Progress Report 2024

Department of Computational Diagnostic Radiology and Preventive Medicine

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<Introduction and Organization>

The Department of Computational Diagnostic Radiology and Preventive Medicine (CDRPM) collects latest biomedical data in preventive medicine field, especially massive image data from advanced imaging modalities, develops a detailed database and researches on preventive medicine, image processing and automatic diagnosis algorithms.

Our department conducts a health-screening program over the long term in association with HIMEDIC Co., Ltd. in order to develop a detailed and reliable database. We also promote epidemiological study in preventive medicine field in association with Yamanakako Clinic, which originated the health-screening program using PET. The health-screening program was contracted to University of Tokyo Hospital. Our department was assigned the actual practice of health screening program. It is also the field work to acquire the data for research on image analysis and epidemiology. The health screening program includes PET/MRI (Positron Emission Tomography/ magnetic resonance imaging), ultra-high field MRI, ultrasonography and mammography with the

latest technology, in addition to standard screening tests in the Health-screening Center of Computational Diagnostic Radiology and Preventive Medicine on the ninth floor of Central Care 2.

In regard to image processing and image analysis, we cooperate with the Department of Radiology, Graduate School of Medicine, The University of Tokyo, and collaborate with UT Radiology / Image Computing and Analysis Laboratory to develop image processing software. Moreover, we promote collaborative study with other researchers on CAD (computer assisted detection) through Open CAD project.

<Research Activities>

a) Database development

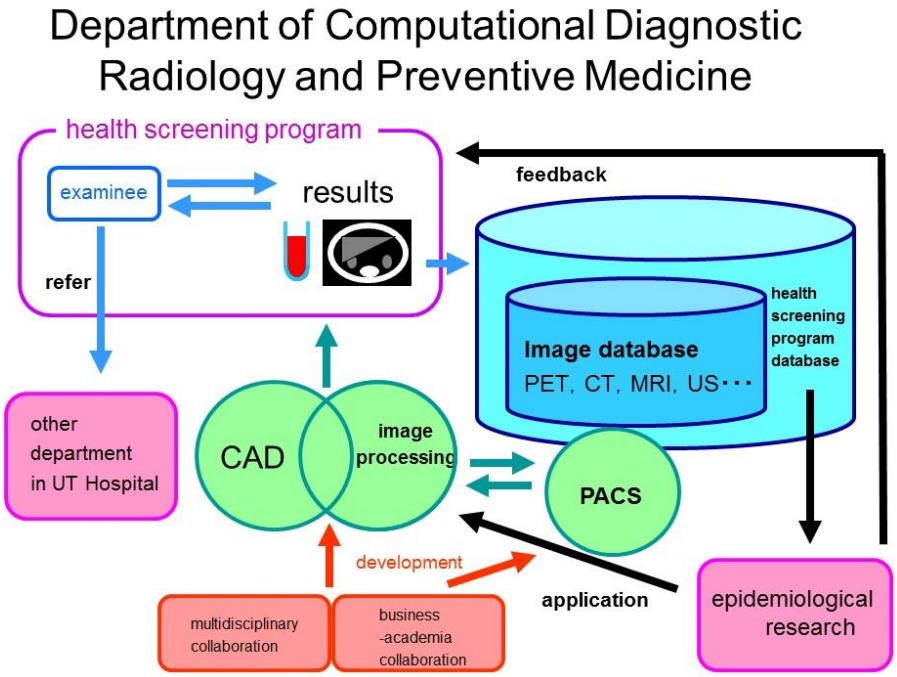
Our department conducts a comprehensive health-screening program. Examinees periodically undergo the program and are followed up over a long period. Their clinical, laboratory and imaging data are stored in a detailed and reliable database and used for research purposes. Among others, volume data using advanced imaging modalities including FDG-PET, multidetector CT and 3T-MRI are collected to detect subtle early-stage disease throughout the body.

b) Big image data processing

We develop basic image processing system to deal multiphase and multimodality images as multidimensional data. And we study algorithms to detect subtle abnormal findings automatically from massive multidimensional data. We develop image processing software in collaboration with UT Radiology / Image Computing and Analysis Laboratory, Department of Radiology, Graduate School of Medicine, The University of Tokyo. We especially focus on development and clinical application of CAD software and work toward practical use of CAD in clinical radiology.

c) Cohort study

We analyze various clinical data from health screening program over time. We verify clinical utility of abnormal findings in novel laboratory and imaging examination to predict development and prognosis of diseases.



<Future work>

a) Database development

We have already established research infrastructure for database and CAD. We continue to store detailed and reliable data from health screening program and to improve the database so that various researchers can use the data for research purposes.

b) Big image data processing

CAD developing system is in practical use. It supports development of software to detect lung nodules on CT images and to measure visceral fat volume using CT images. With regard to clinical application, we start to operate clinical CAD server with software to detect cerebral aneurysms on MRA and to detect lung nodules on CT images. Hereafter, we will clinically try out more created software on clinical CAD server, and begin new software development.

c) Cohort study

We research on relationship between laboratory data findings, imaging findings and long-term prognosis, because such clinical data has been insufficiently studied. Recently, metabolic syndrome based on visceral obesity has attracted attention. It is suggested that metabolic syndrome occurs in the context of functional abnormality of visceral fat tissue as an organ. Using CT images, we try to evaluate human's fat tissue, which has

been difficult to be visualized and quantitated. We will study correlation between indices from CT images and conventional biomarkers including insulin resistance and serum lipid profile, and demonstrate clinical utility of such indices. Moreover, we will study correlation between function of fat tissue and other clinical biomarkers including biomarkers of atherosclerosis (intima-media thickness, plaque and stenosis of carotid arteries), various adipocytokines, and try to explain the role played by functional abnormality of fat tissue in development of metabolic syndrome in humans. We also plan to conduct a follow-up study to examine prediction of cardiovascular events and effect of intervention including nutritional guidance, weight reduction, exercises and drug therapy.

<Papers in English>

1. Fukuma N, Tokiwa H, Numata G, et al. Endothelial oestrogen–myocardial cyclic guanosine monophosphate axis critically determines angiogenesis and cardiac performance during pressure overload. *Cardiovasc Res*. 2024;120(15):1884–1897. https://doi.org/10.1093/cvr/cvae202. Accessed 4/7/2025. doi: 10.1093/cvr/cvae202.

2. Shibata H, Hanaoka S, Koshino S, Miki S, Sonoda Y, Abe O. Identity Diffuser: Preserving Abnormal Region of Interests While Diffusing Identity. Applied Sciences 2024;14(18).

3. Shibata H, Hanaoka S, Nakao T, Kikuchi T, Nakamura Y, Nomura Y, Yoshikawa T, et al. Practical Medical Image Generation with Provable Privacy Protection Based on Denoising Diffusion Probabilistic Models for High-Resolution Volumetric Images. Applied Sciences 2024;14(8).

4. Dai Z, Ko T, Fujita K, et al. Myocardial DNA damage predicts heart failure outcome in various underlying diseases. *JACC Heart Fail*. 2024;12(4):648–661. doi: 10.1016/j.jchf.2023.09.027.

5. Kikuchi T, Hanaoka S, Nakao T, Nomura Y, Mori H, Yoshikawa T. Impact of CT-determined low kidney volume on renal function decline: a propensity score-matched analysis. Insights Imaging 2024 April 05;15(1):102–2.

6. Isa K, Suzuki T, Nomura S, Miyoshi T, Fujita K, et al. Demographic determinants influencing the adoption of genetic testing for cardiovascular diseases in japan - insights from a large-scale online survey. *Circ Rep*. 2024;6(5):178–182. doi: 10.1253/circrep.CR-24-0028.

7. Itoh H, Amiya E, Jimba T, Shimbo M, et al. Efficacy and safety of remote cardiac rehabilitation in the recovery phase of cardiovascular diseases (RecRCR study): A multicenter, nonrandomized, and interventional trial in japan. *Int J Cardiol Heart Vasc*. 2024;52:101421. doi: 10.1016/j.ijcha.2024.101421.

8. Goto K, Soma K, Tokiwa H, et al. Tricuspid regurgitation stratification predicts the time course of systemic right ventricle dysfunction among patients on ACE-I/ARB. *CJC Pediatr Congenit Heart Dis*. 2024;3(5):191–199. doi: 10.1016/j.cjcpc.2024.07.002.

9. Katoh M, Nomura S, Yamada S, Ito M, Hayashi H, Katagiri M, Heryed T, Fujiwara T, Takeda N, Nishida M, Sugaya M, Kato M, Osawa T, Abe H, Sakurai Y, Ko T, Fujita K, et al. Vaccine therapy for heart failure targeting the inflammatory cytokine Igfbp7. *Circulation*. 2024;150(5):374–389. doi: 10.1161/CIRCULATIONAHA.123.064719.

10. Hirano Y, Hanaoka S, Nakao T, Miki S, Kikuchi T, Nakamura Y, Nomura Y, Yoshikawa T, et al. GPT-4 turbo with vision fails to outperform text-only GPT-4 turbo in the japan diagnostic radiology board examination. *Jpn J Radiol*. 2024;42(8):918–926. doi: 10.1007/s11604-024-01561-z.

11. Nomura Y, Hanaoka S, Hayashi N, Yoshikawa T, Koshino S, Sato C, Tatsuta M, Tanaka Y, Kano S, Nakaya M, Inui S, Kusakabe M, Nakao T, Miki S, et al. Performance changes due to differences among annotating radiologists for training data in computerized lesion detection. *Int J Comput Assist Radiol Surg*. 2024;19(8):1527–1536. doi: 10.1007/s11548-024-03136-9.

12. Yamada A, Hanaoka S, Takenaga T, Miki S, Yoshikawa T, Nomura Y. Investigation of distributed learning for automated lesion detection in head MR images. *Radiol Phys Technol*. 2024;17(3):725–738. doi: 10.1007/s12194-024-00827-5.

13. Ito M, Katoh M, Sassa T, Ko T, Fujita K, et al. LMNA Q353R mutation causes dilated cardiomyopathy through impaired vitamin D signaling. *Circulation*. 2024;150(12):971–974. doi: 10.1161/CIRCULATIONAHA.124.069972.

14. Hanaoka S, Nomura Y, Yoshikawa T, Nakao T, et al. Detection of pulmonary nodules in chest radiographs: Novel cost function for effective network training with purely synthesized datasets. *Int J Comput Assist Radiol Surg*. 2024;19(10):1991–2000. doi: 10.1007/s11548-024-03227-7.

15. Kikuchi T, Nakao T, Nakamura Y, Hanaoka S, Mori H, Yoshikawa T. Toward Improved Radiologic Diagnostics: Investigating the Utility and Limitations of GPT-3.5 Turbo and GPT-4 with Quiz Cases. AJNR Am J Neuroradiol 2024 October 03;45(10):1506–1511.

16. Dai Z, Ko T, Inoue S, Nomura S, Fujita K, et al. Myocardial DNA damage is responsible for the relationship between genotype and reverse remodeling in patients with dilated cardiomyopathy. *Circ Heart Fail*. 2024;17(11):e011879. doi: 10.1161/CIRCHEARTFAILURE.124.011879.

17. Fukuda K, Matsuzaki H, Kawahara T, Yamaguchi T, Saito A, Yamamichi N, Kage H, Yoshikawa T, Prevalence and characteristics of minimal pleural fluid on screening chest MRI. *Respir Investig*. 2024;62(6):1109–1116. doi: 10.1016/j.resinv.2024.09.014.

18. Hayashi H, Ko T, Dai Z, Fujita K, et al. TRAITER: Transformer-guided diagnosis and prognosis of heart failure using cell nuclear morphology and DNA damage marker. *Bioinformatics*. 2024;40(11):btae610. doi: 10.1093/bioinformatics/btae610. doi: 10.1093/bioinformatics/btae610.

19. Hirano Y, Hanaoka S, Nakao T, Miki S, Kikuchi T, Nakamura Y, Nomura Y, Yoshikawa T, et al. No improvement found with GPT-4o: Results of additional experiments in the japan diagnostic radiology board examination. *Jpn J Radiol*. 2024;42(11):1352–1353. doi: 10.1007/s11604-024-01622-3.

20. Yoshikawa M, Asaba K. CCN3/NOV as a potential therapeutic target for diverticular disease: A proteome-wide mendelian randomization study. *Medicine (Baltimore)*. 2024;103(45):e40467. doi: 10.1097/MD.0000000000040467.

21. Imai Y, Kusano K, Aiba T, Ako J, Asano Y, Harada-Shiba M, Kataoka M, Kosho T, Kubo T, Matsumura T, Minamino T, Minatoya K, Morita H, Nishigaki M, Nomura S, Ogino H, Ohno S, Takamura M, Tanaka T, Tsujita K, Uchida T, Yamagishi H, Ebana Y, Fujita K, et al. JCS/JCC/JSPCCS 2024 guideline on genetic testing and counseling in cardiovascular disease. *Circ J*. 2024;88(12):2022–2099. doi: 10.1253/circj.CJ-23-0926.

22. Shimbo M, Hatano M, Katsushika S, et al. Deep learning to detect pulmonary hypertension from the chest X-ray images of patients with systemic sclerosis. *Int Heart J*. 2024;65(6):1066–1074. doi: 10.1536/ihj.24-111.

23. Togashi T, Baatartsogt N, Nagao Y, Kashiwakura Y, Hayakawa M, Hiramoto T, Fujiwara T, et al. Cure of congenital purpura fulminans via expression of engineered protein C through neonatal genome editing in mice. *Arterioscler Thromb Vasc Biol*. 2024;44(12):2616–2627. doi: 10.1161/ATVBAHA.123.319460.

24. Nakamura Y, Sonoda Y, Yamagishi Y, Kikuchi T, Nakao T, Miki S, Hanakoka S, Yoshikawa T, et al. It is not time to kick out radiologists. *Asian Bioeth Rev*. 2024;17(1):9–15. doi: 10.1007/s41649-024-00325-1.

25. Hanaoka S, Nomura Y, Hayashi N, Sato I, Miki S, Yoshikawa T, Shibata H, Nakao T, et al. Deep generative abnormal lesion emphasization validated by nine radiologists and 1000 chest X-rays with lung nodules. *PLoS One*. 2024;19(12):e0315646. doi: 10.1371/journal.pone.0315646.

26. Yoshikawa M, Nakayama T, Asaba K. Systematic proteome-wide mendelian randomization to prioritize causal plasma proteins for skin cancers. *Commun Biol*. 2024;7(1):1681–y. doi: 10.1038/s42003-024-07403-y.

27. Fujiwara T, Ishii S, Minatsuki S, Hatano M, Takeda N. Exploring novel therapeutics for pulmonary arterial hypertension. *Int Heart J*. 2025;66(1):3–12. doi: 10.1536/ihj.24-615.

28. Letchumanan N, Hanaoka S, Takenaga T, Suzuki Y, Nakao T, Nomura Y, Yoshikawa T, et al. Predicting the risk of type 2 diabetes mellitus (T2DM) emergence in 5 years using mammography images: A comparison study between radiomics and deep

learning algorithm. *J Med Imaging (Bellingham)*. 2025;12(1):014501. doi: 10.1117/1.JMI.12.1.014501.

29. Shimbo M, Nakayama A, Fukue N, et al. A national survey of career development according to gender and subspecialties among cardiologists in japan. *PLoS One*. 2025;20(1):e0317029. doi: 10.1371/journal.pone.0317029.

30. Yamagishi Y, Nakamura Y, Hanaoka S, Abe O. Large language model approach for zero-shot information extraction and clustering of japanese radiology reports: Algorithm development and validation. *JMIR Cancer*. 2025;11:e57275. doi: 10.2196/57275.

31. Tsukada YT, Aoki-Kamiya C, Mizuno A, Nakayama A, Ide T, Aoyama R, Honye J, Hoshina K, Ikegame T, Inoue K, Bando YK, Kataoka M, Kondo N, Maemura K, Makaya M, Masumori N, Mito A, Miyauchi M, Miyazaki A, Nakano Y, Nakao YM, Nakatsuka M, Nakayama T, Oginosawa Y, Ohba N, Otsuka M, Okaniwa H, Saito A, Saito K, Sakata Y, Harada-Shiba M, Soejima K, Takahashi S, Takahashi T, Tanaka T, Wada Y, Watanabe Y, Yano Y, Yoshida M, Yoshikawa T, Yoshimatsu J, Abe T, Dai Z, Endo A, Fukuda-Doi M, Ito-Hagiwara K, Harima A, Hirakawa K, Hosokawa K, Iizuka G, Ikeda S, Ishii N, Izawa KP, Kagiyama N, Umeda-Kameyama Y, Kanki S, Kato K, Komuro A, Konagai N, Konishi Y, Nishizaki F, Noma S, Norimatsu T, Numao Y, Oishi S, Okubo K, Ohmori T, Otaki Y, Shibata T, Shibuya J, Shimbo M, et al. JCS/JCC/JACR/JATS 2024 Guideline on Cardiovascular Practice With Consideration for Diversity, Equity, and Inclusion. 2025 Feb 20;

32.Numata G, Otsu Y, Nakamura S, Toyoda M, Tokiwa H, et al. In vivo effects of cardiomyocyte-specific beta-1 blockade on afterload- and frequency-dependent cardiac performance. *Am J Physiol Heart Circ Physiol*. 2025;328(3):H543–H549. doi: 10.1152/ajpheart.00795.2024.

33. Kanemaru N, Yoshikawa T, Miki S, Nakao T, Nakamura Y, Fujimoto K, et al. Axillary lymphadenopathy after COVID-19 vaccination: Follow-up for enlarged lymph nodes on MR imaging. *Magn Reson Med Sci*. 2025;24(2):176–183. doi: 10.2463/mrms.mp.2023-0147.