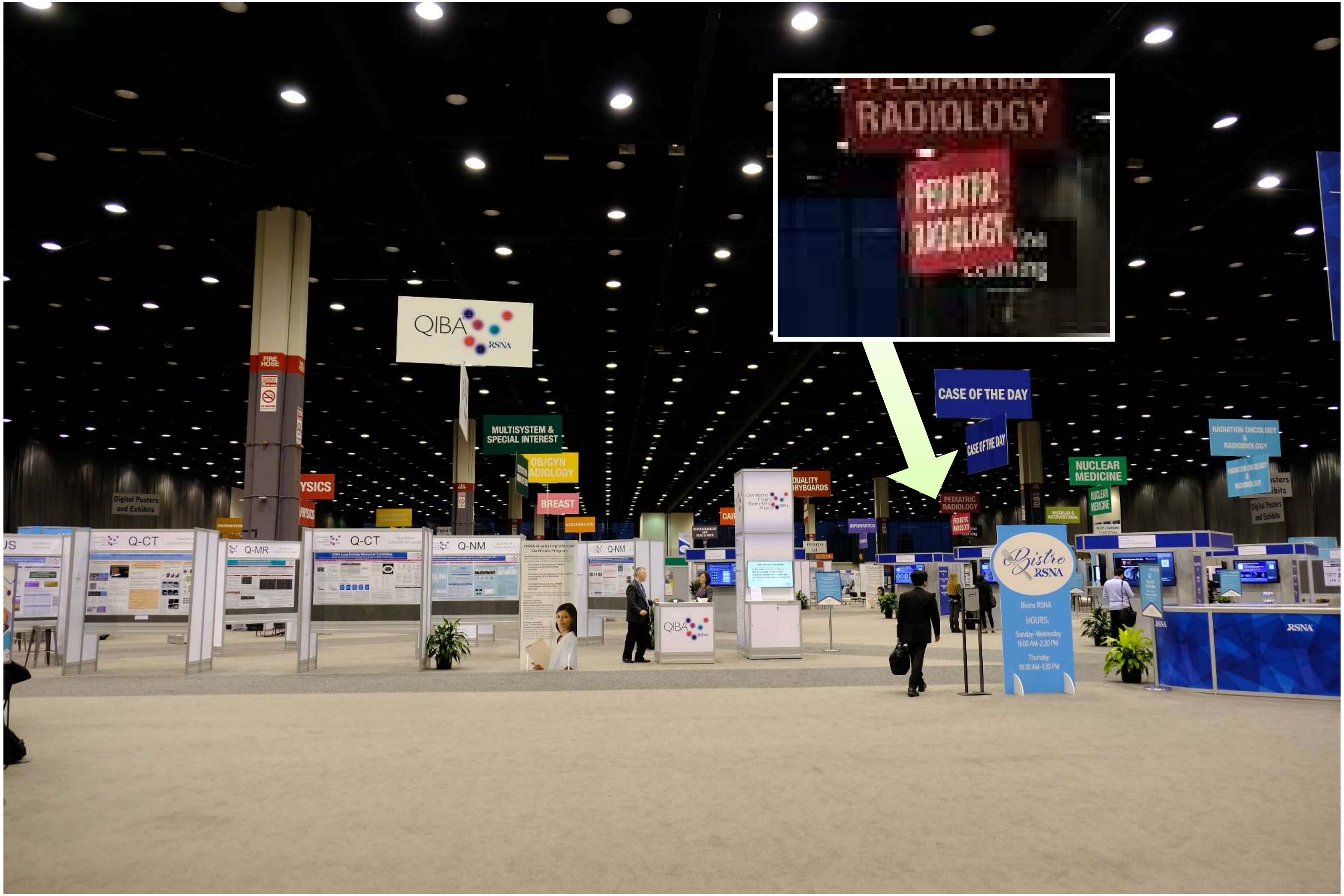
Refraction X-ray



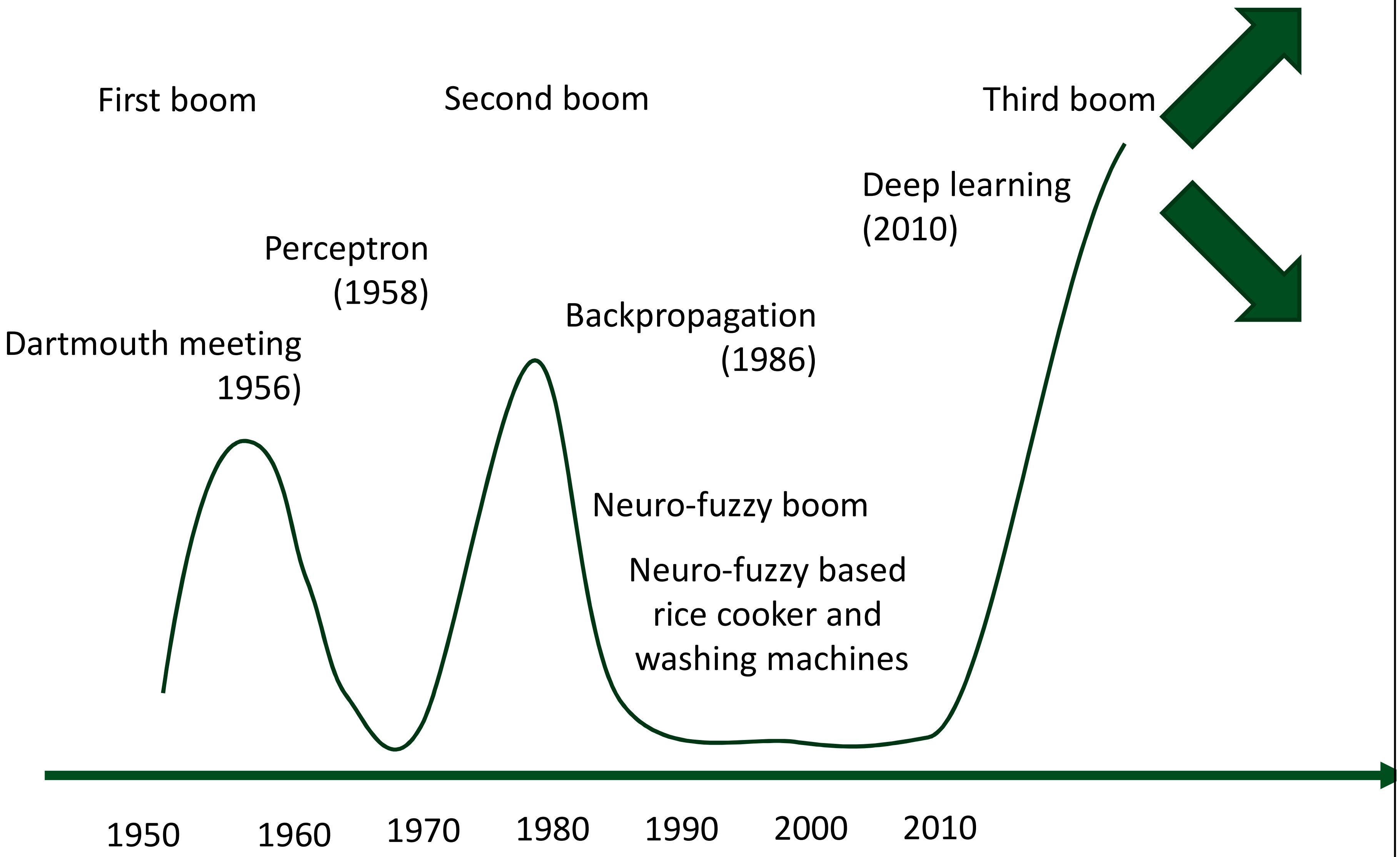
RSNA (Radiological Society of North America)

- 40k – 50k attendees
- ML is big trend in RSNA 2017
- All of ML-related sessions are fully packed

Machine learning is now subspeciality in RSNA

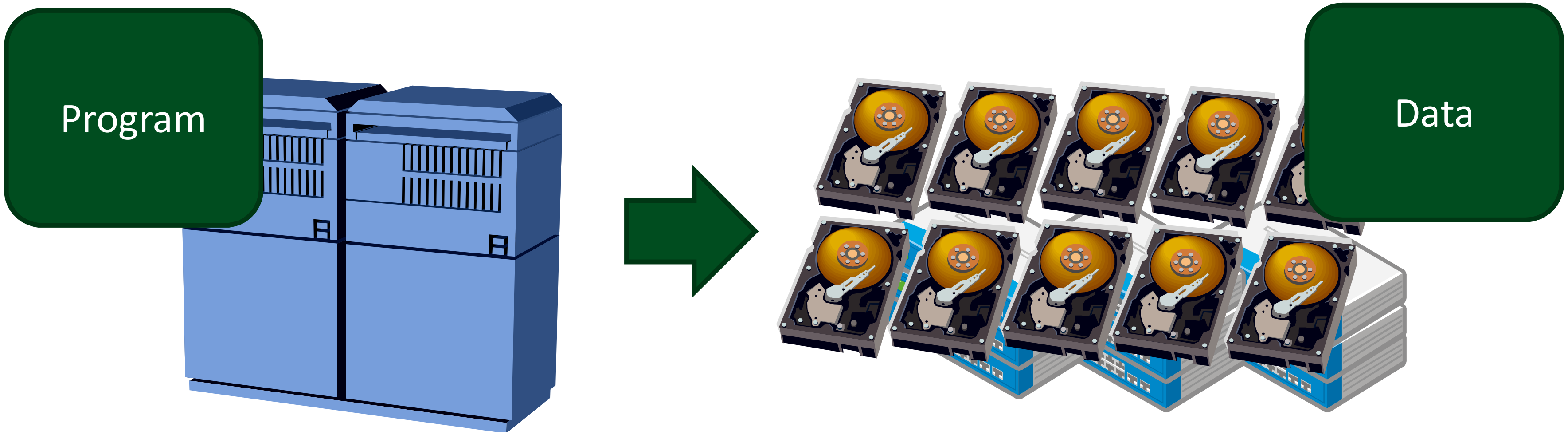


Neural network boom



Trends in information processing

- From Process Driven to Data Driven
  - Reduction of computation and data storage cost
- Data Intensive Computing



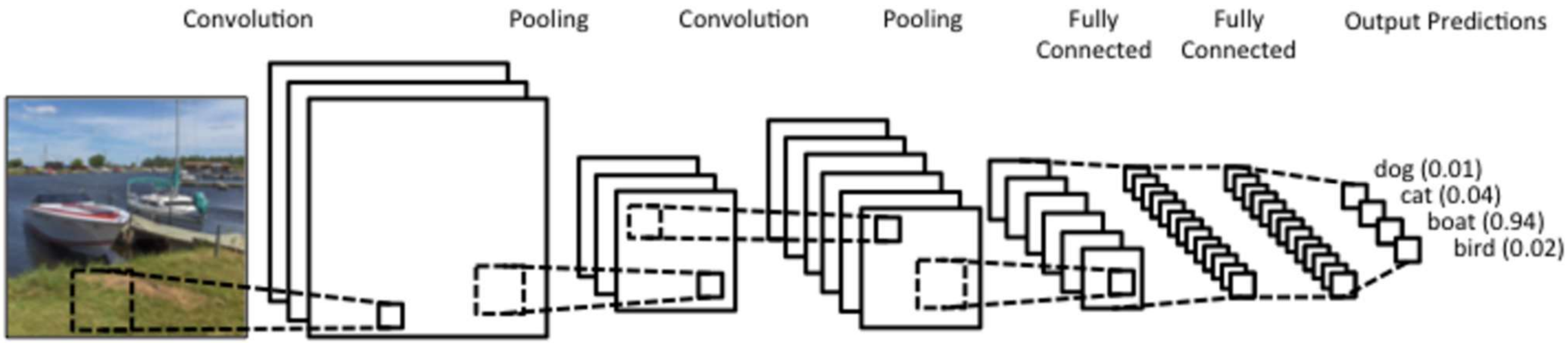
Program is knowledge

Data is knowledge

Everyone is using caffe / tensorflow / chainer
Data is different

Convolutional Neural Network

- Neural network for recognizing images
  - Neocognitron is an origin of CNN [Fukushima]
- Input is image; Output are likelihood of categories
- Convolution layers, maxpooling



http://d3kbpzbmcynnmx.cloudfront.net/wp-content/uploads/2015/11/Screen-Shot-2015-11-07-at-7.26.20-AM.png

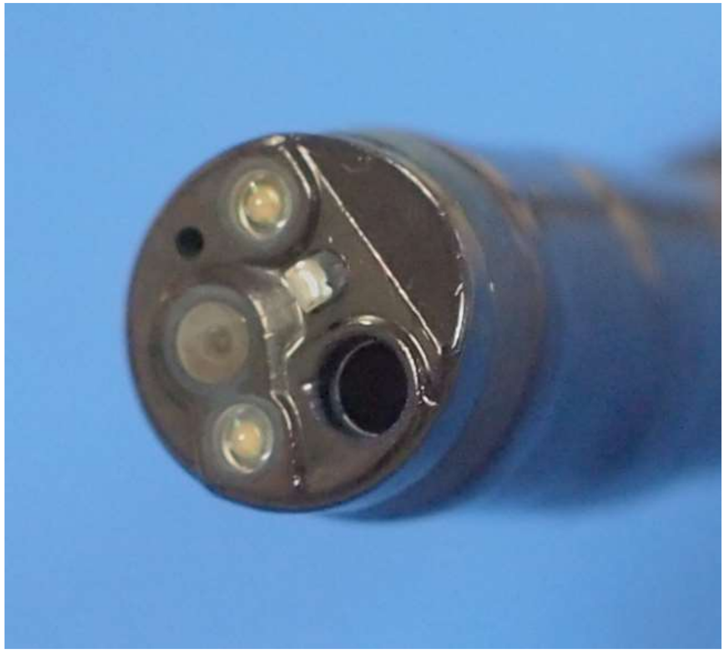
All of medical images will be fully annotated by DL in next five years

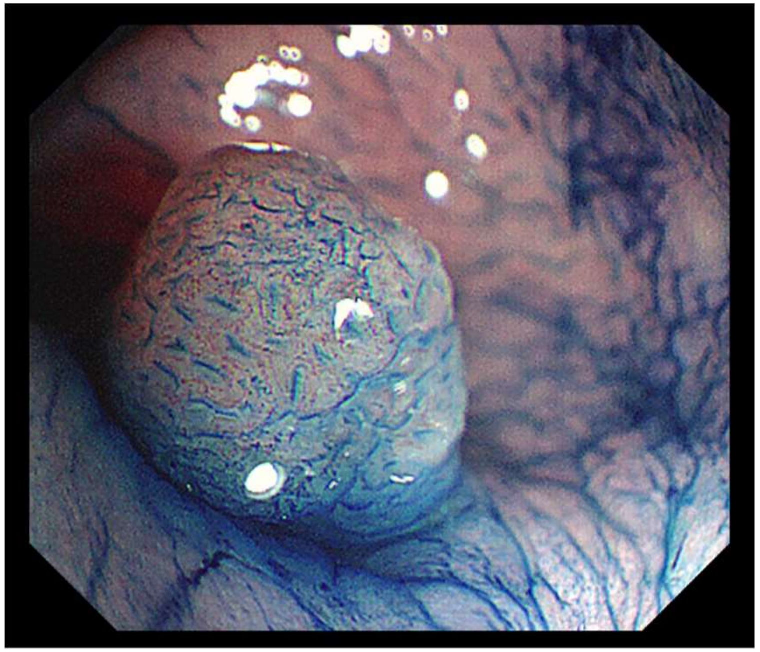
Machine learning in medical system

- Will be used and become very common in many medical fields in next five years?
- Machine intelligence
  - Supporting diagnosis and treatment
  - (Question) autonomous diagnosis and treatment

Endocytoscopy

- Over 500x magnifications
- Real-time observation of cells
- Optical Biopsy





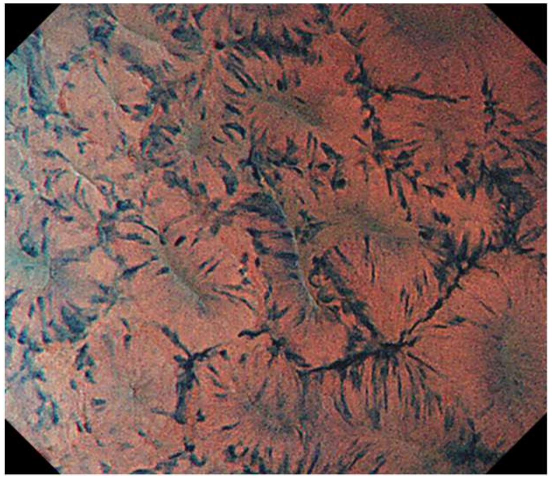
*Inoue H, et al. **Nat Clin Pract Gastroenterol Hepatol** 2005
*Kumagai Y, et al. **Endoscopy** 2004
*Fujishiro M, et al. **Gastrointest Endosc** 2007
*Kudo S, et al. **Endoscopy** 2011
*Mori Y, et al. **Endoscopy** 2013
*Kudo T, et al. **DEN** 2015

New medical device and ML

- Medical devices advance continuously
- More skills are needed to use them and diagnose information obtained from them
- Advanced medical systems should have more intelligence for supporting doctors

Colorectal cancer

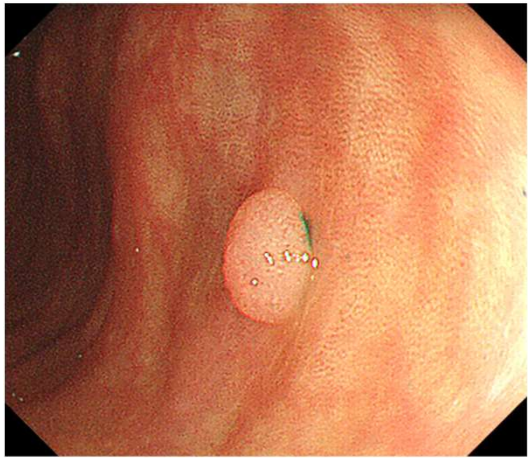
- Colorectal cancer
  - No. 1 cancer in Japan
  - Possible to completely care for early stage cancers
  - Necessary for arly diagnosis and treatment by endoscopy
  - Lack of colorectal endoscopist and pathologist
- Endocytoscopy
  - New endoscope
  - 380x – 500x magnification
  - Cell-level observation
  - Optical biopsy



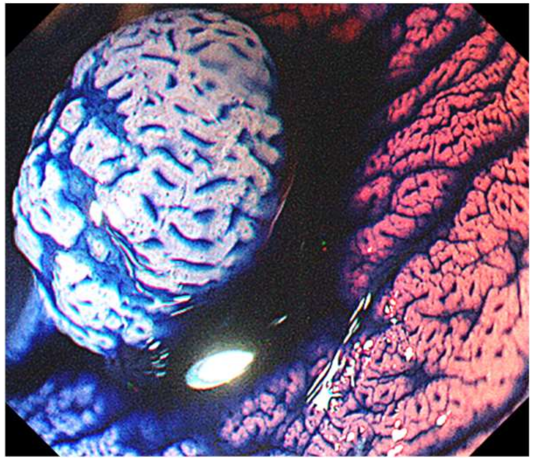
Endocytoscopic image

Classification of tumor or non-tumor

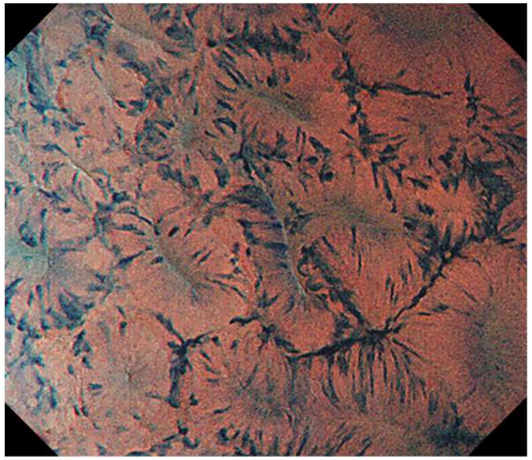
- Conventinoal colonoscope
  - 70-80% accuracy
- Endocytoscopy
  - Accuracy: >90% (experts), 80% (non expert)
  - Long time training for achieve high-accuracy diagnosis



Colonoscopic image



Magnified colonoscopic image



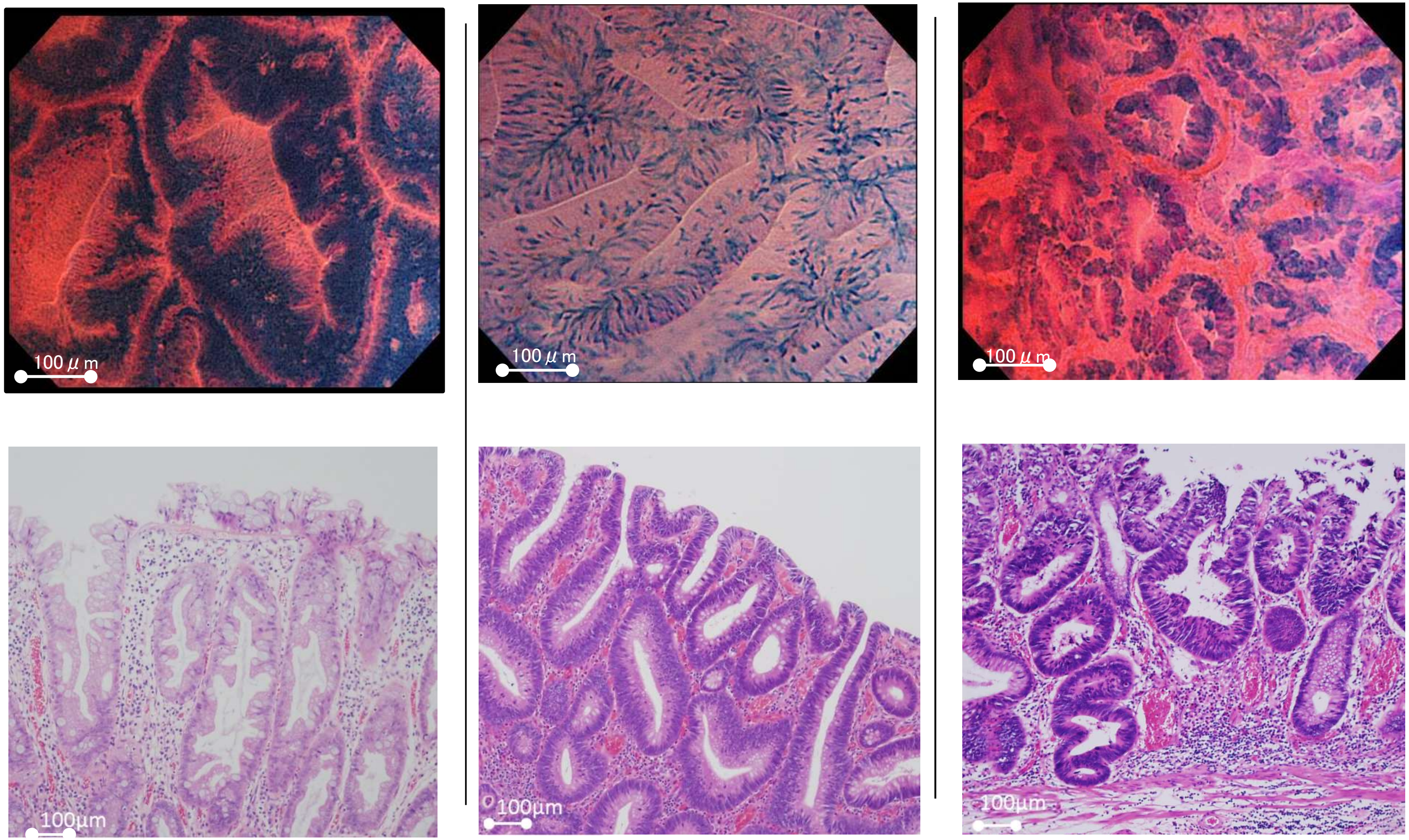
Endocytoscopic image

Similarity between EC images and HE images

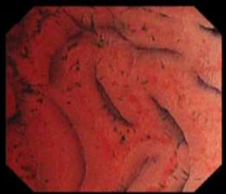
Hyperplastic polyp | Adenoma | Cancer

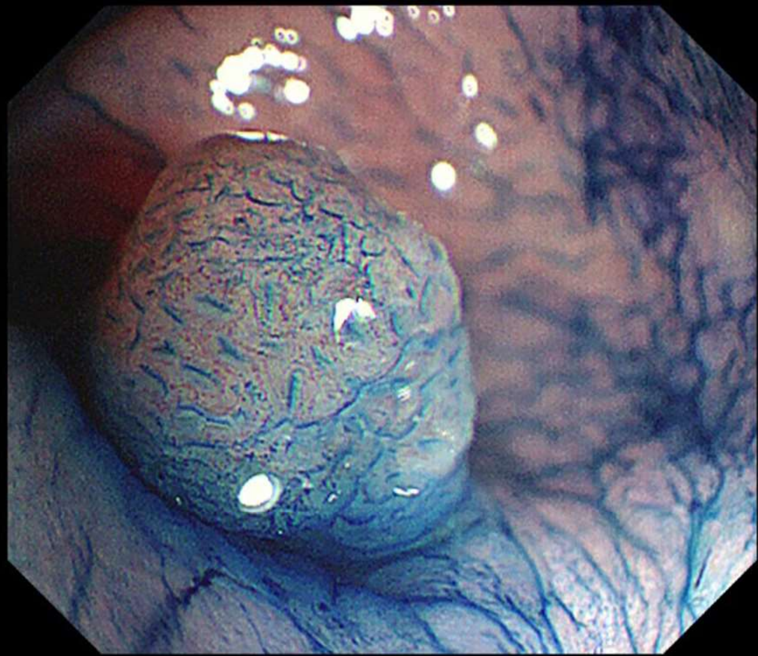
EC

Pathology

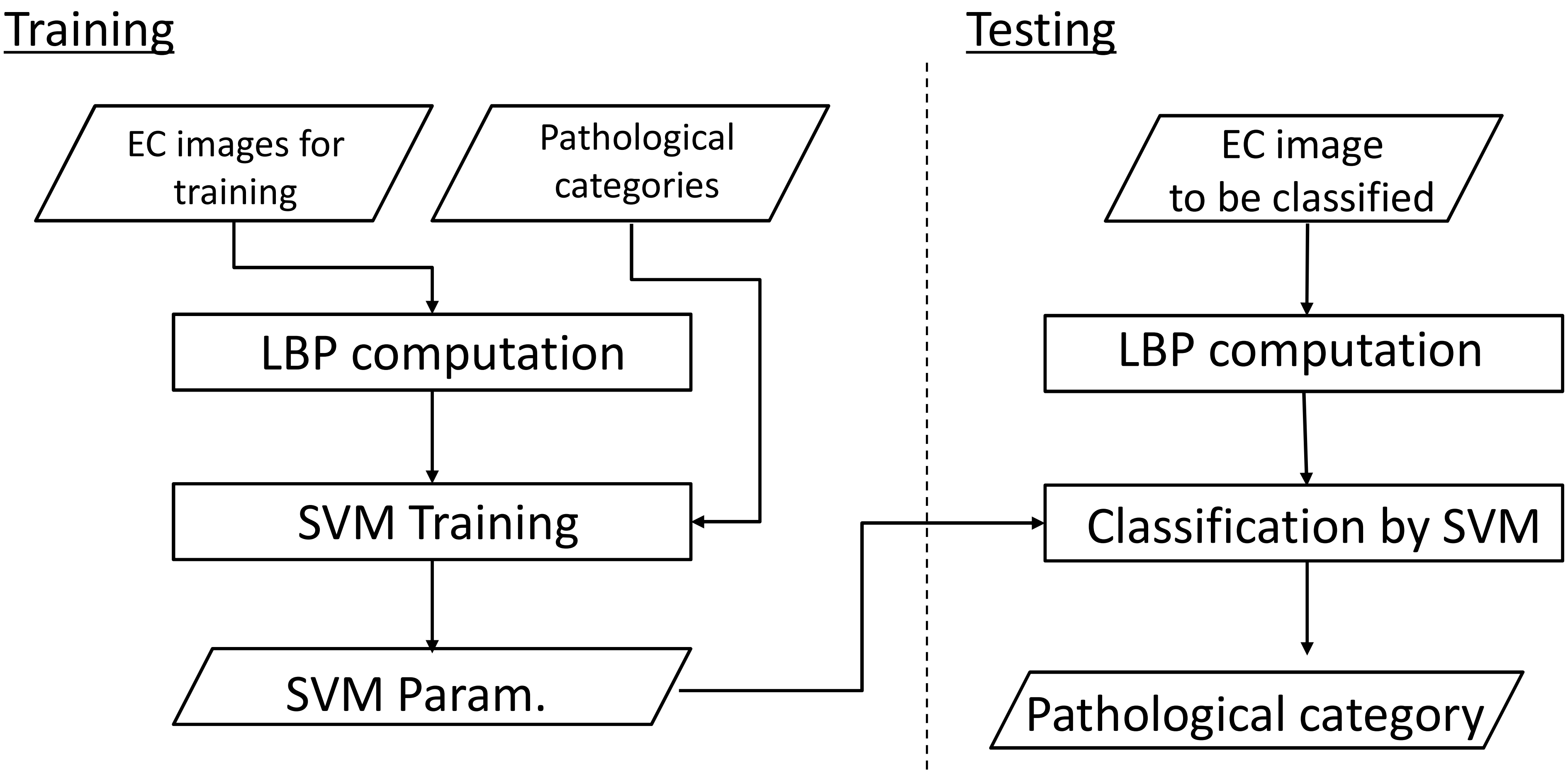


Automated endocytoscopic video analysis

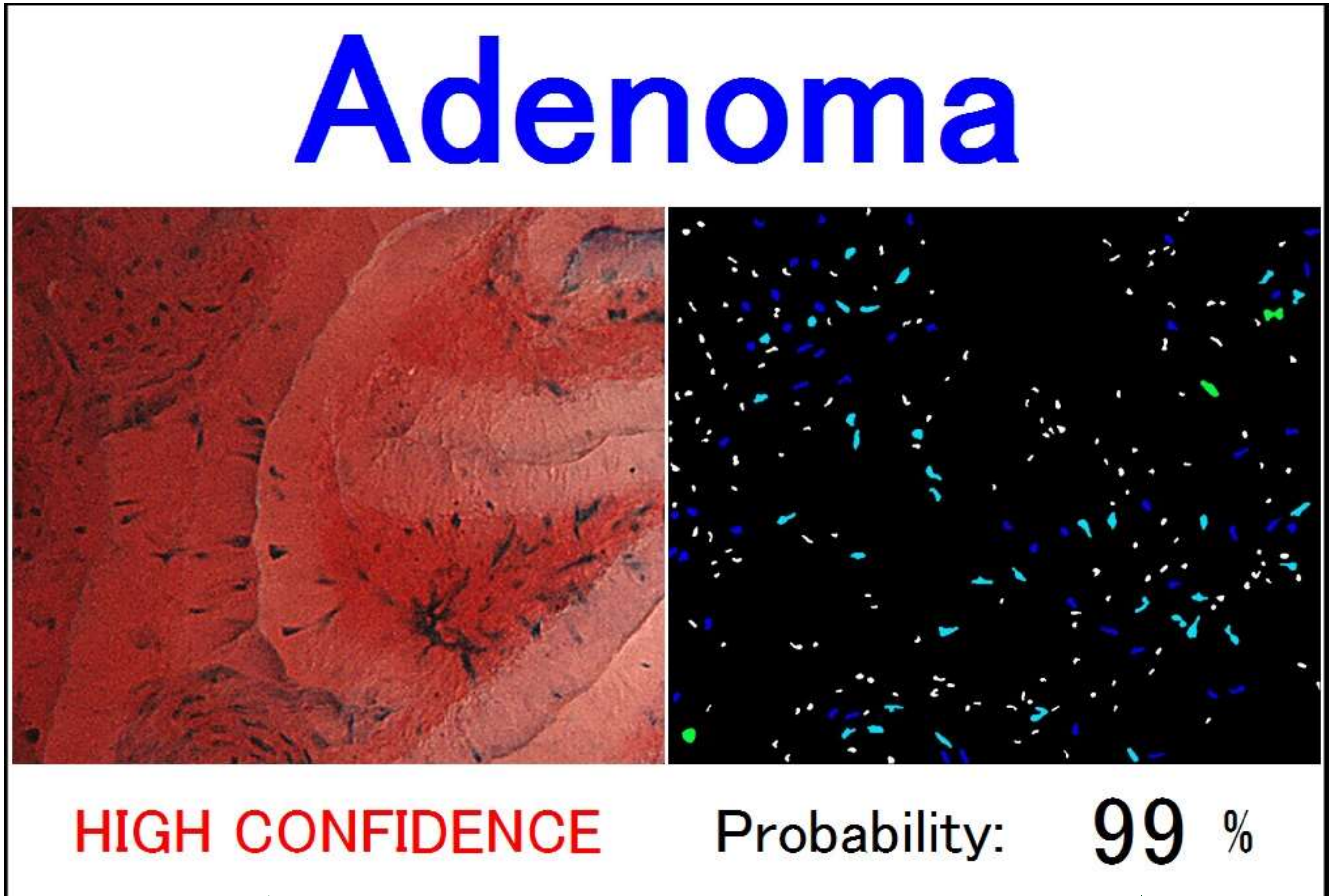




Processing flow



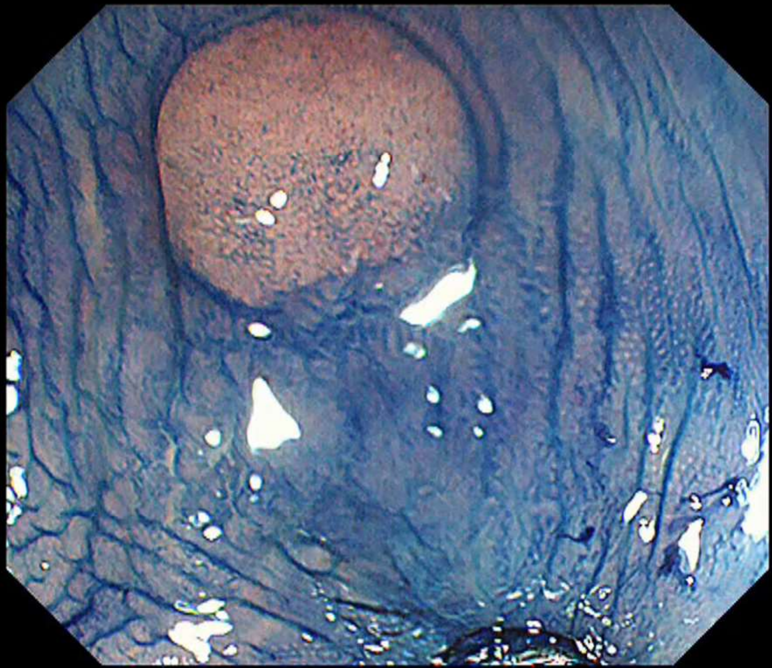
Output images

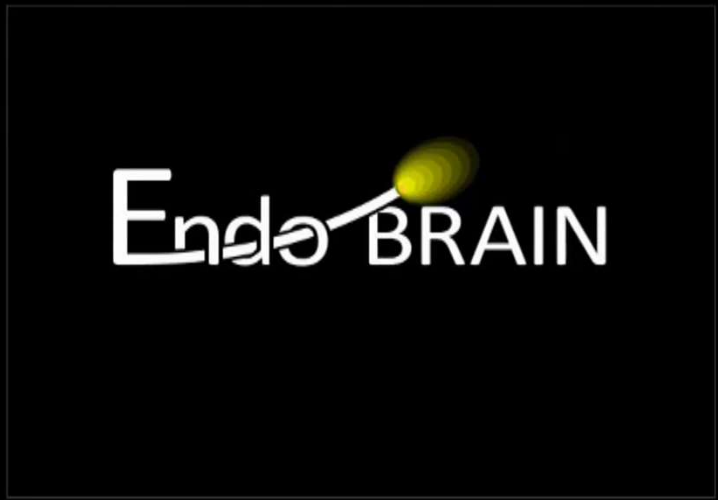


if confidential probability is over 90% we output ”High confidence”

Diagnostic probability

Next, VIDEO




EndoBRAIN

NAGOYA UNIVERSITY

Impact of an automated system for endocytoscopic diagnosis of small colorectal lesions: an international web-based study

Authors Yuichi Mori[1], Shin-ei Kudo[1], Philip Wai Yan Chiu[2], Rajvinder Singh[3], Masashi Misawa[1], Kunihiko Wakamura[1], Toyoki Kudo[1], Takemasa Hayashi[1], Atsushi Katagiri[1], Hideyuki Miyachi[1], Fumio Ishida[1], Yasuharu Maeda[1,4], Haruhiro Inoue[5], Yukitaka Nimura[6], Masahiro Oda[7], Kensaku Mori[8]

Institutions Institutions are listed at end of article.

submitted
28. February 2016
accepted after revision
4. July 2016

Background and study aims: Optical diagnosis of colorectal polyps is expected to improve the cost-effectiveness of colonoscopy, but achieving a high accuracy is difficult for trainees. Computer-aided diagnosis (CAD) is therefore receiving at-

for high confidence optical diagnoses of diminutive polyps.
Results: Of the 205 small polyps (147 neoplastic and 58 non-neoplastic), 139 were diminutive. CAD was accurate for 89% (95% confidence inter-

Mori et al., “Impact of an automated system for endocytoscopic diagnosis of small colorectal lesions: an international web-based study,” Endoscopy, 48, 2016

EC-CAD v.s. Experts or Non-experts (>=5mm)

Table 2 Diagnostic performance of the computer-aided diagnosis system for endocytoscopic imaging (EC-CAD), the experts, and the non-experts for the 139 diminutive (≤ 5 mm) lesions.

	EC-CAD		Experts (N = 3)		Non-experts (N = 10)		*P* value	
	n/n	% (95 %CI)	n/n	% (95 %CI)	n/n	% (95 %CI)	EC-CAD vs. experts	EC-CAD vs. non-experts
Sensitivity	80/91	88 (79 – 94)	248/273	91 (87 – 94)	646/910	71 (68 – 74)	0.256[1]	< 0.001[1]
Specificity	44/48	92 (80 – 98)	128/144	89 (83 – 94)	374/480	78 (74 – 82)	0.540[1]	< 0.001[1]
Accuracy	124/139	89 (83 – 94)	376/417	90 (87 – 93)	1020/1390	73 (71 – 76)	0.703[1]	< 0.001[1]
PPV	80/81	99 (93 – 100)	248/264	94 (90 – 96)	646/752	86 (83 – 88)	0.137[2]	< 0.001[2]
NPV	44/52	85 (72 – 93)	128/153	84 (77 – 89)	374/638	59 (55 – 62)	0.871[3]	< 0.001[3]
Rate of high confidence diagnosis	113/139	81 (74 – 87)	327/417	78 (74 – 82)	1117/1390	80 (78 – 82)	0.470[3]	0.791[3]
NPV when diagnosing all polyps with high confidence	43/46	93 (82 – 99)	115/125	92 (86 – 96)	319/487	66 (61 – 70)	1.000[2]	< 0.001[2]
NPV when diagnosing rectosigmoid polyps with high confidence	34/35	97 (85 – 100)	97/98	99 (94 – 100)	258/312	83 (78 – 87)	0.459[2]	0.026[2]
Average time for diagnosis (95 %CI), seconds		0.2 (0.2 – 0.2)		10 (9 – 10)		15 (14 – 15)	< 0.001[4]	< 0.001[4]

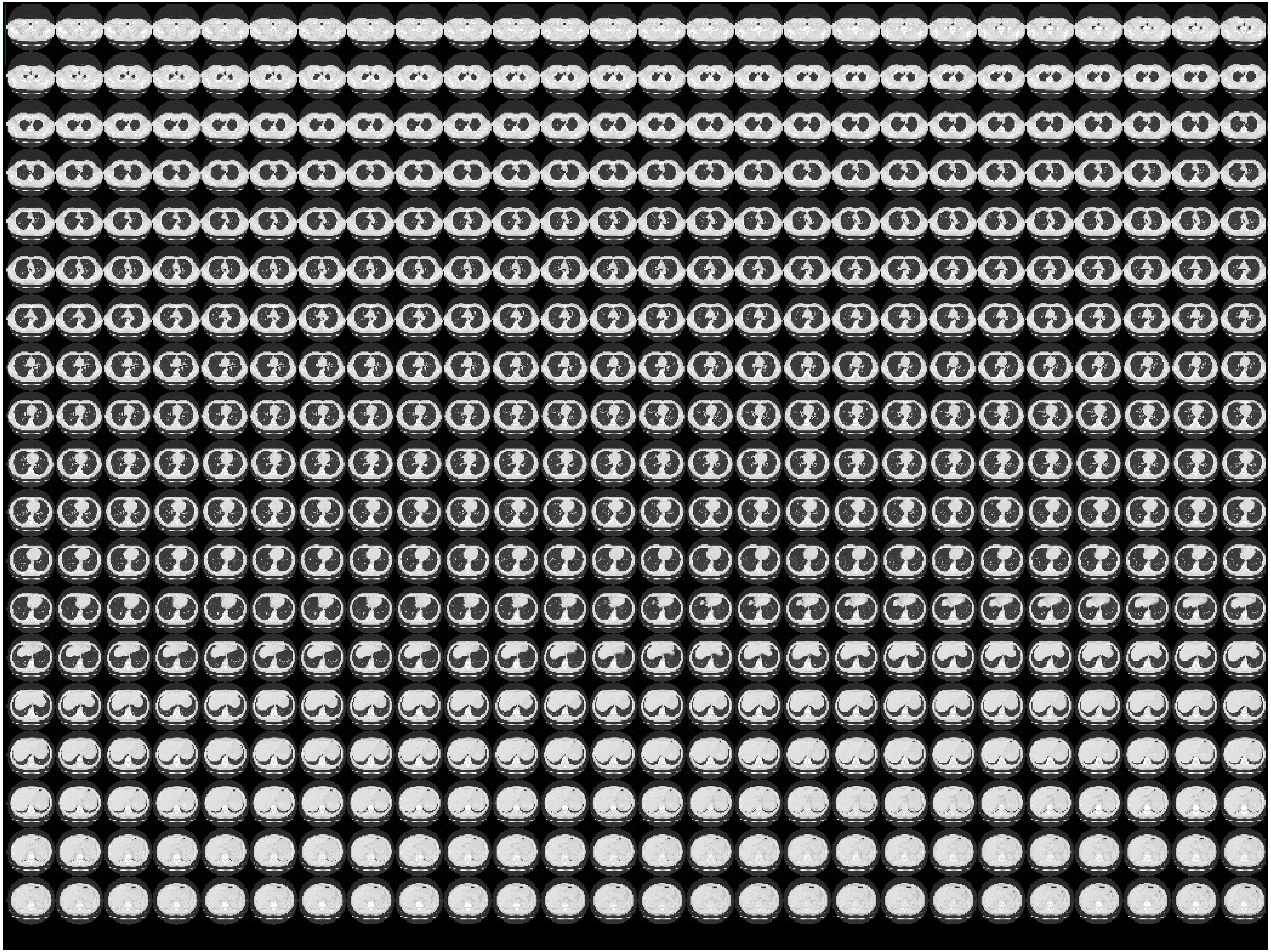
CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.
[1] McNemar test.
[2] Fisher's exact test.
[3] Chi-squared test.
[4] Kruskal –Wallis one-way analysis of variance.

no significant difference significant difference

Experts (90%) > EC-CAD (89%) >> Non-experts (73%)

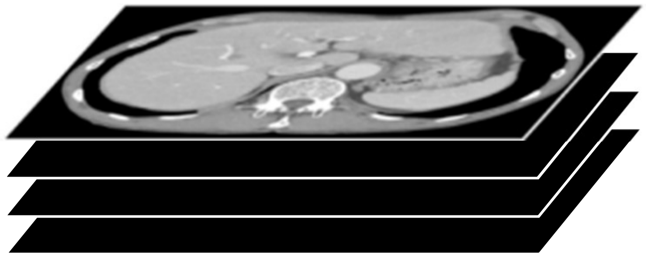
Mori et al., "Impact of an automated system for endocytoscopic diagnosis of small colorectal lesions: an international web-based study," Endoscopy, 48, 2016

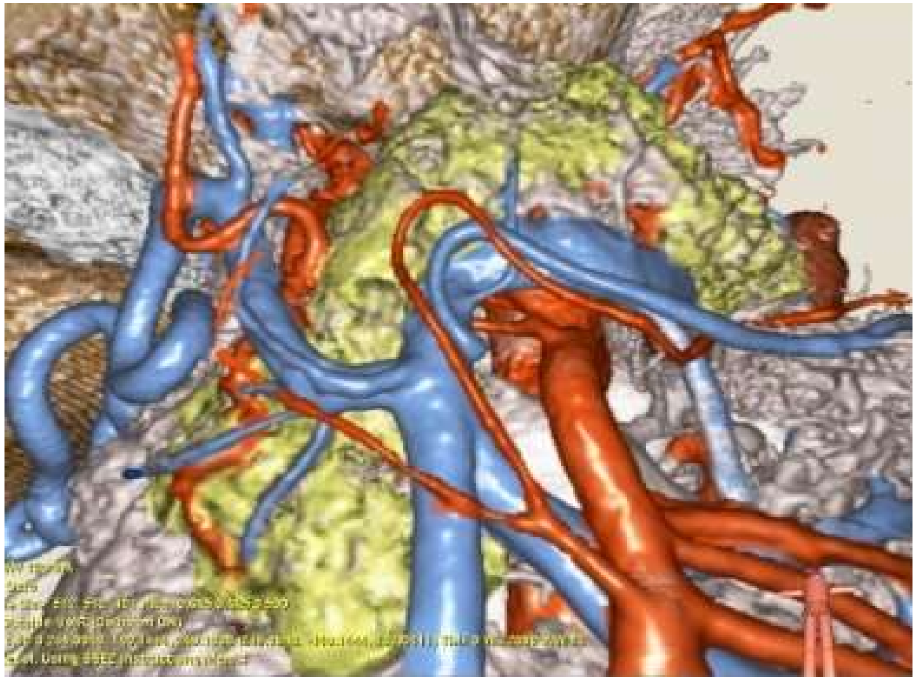
Colonic polyps detection from colonoscopic videos

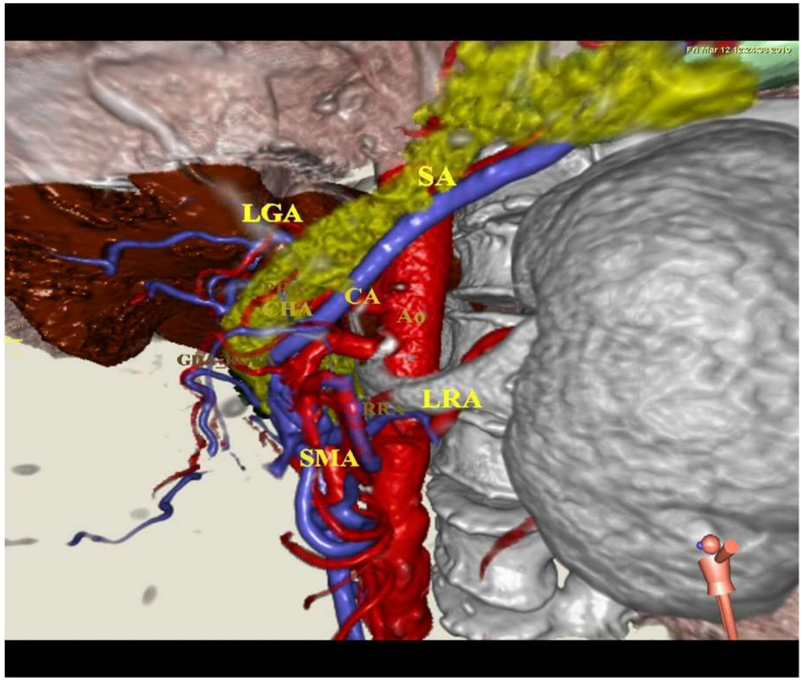


Important information for surgical navigation

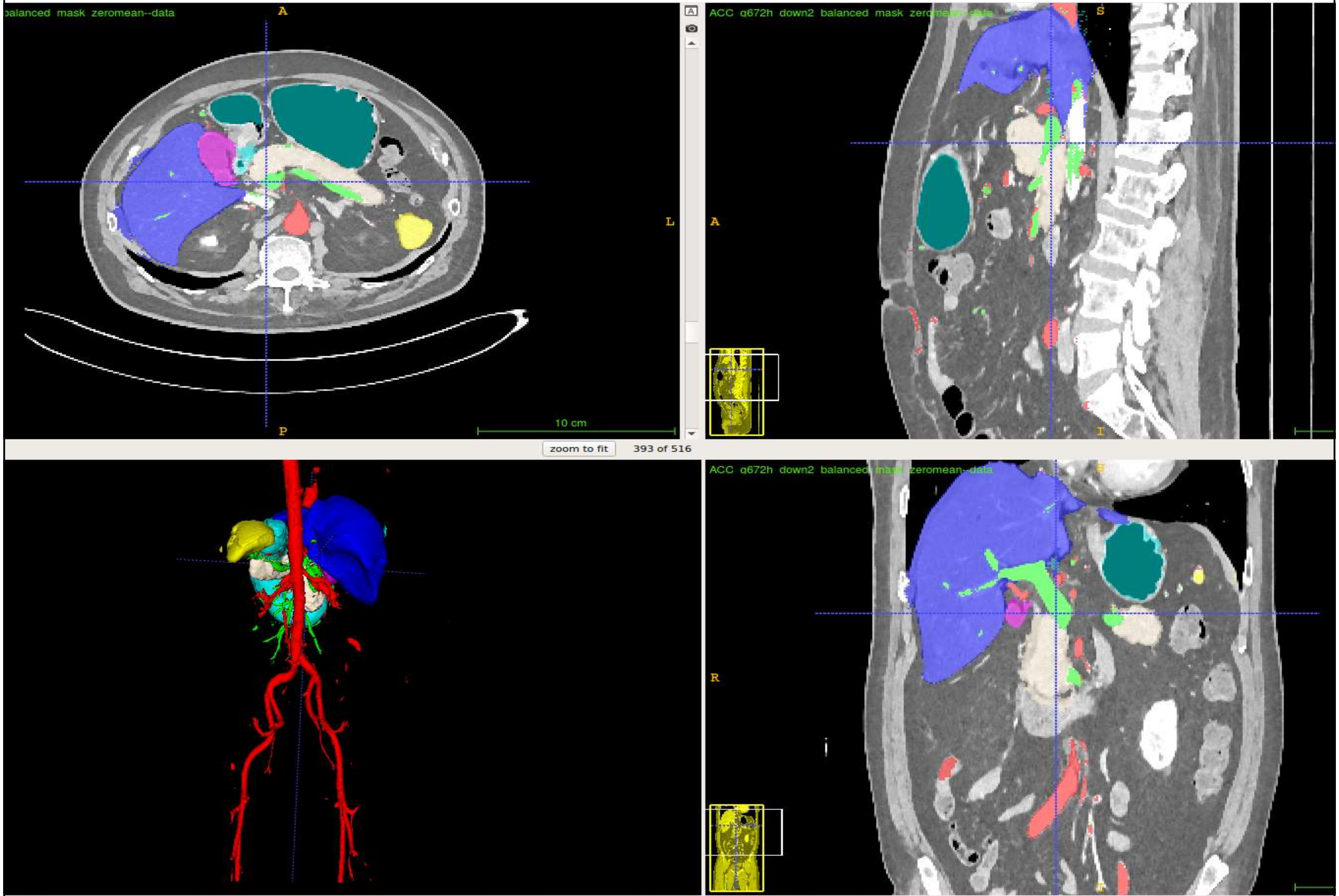
- Tracking information
- Anatomical structure information
- Anatomical name information
- Anatomical variation information







Organ segmentation


balanced mask zeromean--data
A
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10 cm
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393 of 516
ACC q672h down2 balanced mask zeromean--data
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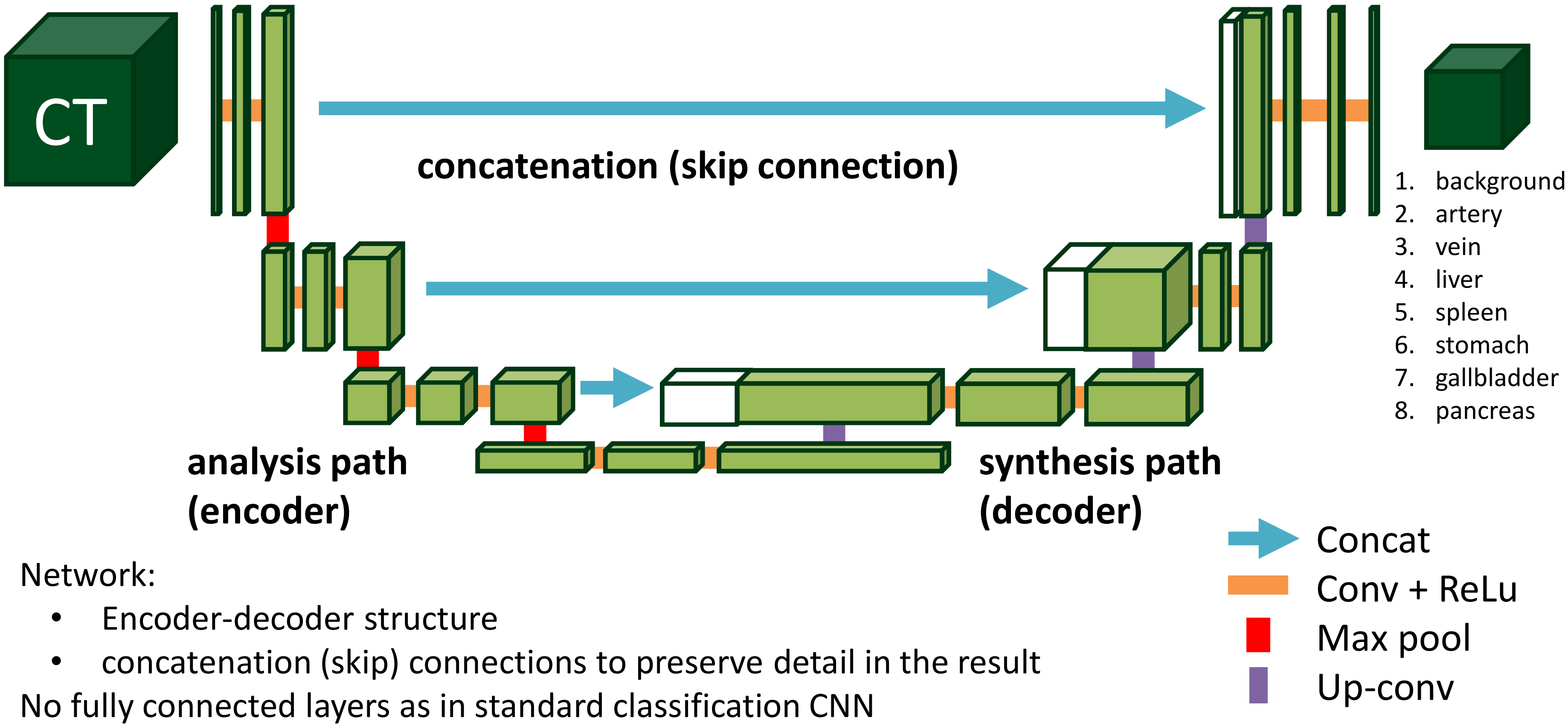
Fully convolutional architectures (3D U-Net)

Input:
132x 132x 116 x **1**

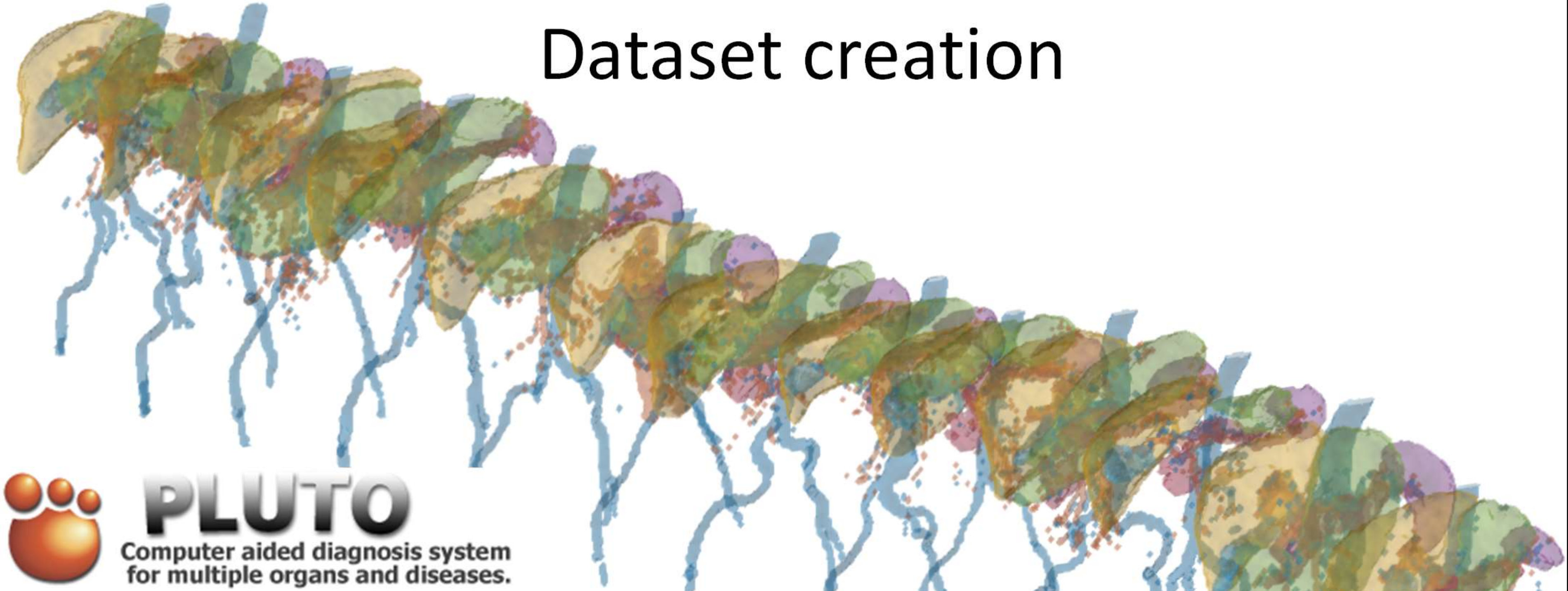
Output:
44 x 44 x 28 x **8**



- Network:
  - Encoder-decoder structure
  - concatenation (skip) connections to preserve detail in the result
- No fully connected layers as in standard classification CNN
- 19 million learnable parameters
- Fits on one 12GB GPU (NVIDIA TITAN X) for training
- Implementation in *Caffe*

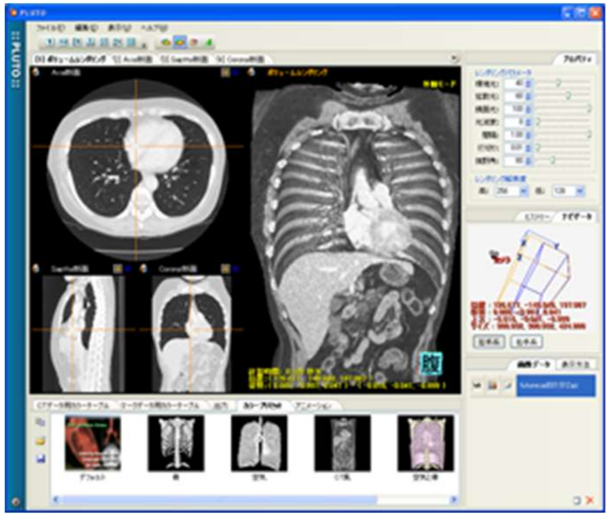
Figure after 3D U-Net [Çiçek et al. MICCAI 2016]

Dataset creation



PLUTO

Computer aided diagnosis system for multiple organs and diseases.

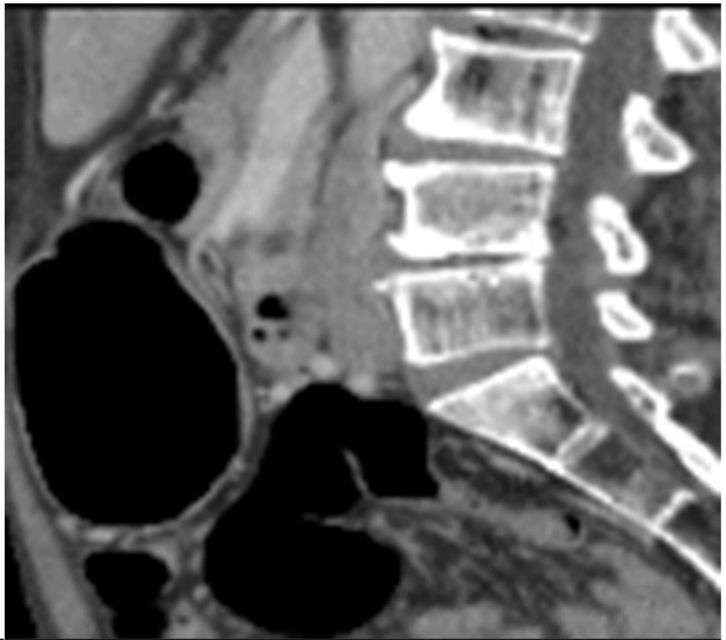


- semi-automated segmentation tools
  - graph-cuts
  - region growing
- data collected from 2009~2017 (330 cases)

http://pluto.newves.org

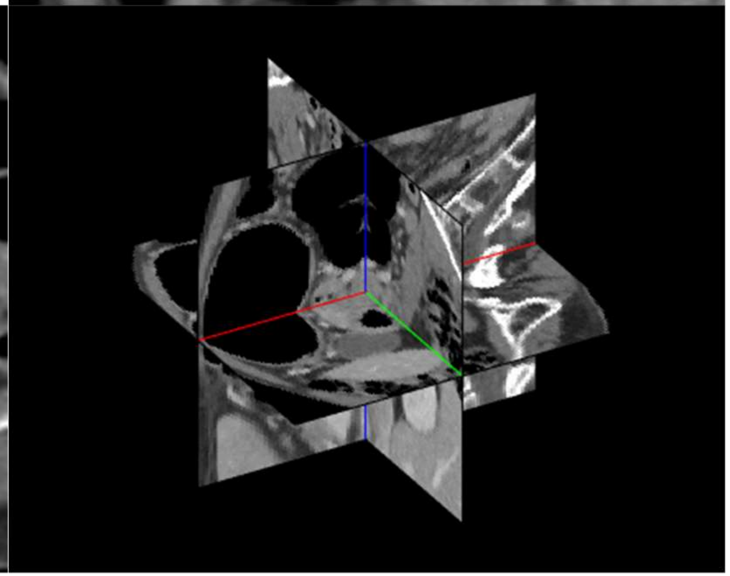
Data augmentation

- random cropping
- random rotations
- elastic B-spline deformations



'CreateDeformation' and *'ApplyDeformation'* layers

3D U-Net [Cicek et al. MICCAI 2016]

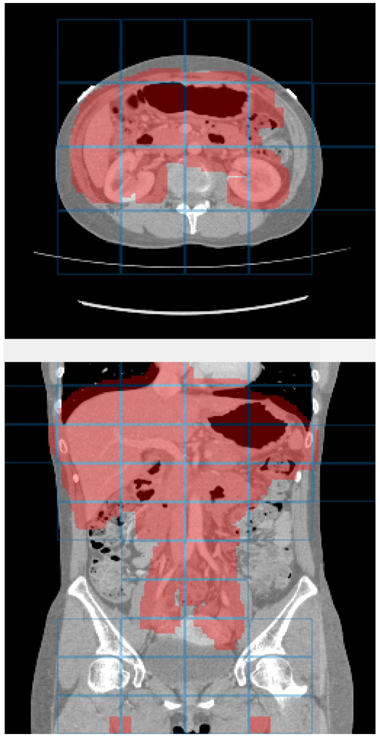


Ground truth

(a)

Stage 2 – Tiling

(b)



Stage 2 result

(c)

Example of the validation set with

(a) ground truth and illustrating

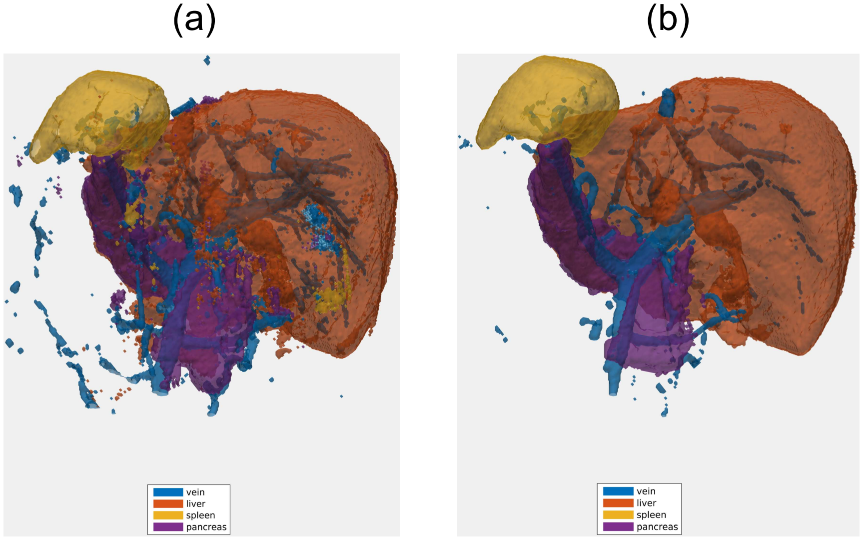
(b) Tiling approach on 2nd stage candidate region, Resulting segmentation is shown in (c).

Note that the grid shows the output tiles of size 44 × 44 × 28 (x,y,z-directions). Each predicted tile is based on a larger input of 132 × 132 × 116 that the network processes as defined by GPU requirements (12 GB)

H. Roth et al. arXiv 1704.06382

Test on **unseen** dataset

H. Roth et al. arXiv 1704.06382



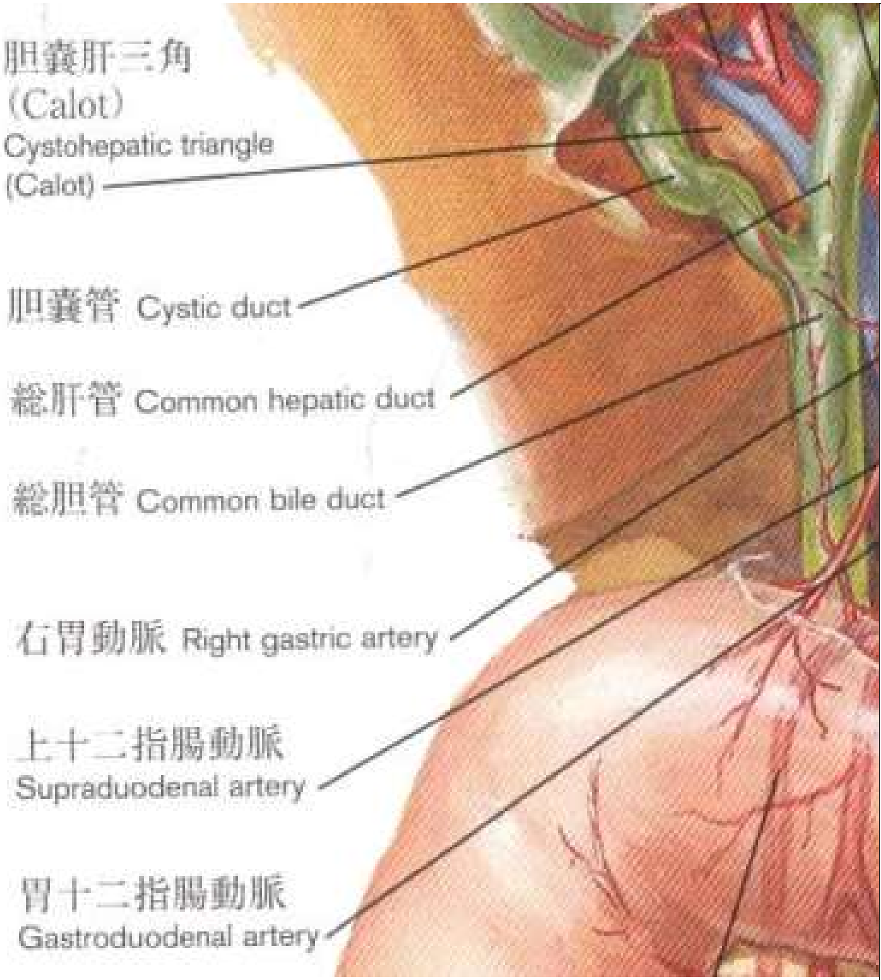
Surface renderings: (a) result of proposed method in first stage and (c) the second-stage results using and overlapping (OL) tiles strategy.

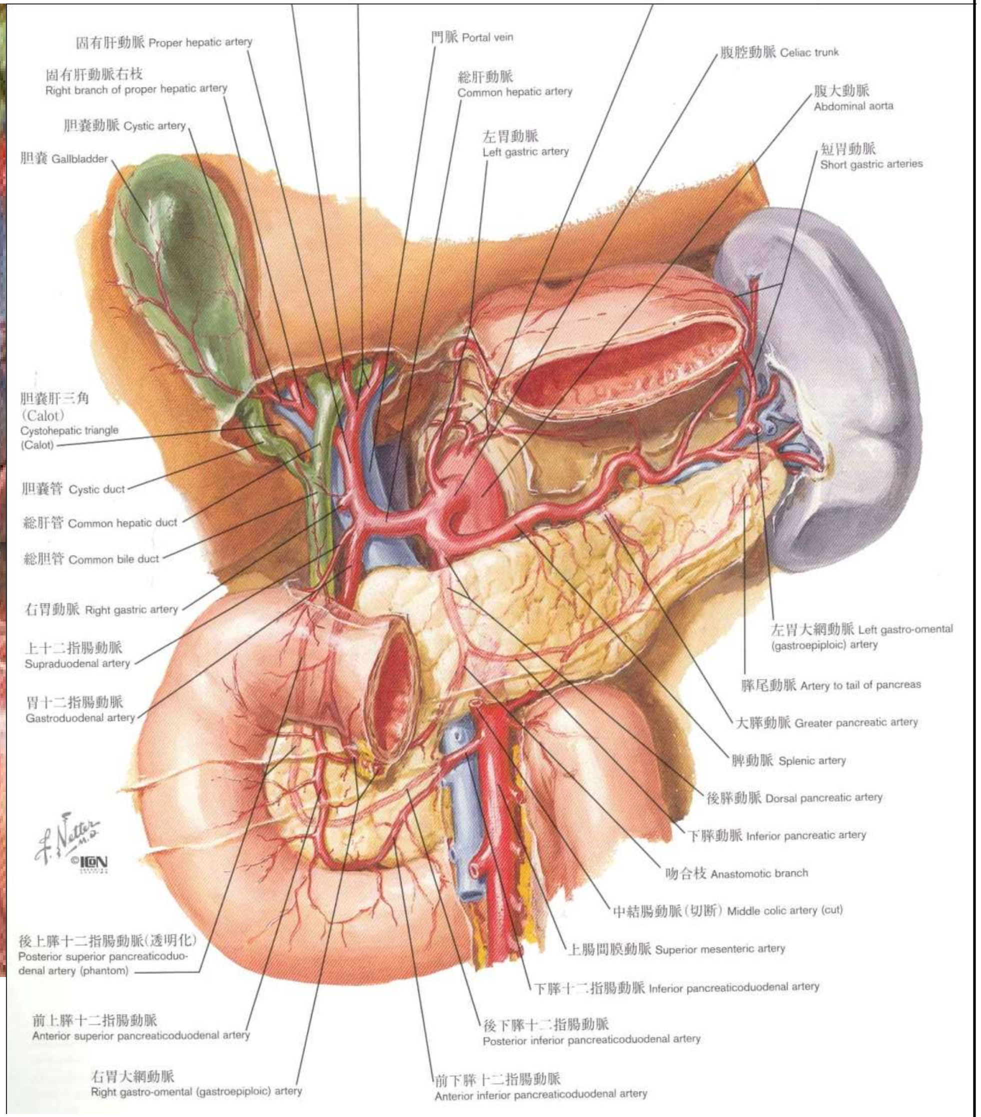
Table 2: **Testing on unseen dataset:** Dice similarity score [%] of different stages of FCN processing.

	Stage 1: Non-overlapping			Stage 2: non-overlapping			Stage 2: Overlapping		
Dice	**liver**	**spleen**	**pancreas**	**liver**	**spleen**	**pancreas**	**liver**	**spleen**	**pancreas**
Mean	93.6	89.7	68.5	94.9	91.4	81.2	95.4	92.8	82.2
Std	2.5	8.2	8.2	2.1	8.9	10.2	2.0	8.0	10.2
Median	94.2	91.8	70.3	95.4	94.2	83.1	96.0	95.4	84.5
Min	78.2	20.6	32.0	80.4	22.3	1.9	80.9	21.7	1.8
Max	96.8	95.7	82.3	97.3	97.4	91.3	97.7	98.1	92.2

150 abdominal ceCTs from different hospital and scanner

Anatomical name understanding

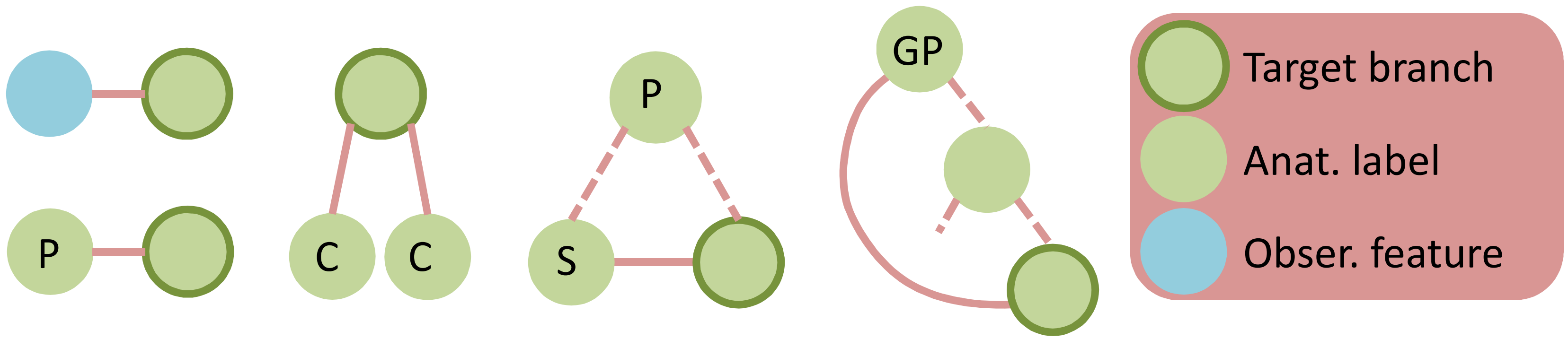




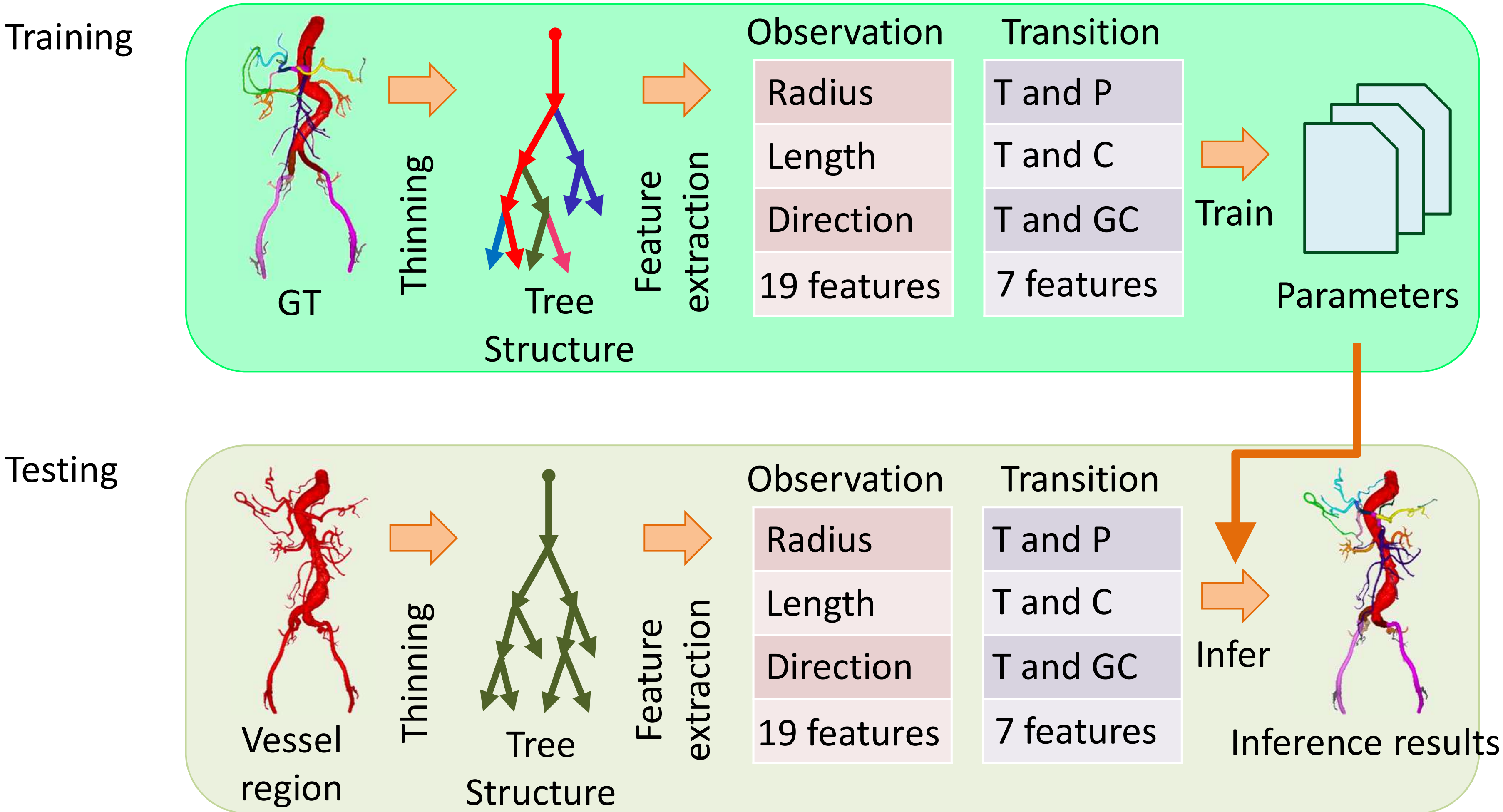
Anatomical labeling by structure learning

- Structure learning
  - Representation of features and labels
  - Possible to represent global structure of branching pattern
  - Possible to infer optimal blood vessel labels
- Conditional random field
  - Learn observation features and anatomical labels
  - Observation features (19)
  - Transition features (7)
    - Relationship of target branch and other branches

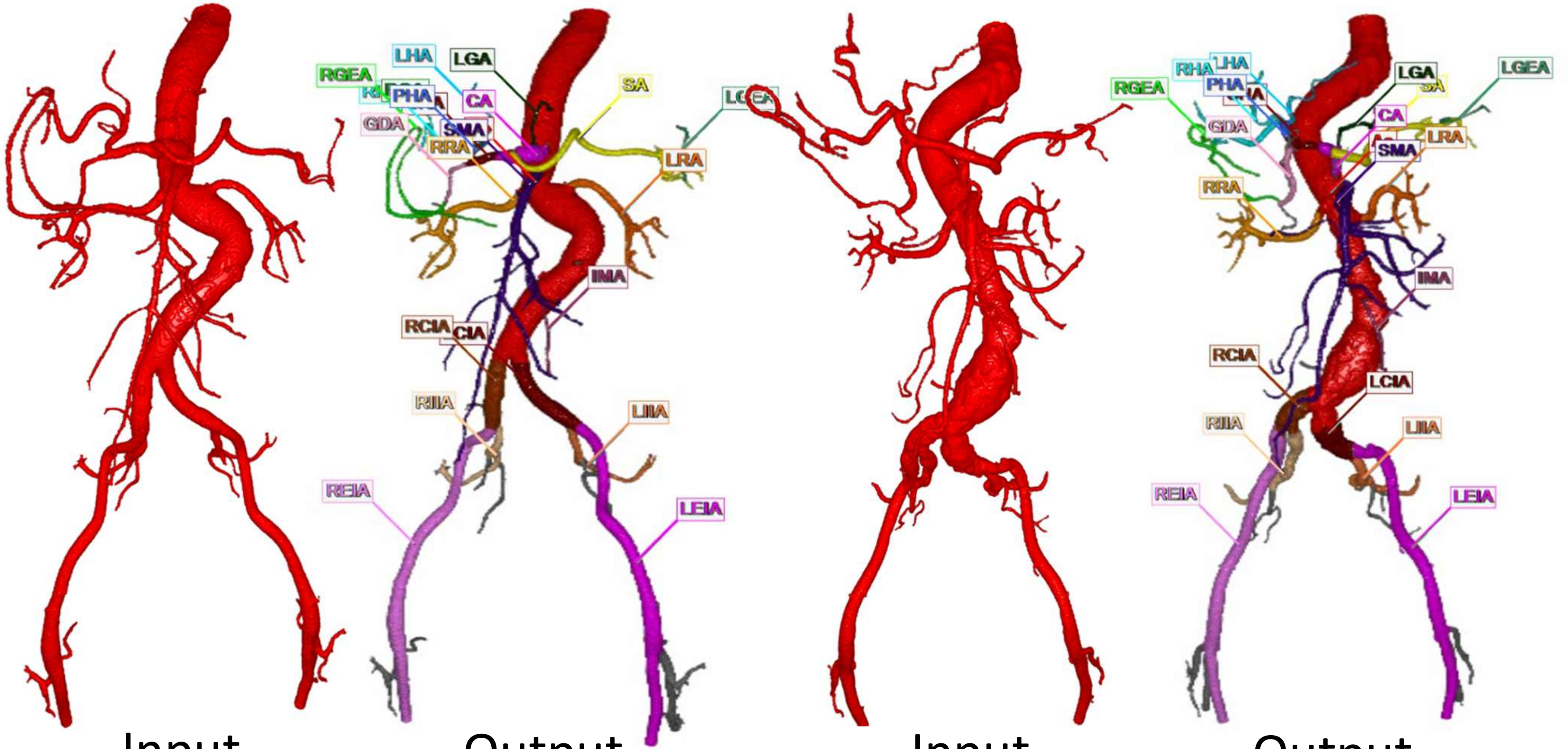
Ex.



Conditional random field



Results – Cases of 100% F-value



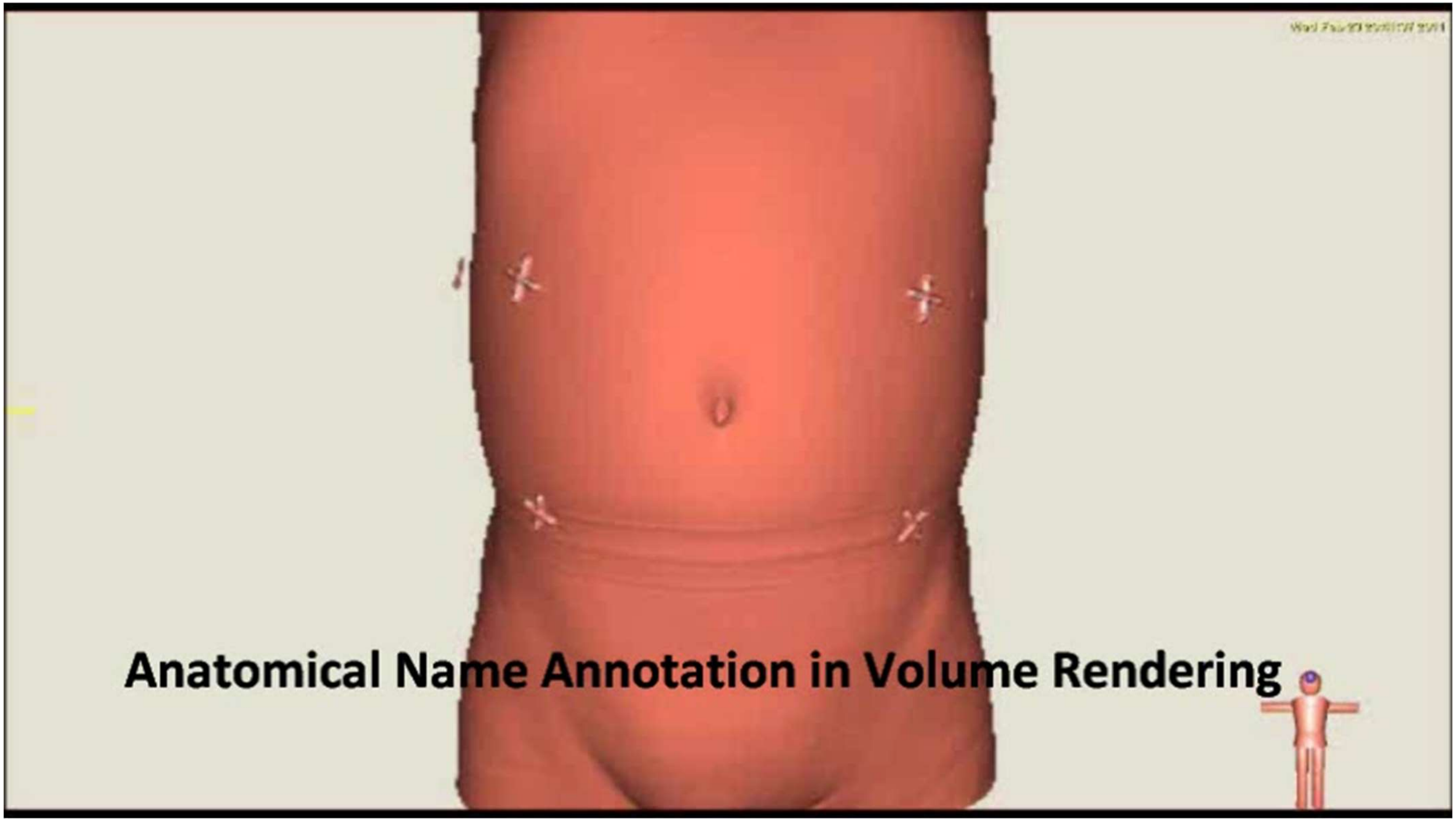
Input Output

F-value 99.6%

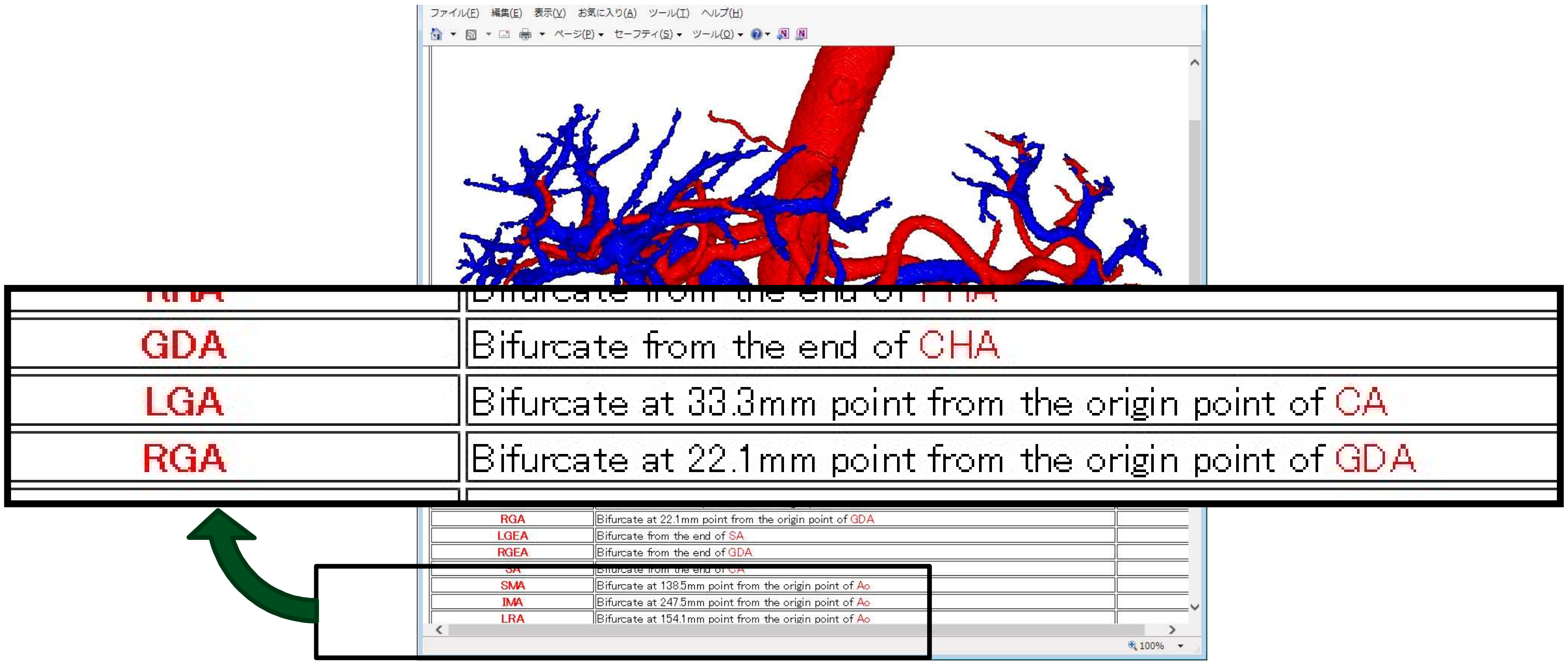
Input Output

F-value 99.6%

Anatomical name rendering on virtual anatomy



Branching structure reporting system



Oda, et al.
SPIE MI 2015

Oncological area

NAGOYA UNIVERSITY

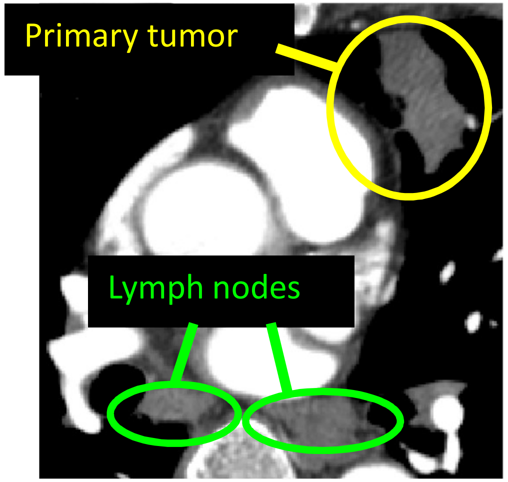
3D U-net for lymph node detection

Hirohisa Oda, Kanwal K. Bhatia, Holger R. Roth,
Masahiro Oda, Takayuki Kitasaka, Shingo Iwano,
Hirotoshi Homma, Hirotsugu Takabatake, Masaki Mori,
Hiroshi Natori, Julia A. Schnabel, Kensaku Mori

Accepted for SPIE Medical Imaging 2018

Mediastinal lymph nodes

- Lung cancer
  - Most common cause of cancer death
    - 1.69 million deaths worldwide in 2015
  - Treatment strategy depends on image diagnosis of lymph nodes
  - Image diagnosis of lymph nodes on chest CT volumes is a hard work for radiologists
- Automated mediastinal lymph node detection is desired
  - prevent overlooking of lymph nodes
  - 3D U-net based segmentation



Chest CT image

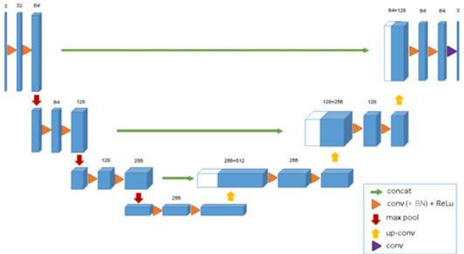
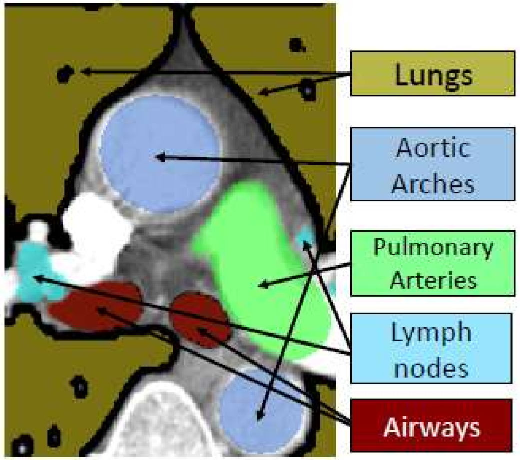


Fig.2 from [Cicek16]

[WHO15] http://www.who.int/mediacentre/factsheets/fs297/en/

Using surrounding anatomies

- Several anatomies around mediastinum
  - Lung, airways, aorta, and pulmonary artery
  - Easily segmented by thresholding, circle fitting, etc.



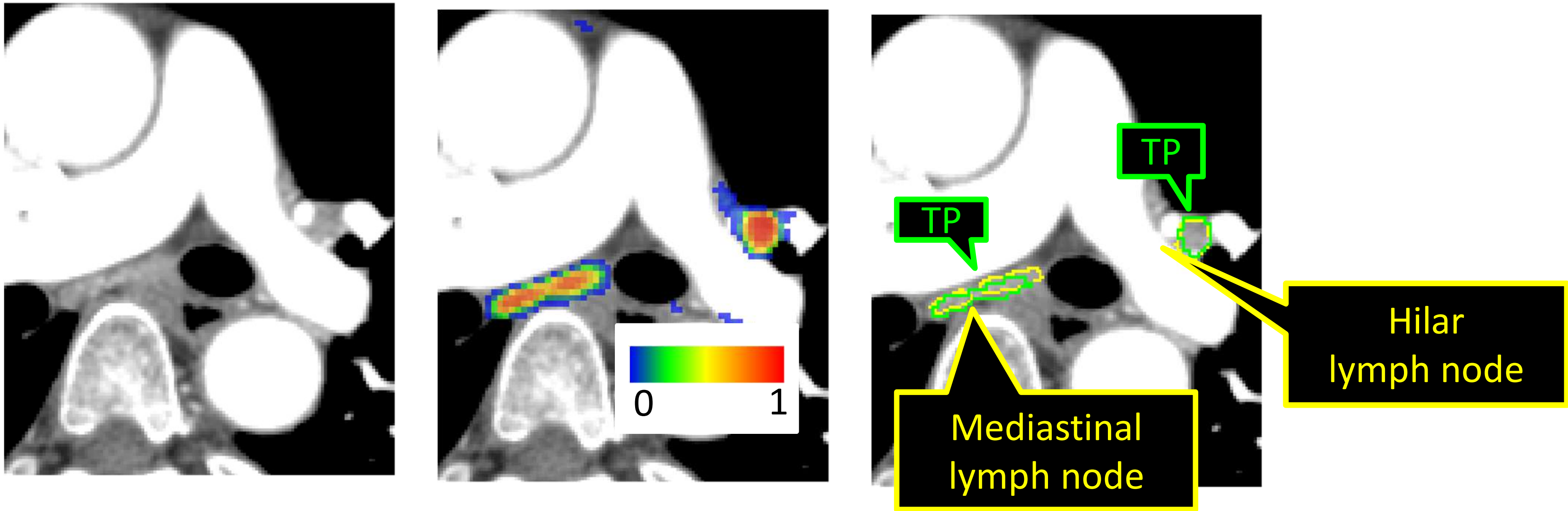
- Weighting regarding size of each class
  - Smaller class should have larger weight for training
  - Especially lymph nodes are much small regions than organs or major blood vessels

$$\mathcal{L} = -\frac{1}{N}\sum_{i=1}^{K}\lambda_i\left(\sum_{x\forall N_i}\log(\hat{p}_k(\mathbf{x}))\right)$$

$$\lambda_i = \frac{1-N_i/N_C}{K-1}$$

Examples

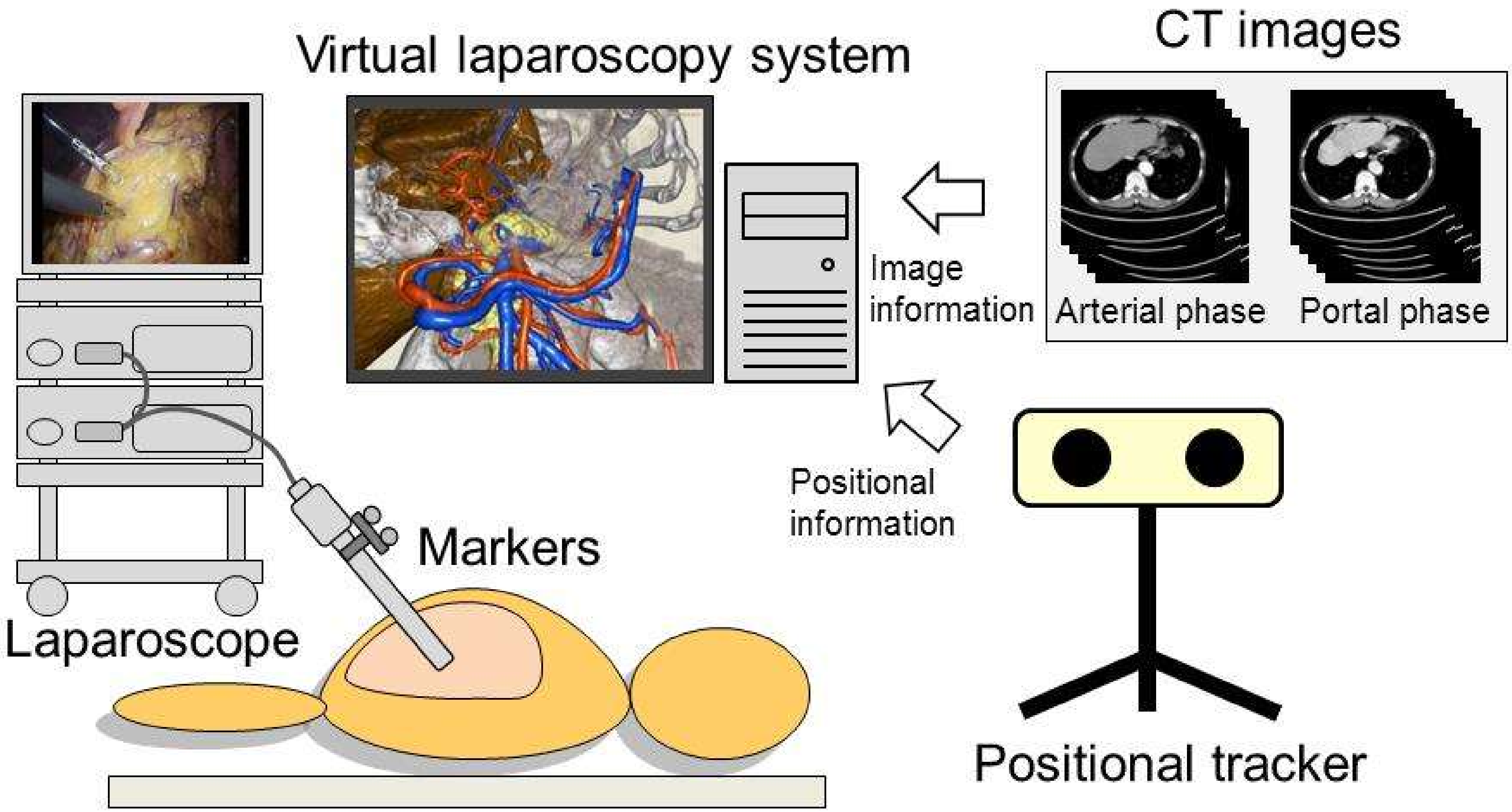
- Lymph nodes were properly detected
  - Segmentation accuracy also looks good



Input volume — Lymph node probabilities — Detection results ($t = 0.5$)

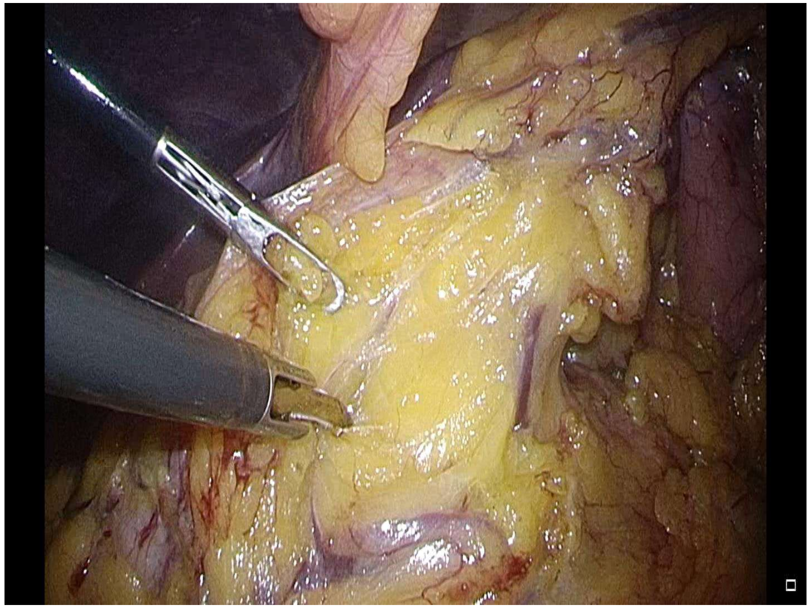
AI goes to operating theater

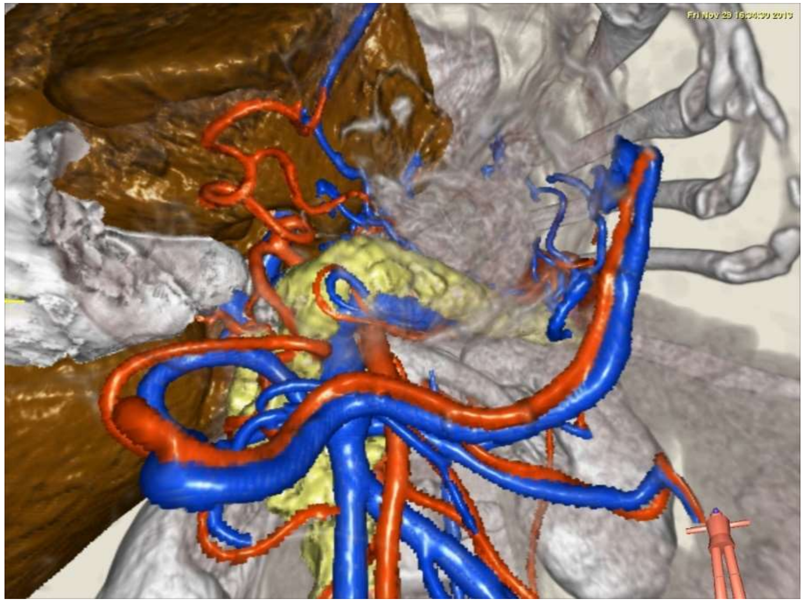
Laparoscopic surgery navigation

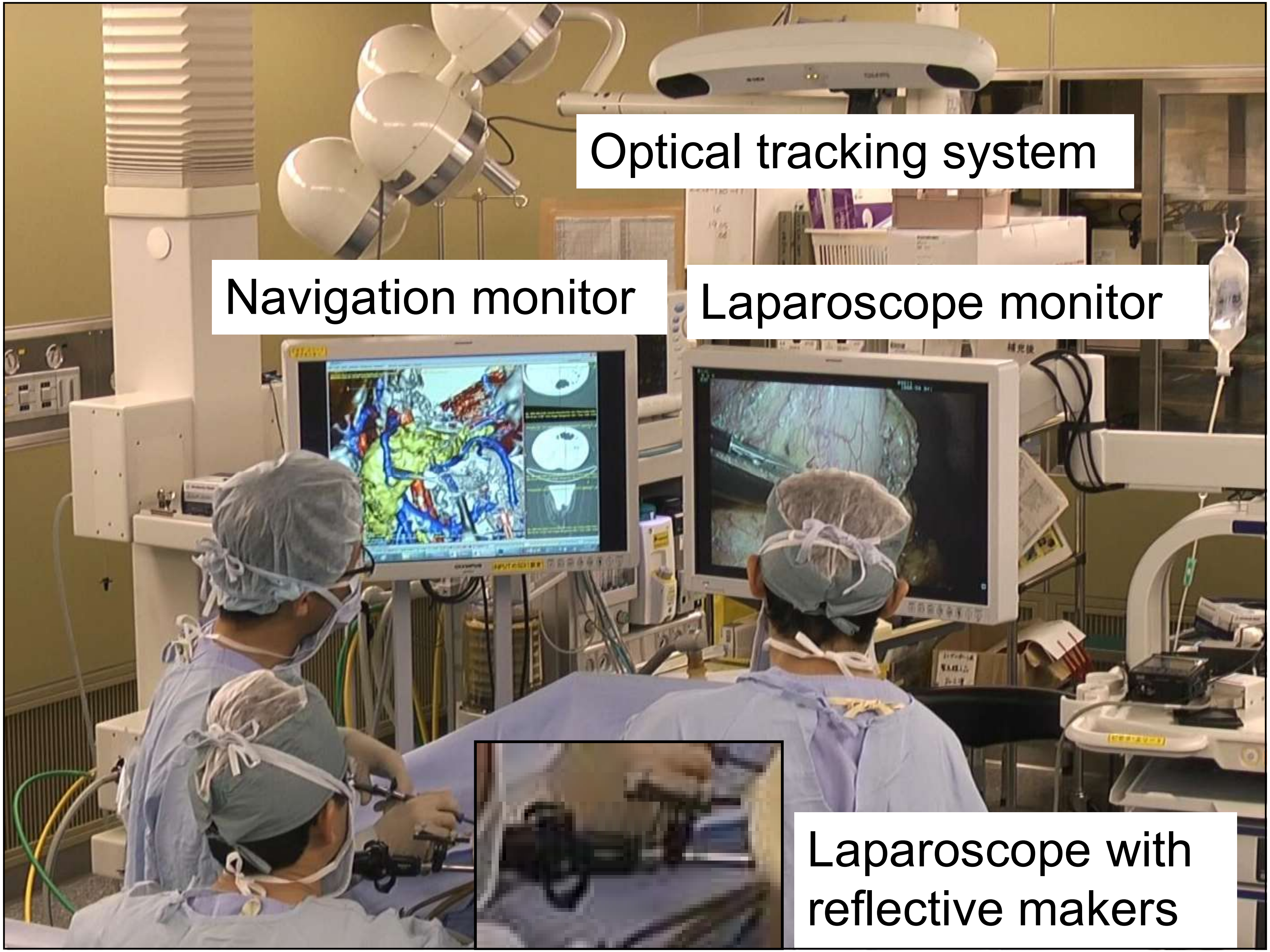


Surgical navigation of gastrectomy [Hayashi IJCARS2015]

- Comprehension of anatomical structure is important in laparoscopic surgery.
- 3D virtual laparoscopic views (3D VLVs) generated from preoperative CT images help surgeons to understand patients’ anatomical structures.





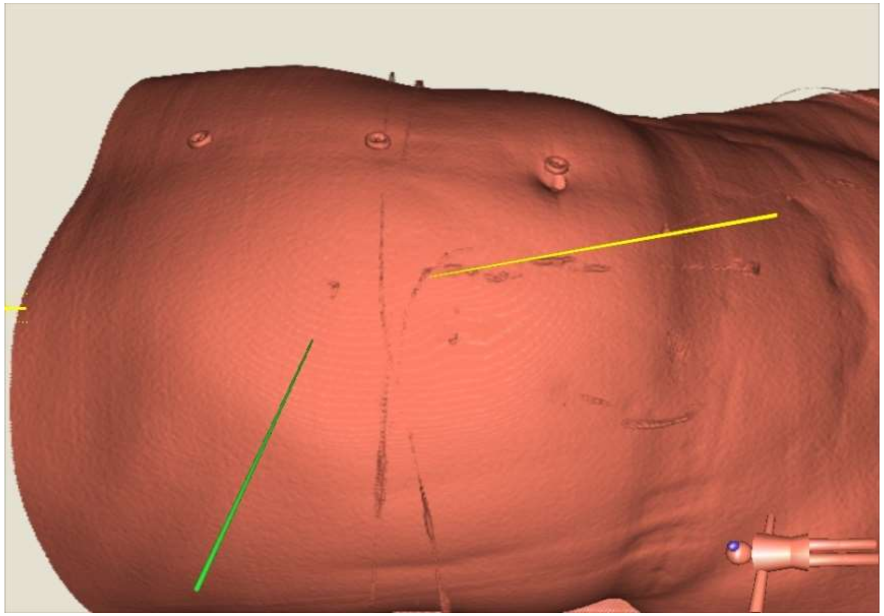

Optical tracking system
Navigation monitor
Laparoscope monitor
Laparoscope with
reflective makers

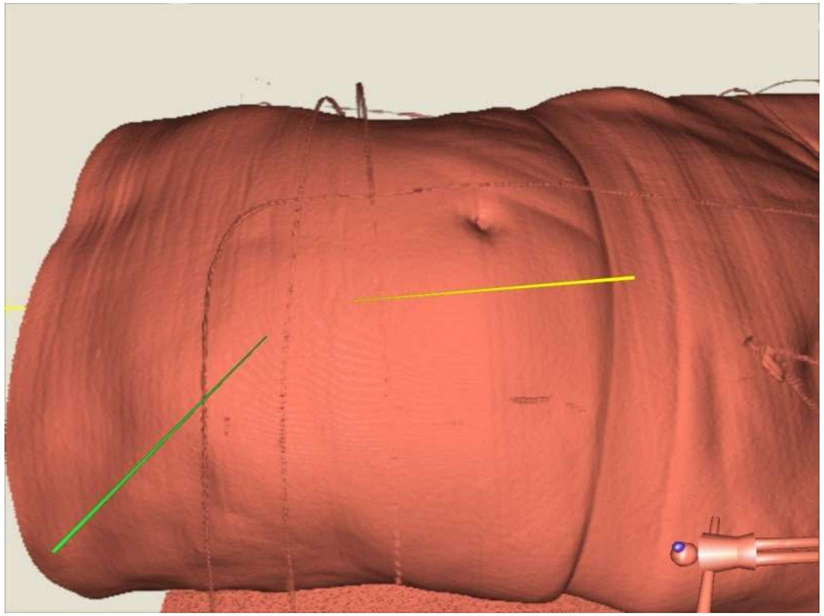
Laparoscopic gastrectomy navigation

NAGOYA UNIVERSITY

Purpose

- Port (trocar) location planning system
  - Determine port location based on anatomical structure
  - RGA and LGA



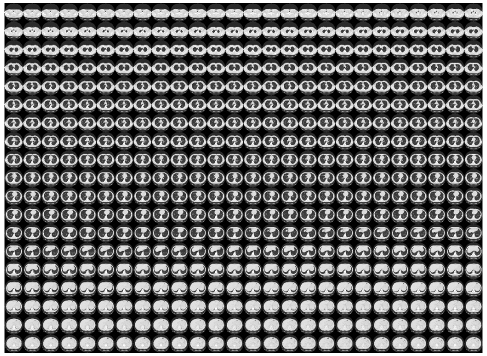


[1] Hayashi Y et al. Port placement planning assistance for laparoscopic gastrectomy based on anatomical structure analysis. Int J CARS 2016; 11 (Sup.1): S265-S266.


SONY

VR

Easy to obtain, not suitable for supervised learning

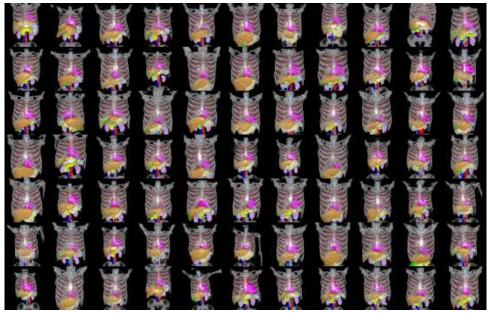


Raw big data

Just data

Big data

How to bridge the gap!
How to convert!



Just knowledge

Annotated big data

Good for supervised learning, but very hard to collect

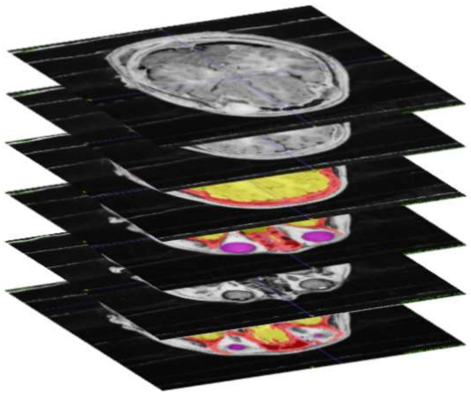
Biomedical big data

Many cases, large data per case

Many cases, small data per case

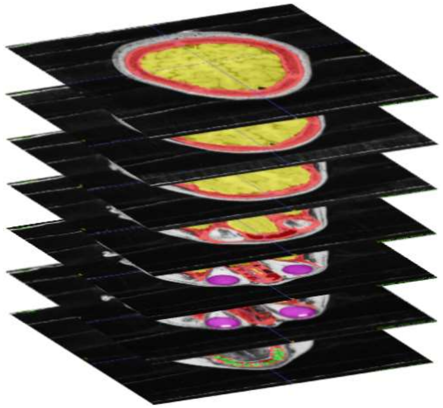
Small cases, huge data per case

From sparse annotation to full annotation



unannotated
unannotated
annotated
annotated
unannotated
annotated

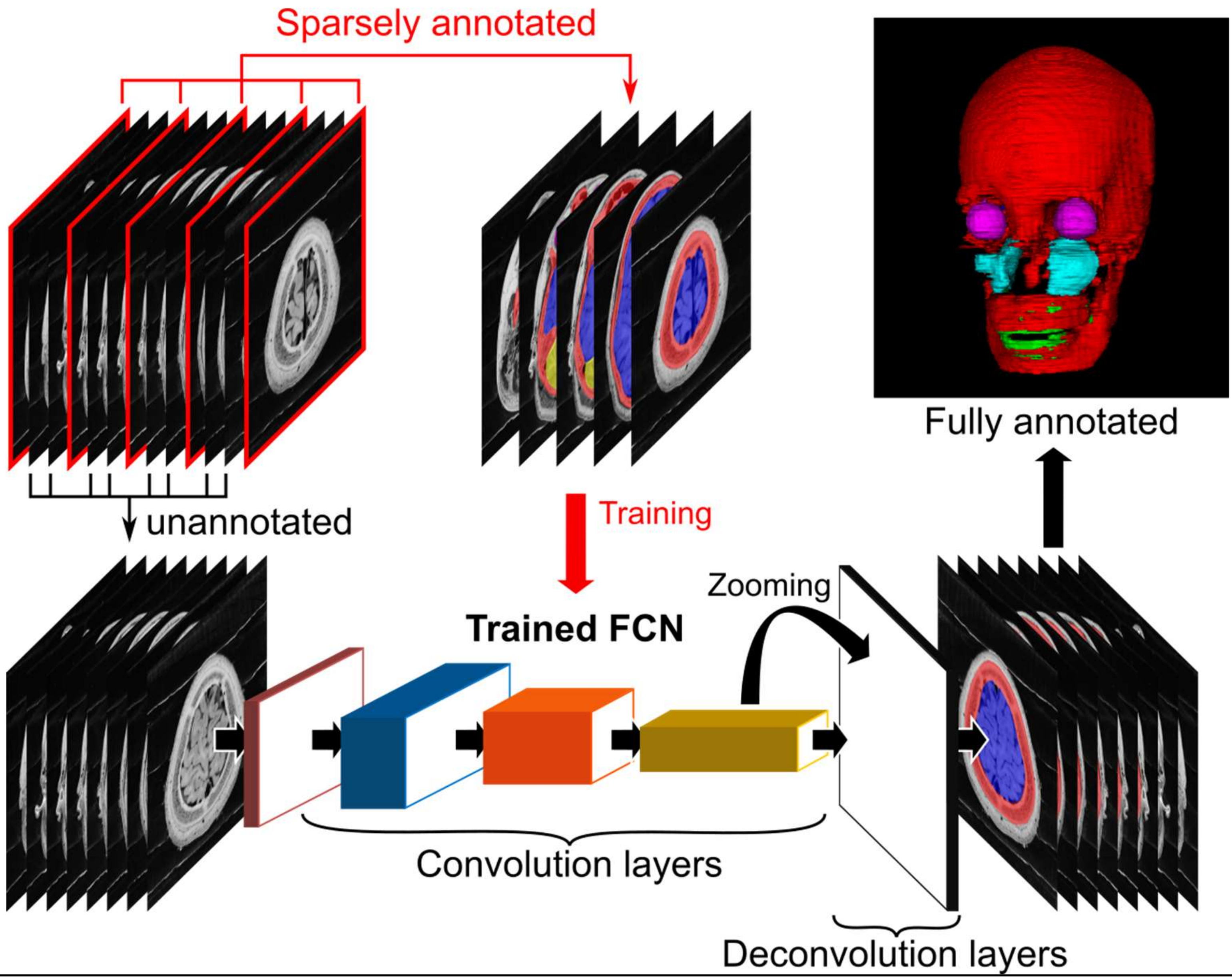
Sparse annotation



annotated
annotated
annotated
annotated
annotated
annotated
annotated

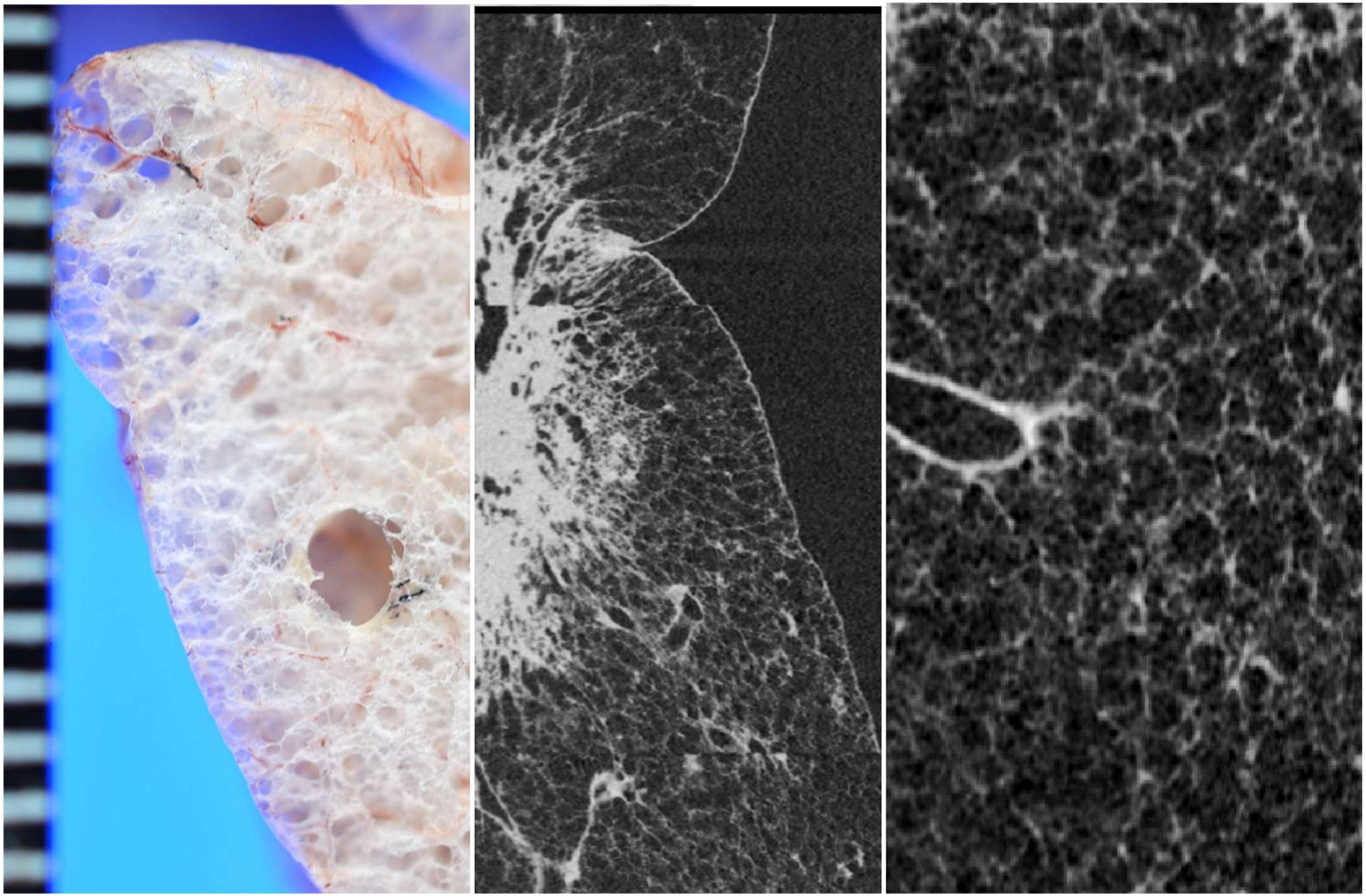
Full annotation

Segmentation based on sparse annotation



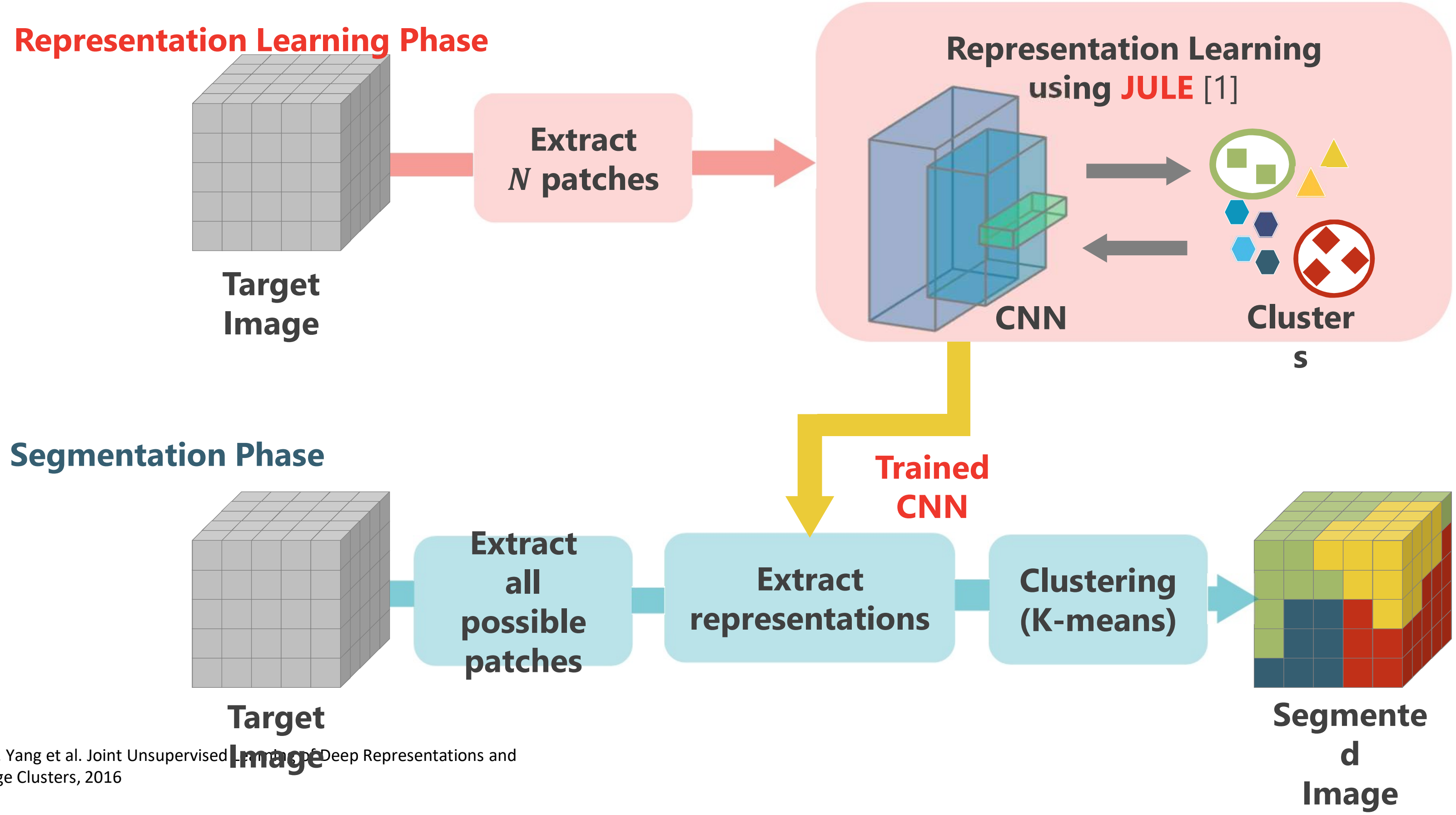
Lung specimen

Micro CT scanner (up to 5um/voxel)



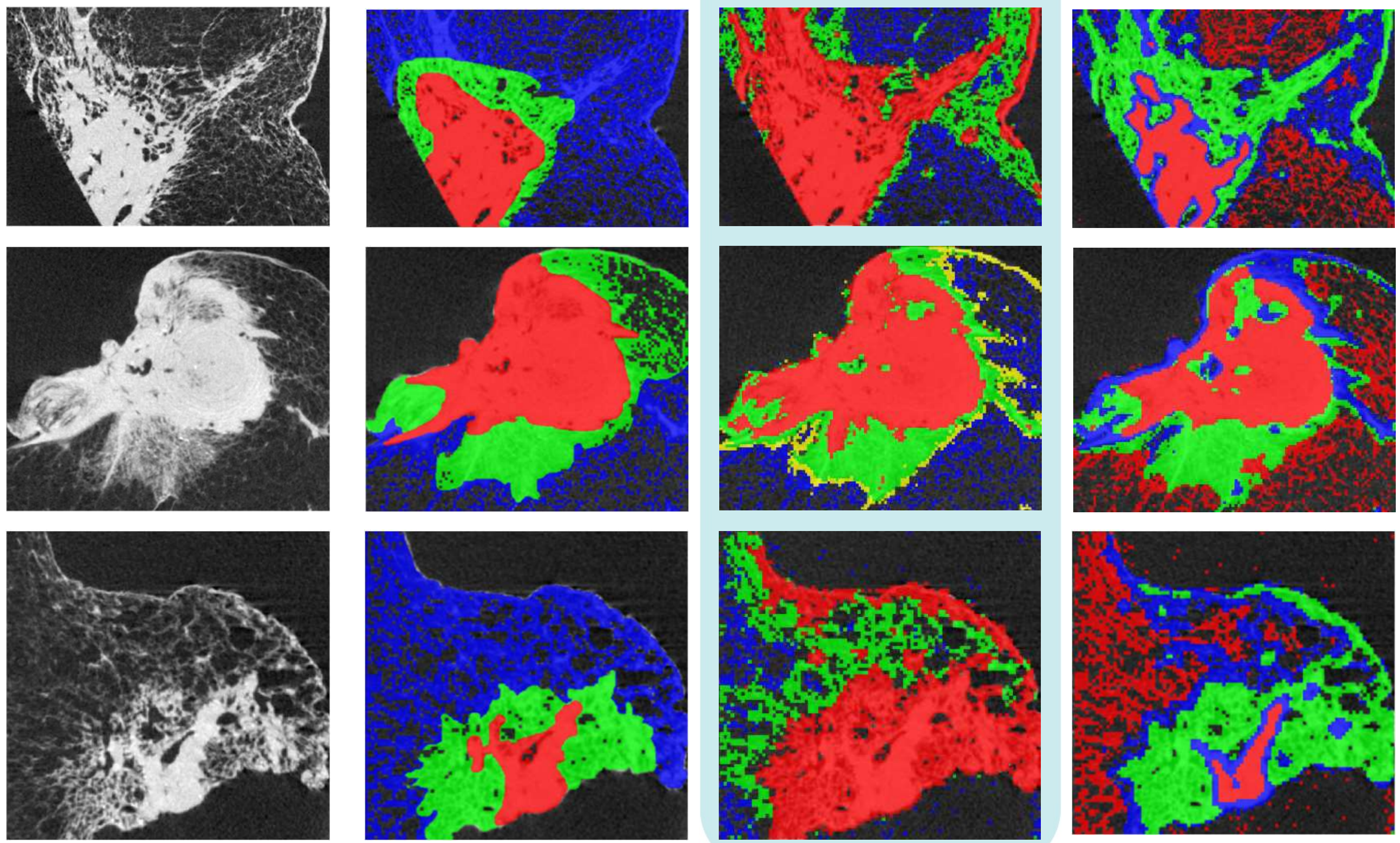

NewVES
File Edit View Window Rendering Network Joystick Navigation Context
Full-function
PATH
video
VolR Table
Ctrl
Pad
Mark
WebとWindowsを検索
18:20
2016/02/07

Unsupervised segmentation of uCT



[1] J. Yang et al. Joint Unsupervised Learning of Deep Representations and Image Clusters, 2016

Segmentation of uCT volume of lung cancer



Medical images will be fully annotated by computers

Future

- All of medical imaging data will be annotated by machine learning in future
- This already happens in digital photography area
  - Many cloud-based photo services automatically annotated photos by ML
- How does this change our medical world?
  - Medical doctor / Engineers / Patient
  - ML-based medicine comes home for monitoring daily health conditions?

Conclusions (and open questions)

- Machine learning (AI)
  - Medical image diagnosis
  - Computer assisted intervention
- ML will become indispensable technique in medicine
  - All of supportive tools will be based on ML
- How to integrate ML/AI into clinical workflow
  - c.f.) Surgeons refer surgical navigation in very short time during surgery. But it is very critical point.
- Big data and lack of supervised data
  - Data is a lot but not structured or not annotated
  - Unsupervised learning and weak annotation will be a key
  - How to create big supervised data from small supervised data from big data.

Academia, hospital and industry

Hospital

昭和大学

Showa University

Collaboration between medical dept., informatics dept. and industrial dept..

Academia

Nagoya University

Industry

Cybernet systems

Translate university's technologies to market

つくる情熱を、支える情熱。

CYBERNET

OLYMPUS

Conclusions (and open questions)

- Current medical AI is very specific
  - Good performance in specific tasks
  - Lack of observation of real patiens
- Ethics in medical AI
  - Personal information used for training
  - Personal information protection law in Japan
    - Clear distinction of **academic** research use and **industrial** use
  - Overriding medical doctors' decisions
- Cross-border data collection for medical AI
  - Raw data
  - Labeled data
  - Data circulation

Conclusions (and open questions)

- AI is currently led by IT giants
  - Collecting data so much
  - 1984 (George Owell)?