

# A02-3 Function Integrated Diagnostic Assistance Based on Multidisciplinary Computational Anatomy

- Plan of Five Years and Progress Overview FY2014 -

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**Abstract** — This paper describes the purpose and plans with a brief summary of the progress in FY2014 for our research work as a part of the project, “Multidisciplinary Computational Anatomy and Its Application to Highly Intelligent Diagnosis and Therapy,” funded by Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan. The main purposes of our research in this project are to establish a scientific principle of multidisciplinary computational anatomy and to develop computer-aided diagnosis (CAD) systems based on such anatomical models for organ and tissue functions. CAD systems with multidisciplinary information are expected to contribute to the society by enabling super-early detection and prevention of diseases and improving the quality of lives of patients.

## I. INTRODUCTION

Modern medical imaging devices have granted the visualization of metabolic and functional information of a body, raising the enormous interest in quantitative image analysis. In the field of neuroscience, a new diagnostic method by fusion of anatomic and functional information has

been developed. The method is based on the theory of localization of brain function, Brodmann area, and Talairach atlas brain, and established as the statistical image analysis method. On the other hand, such method has not yet been well established in fields other than brain. Therefore, the establishment of a scientific principle for diagnosis of organ and tissue functions and the development of such models would be a valuable scientific achievement. Our world-leading research in this project is expected to bring a tremendous contribution to the medical imaging field.

We have been studying on the development of computational anatomy models of various organs from CT images [1]. Our previous achievements include automatic localization and segmentation of various organs and tissues, standardization of body size and registration to a standard model, and establishment of probabilistic models. In the field of functional imaging, we have been investigating a statistical image analysis method for glucose metabolism in FDG-PET images, computer-aided diagnosis of liver function in MR

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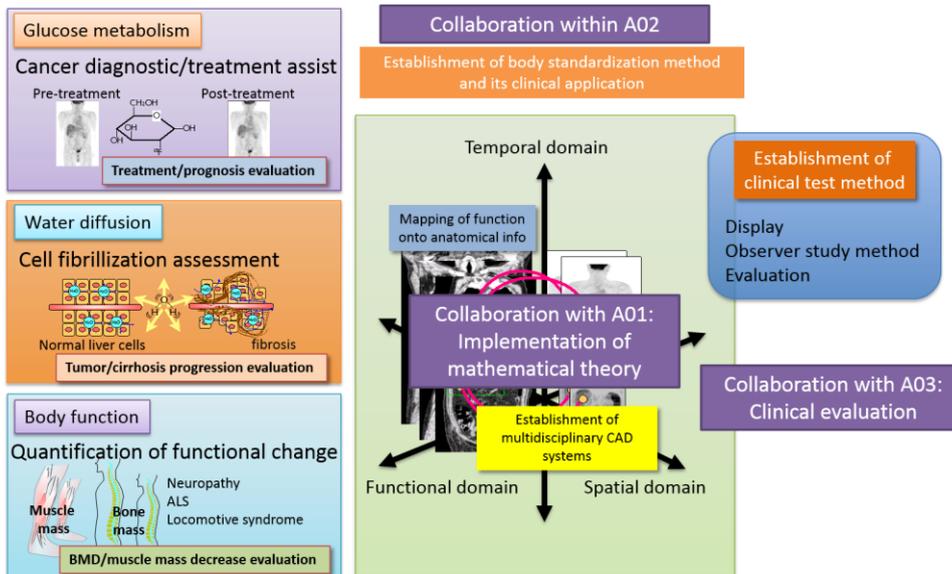


Fig. 1 Schematic diagram of the research project

images, and quantitative analysis of bone mass and muscle mass in relation to body function. However, these analyses are primarily limited within single modalities and not yet well established to take a full advantage of modern imaging technology by combining multidisciplinary information.

As A02-3, our purpose in this project is to investigate an image analysis method based on the anatomic and functional information fusion and to establish a methodology of computer-aided diagnostic (CAD) systems for organ and tissue functions. Specifically, our plan is to investigate on three major topics: CAD system for glycometabolic function, CAD system for water molecular diffusion function, and CAD system for articular and muscular function.

In collaboration with A01 groups, we will embody the mathematical theory established by A01-1 and spatiotemporal, functional and pathological models proposed by A01-2 and 3. Our roles, in collaboration with A02 groups, are to develop the multidisciplinary models by using our knowledge and experience obtained in the development of computational anatomy models and extending it to temporal and functional dimension and to implement the models in CAD systems for contribution to advanced diagnosis and treatment. The developed systems will be pass on to A03 groups for clinical evaluation.

In the following sections, a detailed plan for each of the three major topics along with other potential topics and some preliminary result will be presented.

## II. RESEARCH PLANS AND ACHIEVEMENTS

### A. Fundamental Techniques for Quantifying and Modeling the Human Functions based on Multiple CT and MR Images

#### 1) Purpose

The aim of this research is to quantify the human functions based on multiple imaging modalities such as CT and MR on individual patient, and the goal of this work is to model the

normal functions of human body based on a large database that can cover the human population statistically for supporting the computer-aided diagnosis (CAD) and surgical planning.

#### 2) Background, research plan and current progress

##### a) Image data collection

In our previous work, we constructed a large image database that contained over 4,000 patient cases of torso CT scans. This database enabled our machine-learning approach that accomplished the automatic organ localization successfully [2, 3]. In the present work, we plan to reinforce the database by expanding the scan range of human from torso to whole body and image modalities from single CT to multiple CTs, MR, and so on. Currently, we have passed the examination of Research Ethics Committee of Gifu University Hospital and obtained the permission for this study. Over 40 cases of whole-body CT scans and 10 whole-body MR (T2 + diffusion-weighted image: DWI) scans have been collected. These images enable the initial investigations of this research work. Furthermore, we improved the efficiency of our data-collection system by adding a function to connect our system with a PACS system directly. A demonstration of our system had been presented in [4, 5].

##### b) Anatomical recognition and segmentation

In our previous works, we developed a universal approach to recognize and segment the major organs and tissues on torso CT images by finding its location in CT images, searching the image patterns that are similar to the inputted image in a database, and transferring the anatomical structures in the selected image patterns directly to the inputted image as the references to guide the segmentation. This approach was fully based on machine-learning and data-driven methods that use more image data instead of complex algorithms to enhance the robustness and accuracy of the organ segmentation process [1]. We plan to continually use this consideration and expand the ability of our system to deal with more challenging anatomical structure recognition problems such as individual vertebra

recognition and muscle-skeleton segmentation by using multiple image modalities instead of a single CT image. The progress of the multiple vertebra recognitions will be presented in [6].

### c) Functional quantification

In our previous work, we focused on the motions and deformations of diaphragm and liver by tracing changes of target's shapes on a time series of CT or MR scans from the same patient [7]. In the present work, we plan to introduce the other functional images such as DWI and combine them into anatomical structures that obtained from MR or CT images. The challenge in this work is 3D image registration between different image modalities with high accuracy. We plan to propose a new method to accomplish the multi-modality image registrations based on corresponding landmarks on different images. The efficient landmark discovery and non-rigid image deformation based on landmarks are two major problems that we are focusing on. We recently presented a preliminary work that investigates the local image similarity for landmark detections by using a 3D phase correlation method in [8].

### d) Applications

The needs and feedbacks of the doctors are important guideline of this research works. We plan to develop a user-interface to effectively communicate with the doctors for using and evaluating the results of our research. We are developing a system that can visualize the uterus structures and fibroids in 3D based on MR images to help doctors to make the surgical plans [9]. We also applied 3D-printing techniques to generate the real 3D physical models that show patient specific uterus structures realistically. The investigation on the usefulness of these models will be presented in [10]. The final goal of this user-interface is to combine the functional information to the anatomical structures to show the information virtually on a computer screen or generate a hand-on physical model for easy understanding.

### 3) Conclusion

We plan to quantify the functions of human body from multiple MR images and model these functions by referring the anatomical structures that have been recognized in our previous work. The initial investigations of our approach and image collections are going on smoothly. The potential

usefulness of our research works for supporting surgical planning for uterine fibroids have been confirmed.

## B. Statistical Image Analysis of FDG-PET Images

### 1) Background

The idea of statistical image analysis has been applied to determine activated areas in brain by using PET, fMRI, and SPECT images. The technique involves segmentation technique of objective regions, a construction of a normal model, and a statistical analysis of an objective image and the normal model by pixel by pixel. To expand this scheme of brain function analysis from brain to torso regions, automated segmentation technique of organ and non-linear deformation approach are required. We have developed an automated segmentation technique in torso CT images as mentioned in the previous section. The technique can be applied to the statistical image analysis in torso regions, and the fundamental procedure for image deformation and statistical analysis were developed as an initial work [11].

### 2) Research plan

The whole scheme in five years consists of three objectives: an establishment of a theory of the anatomical standardization method of torso area, an application of the theory to FDG-PET scan and a demonstration of the method by using PET/CT scan images for cancer treatments. Theories and implementation technique from A01 group will be used in the anatomical standardization.

### 3) Recent achievement

In this year, we have applied the segmentation technique of organ regions [12] on diagnostic CT images to CT images in PET/CT devices to construct a fundamental theory of statistical image analysis for torso area, because the segmentation performance in low-dose and low-resolution CT images obtained from PET/CT device has not been evaluated yet. Regions of heart, liver, left and right lungs, stomach, left and right kidneys, pancreas, and bladder were manually segmented in collaboration with A01 group in the previous research works of computational anatomy. We used 50 normal torso CT cases from PET/CT devices (39 males and 11 females, 512x512 pixels with 1.17 mm spatial resolution and 5.0 mm slice thickness). To evaluate the organ segmentation results, we used the two indices: distances between centers of

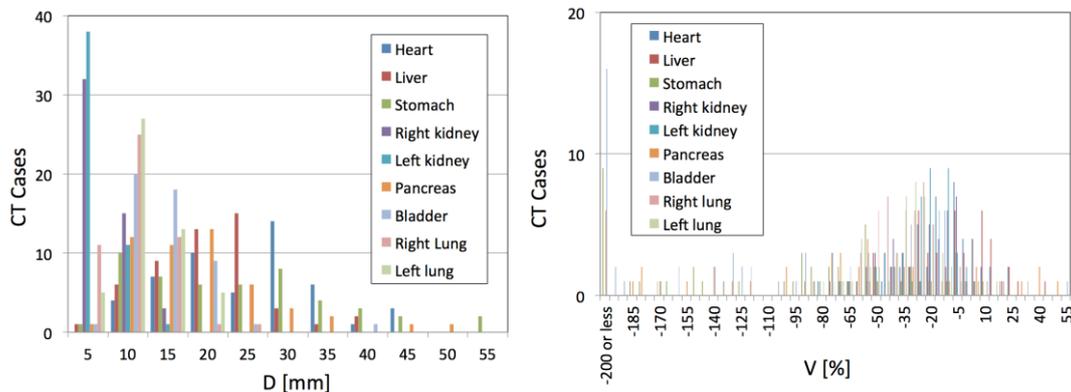


Fig. 2 Distributions of two indices to evaluate organ segmentation performances

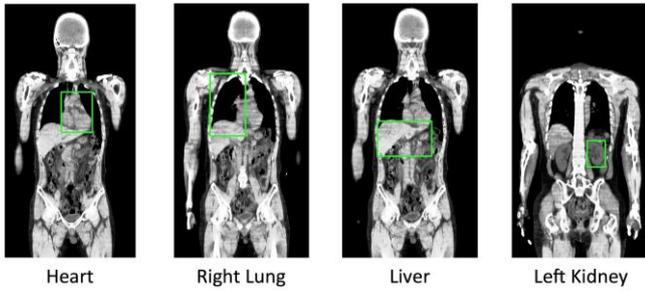


Fig. 3 Examples of bounding boxes on CT images from PET/CT devices

segmented bounding boxes and gold-standard organ regions (D) and volume variance ratios (V), which is defined as the fraction of the volume difference between bounding boxes and GS organ regions. Fig. 2 shows the distributions of Ds and Vs. The distributions of Ds and Vs obtained from every organs were between 0 to 35 mm, and -70 to 10 %, respectively. The distributions of the indices were comparable to those in our previous work [12]. Fig. 3 shows an example of the segmentation results of heart, right lung, liver and left kidney. The bounding boxes illustrate the appropriate boundary to segment each organ from the whole body image. The automated results of organ localization can be applied to establish a new theory of anatomical standardization in torso region because each organ has to be deformed into one shape to construct normal model to describe the functions of organs that were measured by the PET scan images.

### C. Detection and Analysis of Lung Tumors Using PET/CT Images

#### 1) Purpose

Lung cancer is the leading cause of death for males and females worldwide; it is essential to detect the lung cancer at an early stage. PET/CT examination is widely used for detection of early cancer, since it has the high sensitivity and high specificity by using both anatomical and functional information of the body. However, radiologists have to examine more than 1,000 images per patient; it is difficult to maintain the diagnostic accuracy avoiding reading errors. In this study, we develop the automated schemes of lung tumor detection and evaluation of malignancy using the PET/CT images.

#### 2) Research plan

In this study, we will develop the lung CAD scheme by combining the PET/CT images and supplementary information.

First year, we plan to develop the hybrid detection method of lung tumors using both CT and PET information. As for the existing detection method using CT image, it was difficult to detect low-contrast lesions that touch to normal organs such as the chest wall or blood vessels in the lung [13]. In this study, we plan to develop the improved scheme using active contour filters to detect the "difficult tumors" from the previous CAD scheme.

In 2015-2017, we plan to develop the analytical method of determining the malignancy of tumors by a combination of anatomical, functional and supplementary information (past

medical history, family history, and gene information, etc.). At the same time, we will construct a large scale PET/CT image database with pathological information to verify the analytical result of malignancy.

In the final year, we will develop the CAD software introducing above techniques. Clinical effectiveness will be evaluated using this software and image database.

Basically, above techniques can also be applied to tumor detection in other organs. Therefore, we will extend this study to other organs such as pancreas, liver, and breast.

### 3) Resent achievement

A hybrid detection method of lung tumors using active contour technique was developed in our present study [14]. As a result of evaluation of this method using 100 cases, the sensitivity was 89.3 % with the number of false positives (FPs) per case at 6.0; it was 8 % higher than that of the independent detection systems using only CT or PET images and was 6 % higher than our previous CAD scheme using PET/CT images.

Using the same approach as lung CAD, an automated detection of pancreas tumors was developed. In this study, pancreas region in a CT image was estimated using the multi-organ detection scheme developed by our research group [15]. Initial evaluation using 8 cases of screening PET/CT images revealed that the sensitivity of detection was 75 % with the FPs per case of 1.17 [16].

### D. Automated Analysis of Increased Uptake Regions in the Bone Scintigraphy Using SPECT/CT Images

#### 1) Purpose

As an examination of bone scintigraphy, two-dimensional examination is conducted using a gamma-ray camera. Recently, some institutions introduced a whole body SPECT/CT examination. By using SPECT/CT images, it is possible to analyze the uptake regions of the SPECT image while utilizing the information of the bone obtained from the CT image; remarkable improvement of accuracy is expected compared to the existing methods.

However, because the diagnosis using SPECT/CT is based on qualitative judgment, it is difficult to evaluate uptake regions quantitatively and three-dimensionally. In this study, therefore, we develop an automated analytical technique of increased uptake regions using both SPECT and CT images to evaluate the bone metastases and malignancy of tumors.

#### 2) Research plan

In this study, we will develop the CAD scheme to evaluate the bone metastasis and its malignancy by combining the anatomical and functional information obtained from CT and SPECT images, respectively.

In 2014-2015, we will investigate the imaging properties of tumors in SPECT/CT images using a bone-simulated phantom. Based on these results, we plan to develop the automated analytical method of tumors in SPECT/CT images. At the same time, we will construct the SPECT/CT database for evaluation.

In the SPECT/CT images, many benign regions and physiological uptake regions are seen. Therefore we will develop the method for elimination of these regions among initial candidate regions from 2016-2017. To eliminate them, computational modelling of benign regions, physiological uptake regions and malignant tumors will be conducted. Consequently, in the final year, we plan to develop the CAD software including above techniques and to evaluate it using the image database in order to evaluate the effectiveness of this method.

### 3) Recent achievement

We conducted preliminary evaluation using bone-simulated phantom and prototype software. As a result, measured uptake values and volumes of uptake region were well matched to those of designed values [17].

## E. A Model-based Approach to Recognize Skeletal Muscle Region for Muscle Function Analysis

### 1) Purpose

In Japan, CT device, which allows to image entire torso or whole body image, is widespread. In the super-aging society, for rehabilitation and extension of healthy life expectancy, an accurate measurement of skeletal muscle volume is required. Our purposes are to develop the quantitative analysis method of whole body muscle and to quantify the change in muscle function based on this method.

### 2) Overview

In our previous studies, we achieved site-specific recognition of the skeletal muscles in torso regions [18-21]. With this technique, an automatic recognition for skeletal muscles in surface and deep regions was realized. In order to achieve the whole-body analysis of muscle function, it is necessary to realize a complex and stable analysis of the muscles in various regions. Therefore, in order to achieve whole-body muscle analysis, the study of composite analysis of skeletal muscles using whole body CT image has started.

### 3) Results

In this year, in addition to the conventional study, we achieved the automatic recognition of sternocleidomastoid muscle [22] and iliac muscle [23]. Sternocleidomastoid muscle measurement is important in the diagnosis of diseases such as muscular dystrophy and ALS. Using the model construction method and model deformation technique such as FFD, the average concordance rate of 62 % in 20 cases (Fig. 4 left) was achieved in our preliminary investigation. For the iliac muscle,

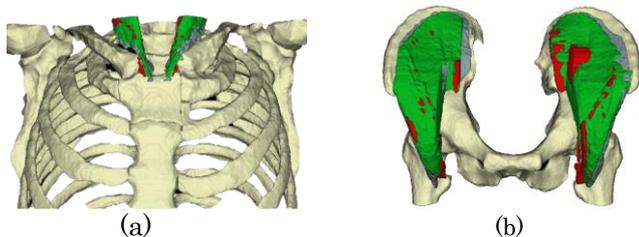


Fig. 4 Recognition result of our initial study. (a) Sternocleidomastoid muscle, (b) Iliac muscle

a muscle related to walking function, the automated recognition method of the psoas major muscle, which is already achieved in previous study, can be applied. With the recognition of iliac muscle region, it is expected to realize the functional analysis of iliopsoas muscle. As an initial step of the automatic recognition of iliac muscle based on the shape model, we obtained an average concordance rate of 77 % in 5 cases. (Fig. 4 right) Currently, the whole-body CTs are collected, and we began to focus on in building a technique for muscle function analysis of whole body, including time-dependent changes.

## F. Quantitative Evaluation of Muscle Function Using US Images

### 1) Background

In recent years, quantitative evaluation of “Locomotive syndrome” caused by musculoskeletal disorders which describes the state of high-risk condition of requiring care is expected [24]. This study aims to quantify the condition of the muscle from a two-dimensional ultrasound image of a quadriceps muscle.

### 2) Method

First, the upper and lower fasciae from the ultrasound B-mode image are extracted. They are approximated by curves, and the area between the curves is set as a region of interest (ROI). Next, we calculate texture features and muscle thickness from the ROI. We build a regression model of the knee extension strength by combining the texture features, the muscle thickness, and physical features. Finally, we substitute the features calculated from the test data into the regression model, and estimate their knee extension strength.

### 3) Results

Fig. 5 shows the result of the experiment using a leave-one-out cross-validation in 48 elderly (14 men and 34 women, mean age  $70.4 \pm 7.3$  years). The vertical axis corresponds to the value measured by using a knee extension strength meter, and the horizontal axis represents the estimated value of the system. As a result, the coefficient of determination (R-squared) was 0.65, and root mean squared error was 5.19 kg.

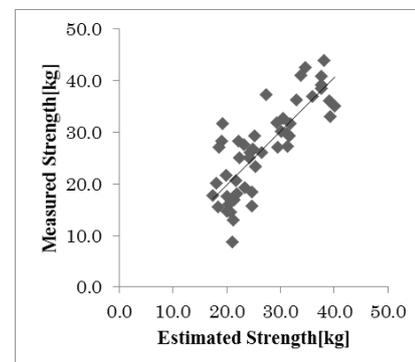


Fig. 5 Relationship between the measured and estimated knee extension

#### 4) Conclusion

The result suggests that the proposed system can estimate the knee extension strength using an ultrasound image of a quadriceps muscle. According to the previous study by Muraki et al. [25], texture features of muscle areas represent the quality of the muscles; therefore, we will consider the system to quantify the quality of the muscles from texture features in the next step.

### III. CONCLUSION

In this paper, our purposes and research plans for this project were described. According to the plan, we have started to construct databases and to investigate in establishing the multidisciplinary anatomy models for various applications. The preliminary results show the promising progress. In the next 4 years, we will proceed with our plans and collaborate with other groups to accomplish the goal of this project.

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