特集／計算解剖学―画像数理，応用システム，臨床応用の最前線―

Model Constructions for Computational Anatomy: Fundamentals and Applications

計算解剖モデルの構築 ― 基礎と応用 ―

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要 旨

本解説論文では，われわれの最近の研究についてその目的と成果の一部を紹介する．本研究は，文部科学省科学研究費補助金・新学術領域研究「医用画像に基づく計算解剖学の創成と診断・治療支援の高度化」の中の一研究プロジェクトである．同領域研究では，計算機による人体の解剖学的構造の完全理解とその診断・手術支援への応用をおもな目的としており，われわれはこの研究目的の実現に向けて，複数の画像モダリティ（CT，MR，FDG-PET，眼底写真，歯科パノラマＸ線写真など）を用いて，計算解剖モデルの構築やモデルの応用に関する研究を進めている．本稿では、われわれの研究成果から４つを選択して紹介する．

キーワード：臓器モデル，解剖学的構造の理解，計算機支援診断，セグメンテーション

This review article describes four parts of our recent progresses in the research which has been performed under the research project “Computational anatomy for computer-aided diagnosis and therapy: Frontiers of medical image sciences” (http://www.comp-anatomy.org/) funded by Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan. The overall purpose of our works under this project is to engage in model constructions for computational anatomy and the applications of the models developed to computer-aided diagnosis (CAD) for automatically recognizing the anatomical structures and analyzing the functions of different organs in a whole body region, all of which are imaged with imaging modalities such as CT, MR, PET, eye fundus photograph, and dental panoramic radiograph. These progresses show the efficiency and potential usefulness of the proposed research works by the promising results.

Key words: Organ modeling, Anatomical structures understanding, Computer-aided diagnosis, Segmentation

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1. Introduction

Nowadays, modern imaging devices represented by CT, MRI, and PET are widely used in clinical practice. High performance of such scanners can provide detailed information of the whole body region,

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not only showing real anatomical structures of a patient in 3D (sometimes even in 4D), but also being able to visualize the functional information of the inner organs. Therefore, these medical images have been regarded as an important reference for screening, precise diagnosis, surgery, and therapy purposes.

A 3D volumetric image typically consists of a large number of axial slices. For example, a CT scan in torso region generally generates 800–1200 2D axial slices, which causes a lot of interpretation burdens for radiologists. Computer-aided detection/diagnosis (CAD) can help to reduce such burden by assisting image interpretation [1]. Especially, an advanced CAD system that aims at multi-disease detection from multi-organs is required to be investigated in torso CT images [2], and even images in other imaging modalities. In order to realize such aim and develop higher-level CAD systems, automatic segmentation/recognition techniques of the detailed anatomical structures by constructing the model of the human body can be often a powerful approach; however, it is still a challenging issue. As one of the solutions, modeling the human anatomy and function for normal and abnormal human bodies based on a large number of medical images is expected as one of the key techniques [3].

In this review article, we introduce our four state-of-the-art research works that focus mainly on organ segmentations based on machine learning and similar image retrieval, muscle segmentations by using shape and relation models, multiple lesion detections by comparing with normal body models, and inferior border of mandible detection by the model selection. These works demonstrate the state-of-the-art techniques for fundamental image segmentation based on the modeling approach and show the usefulness of those techniques on the CAD applications by the promising results [4], all of which have been performed under the research project "Computational anatomy for computer-aided diagnosis and therapy: Frontiers of medical image sciences" (http://www.comp-anatomy.org/) funded by Grant-in-Aid for Scientific Research on Innovative Areas, MEXT, Japan.

2. Examples of modeling and applications

A) A universal organ segmentation approach on torso CT images

Background/Purpose: The aim of this research subject is to develop a universal approach that can be used to automatically segment the different massive organ regions on CT images. The traditional approaches for developing automatic segmentation algorithms put the interests on how to generate an ad-hoc method to extract the specific organ-appearance on CT images by the human designers. A common model that can show the anatomical structures of all organs should be constructed firstly and then used to provide the prior knowledge for guiding the segmentation task. However, generating such a model to represent all the possible anatomical structures in both normal and abnormal CT cases is difficult and sometimes unrealistic, especially in the case that only a limited number of CT images are available during the development. Therefore, the approach that can learn and update the knowledge of the model directly from database and solve the different organ segmentation problems simply and straightforwardly is expected.

Proposed model: We have proposed a new approach [5–11] to modeling the organ segmentation process 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. The proposed approach is 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 (refer to **Fig. 1**). The key point of our proposed approach is to simplify the organ segmentation process as a content-based image retrieval and anatomical structure transformation problem.

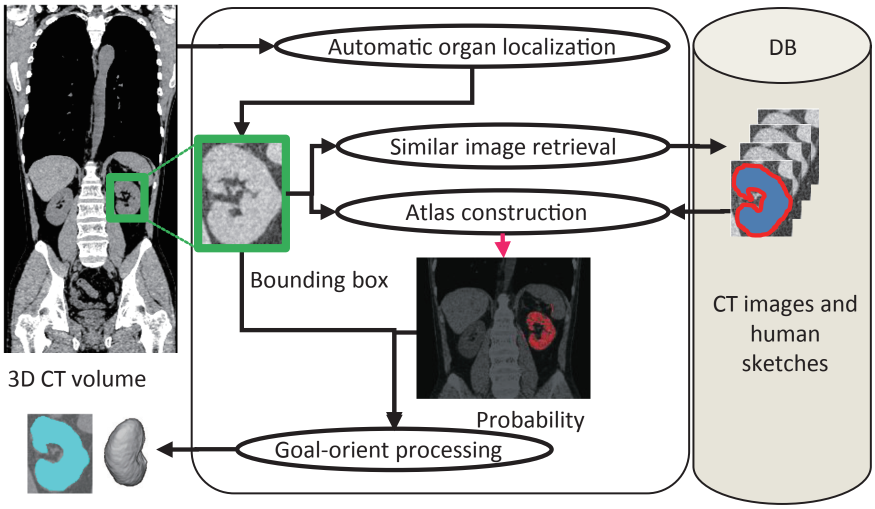

Fig. 1 Processing flow of the proposed organ segmentation approach.

The approach includes three processing steps: (1) automated target organ localization, (2) content-based image retrieval and atlas construction, and (3) atlas-based organ segmentation. Two techniques have been used in this approach; one is fast object localization based on machine-learning [6], and the other is image retrieval by using a phase-correlation registration based on the fast Fourier transform (FFT) [5].

Experiment and Evaluation: A database (DB) that includes 100 cases of 3D volumetric CT cases was used [11]. These CT cases were collected at Gifu University Hospital by two kinds of multi-slice CT scanners (LightSpeed Ultra16 of GE Healthcare and Brilliance 64 of Philips Medical Systems). The heart, liver, spleen, left kidney, and right kidney were selected as the segmentation targets for evaluating the performance of the proposed approach. One of the investigators manually extracted heart regions in 50 CT cases, liver regions in 38 CT cases, spleen regions in 60 cases, left kidneys in 93 cases, and right kidneys in 35 cases. These regions were used as the ground truth for accuracy evaluation. A leave-one-out cross validation was employed in the experiment.

The experimental results showed that the proposed scheme can solve the segmentations of the five different inner organs by using one algorithm. We confirmed that these five target organs were segmented automatically and correctly in all CT cases. The average coincidence ratios determined using the Jaccard similarity coefficient (JSC) values were 0.67 for heart, 0.78 for spleen, 0.86 for liver, 0.77 for right kidney, and 0.73 for left kidney [10].

The results indicate that our proposed method is very robust for different organ segmentations in both normal and abnormal CT cases. The segmentation results were comparable to the ground truths that were manually inputted by a medical expert, and the accuracy may be improved by using shape information in future works [12].

B) Surface muscle recognition on CT images

Background/Purpose: The skeletal muscles in CT images are commonly not paid attention by most of the doctors because their interest lies in the internal organs that are affected by diseases. Therefore, the effective use of image information is expected for the torso CT images, which are originally imaged not for the diagnosis of muscles but for the other purposes (e.g. finding diseased organ (s)).

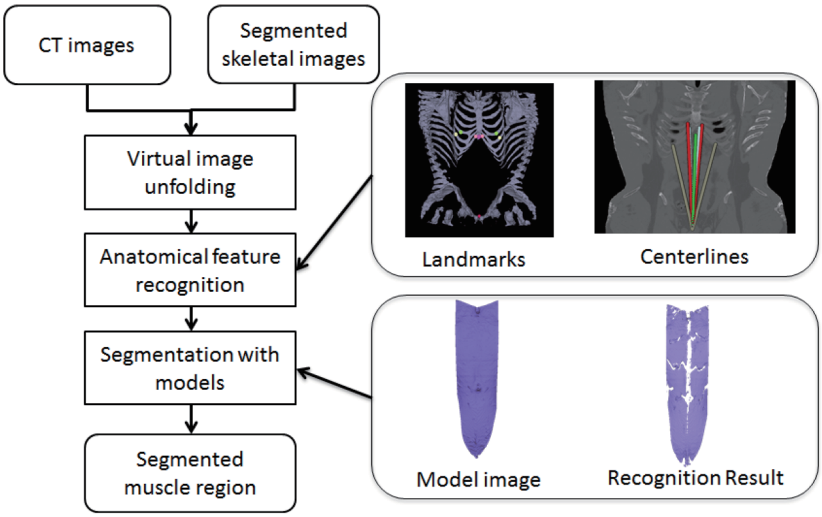

Fig. 2 Processing flow of rectus abdominis muscle recognition.

Since all torso CT slices do contain muscle regions, we have been investigating an effective use of these images.

Proposed model: In our previous work, we have proposed anatomical shape models and applied to the psoas major muscles [13] and the rectus abdominis muscles [14], both of which are generated by the statistical analysis of the training datasets separately. These models represent each muscle's outer shape by approximate functions and the model-based approach was found to be effective for segmenting the muscle regions with characteristic shapes. However, in order to achieve surface muscle segmentation based on the model, for example, for the rectus abdominis muscles and lateroabdominal muscles, one must consider the variations of the body. To overcome this issue, we proposed a new method to normalize the body shape with a virtual image unfolding technique [15, 16].

Experiment and Evaluation: The method consists of three steps [see **Fig. 2**]. Firstly, in order to simplify the body structure, virtually-projected image is produced by virtually unfolding a 3-D human body to a 2-D plane. However, before this procedure, we need to take into account the subcutaneous fat existing on areas of the target muscle, which is a major factor causing the body difference between the cases. Therefore, the subcutaneous fat region is removed on the basis of the density (CT value) difference information before the unfolding processing. Secondary, anatomical features, as landmarks, are recognized on the virtually unfolded image to make a shape model; the landmarks correspond to the origin and insertion of the muscle as anatomical definition. Then the centerline as a fiber line generated by connecting these landmarks is determined (see upper two images in **Fig. 2**). The muscle model is generated by including all muscle fiber lines represented by the centerlines on the virtually unfolded image. Finally, the area overlapping with model image is defined as initial muscle region, then the "true" muscle region is determined on the basis of the gray value (see lower two images in **Fig. 2**).

We applied this method to 10 patients with no evidence of abnormalities in the muscle region. As a result, 89.0% concordance with manual segmentation was achieved.

Thus for the muscle recognition in abdominal regions with large body differences, it was found that the virtually unfolded image technique can be very effective to simplify the body variations. The result suggests the possibility of an application of this method to the other muscle recognitions.

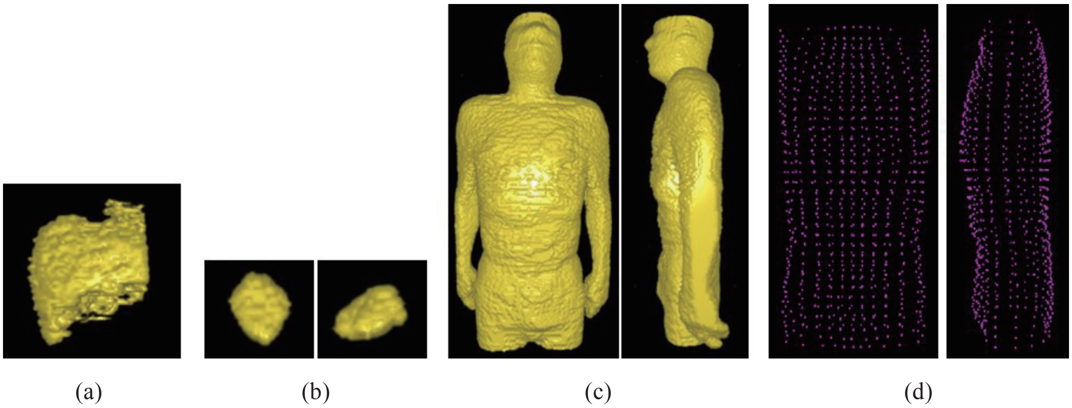

Fig. 3 Example of organ and body shape recognition. (a) Liver surface on FDG-PET scan, (b) two examples of bladder surface, (c) standard body surface deformed, and (d) landmark distribution set on the body surface deformed by TPS.

C) Anatomical standardization and temporal subtraction on FDG-PET

Background/Purpose: Diagnostic imaging on FDG-PET scans is often used to evaluate chemotherapy results of cancer patients. The interpretation of SUV (standardized uptake value) requires experiences to distinguish the activity index from the background signal depending on each organ or tissue. Anatomical standardization approach for molecular imaging on brain functions has been proposed to analyze region specific activities by comparing with those in normal database and to obtain statistical results to indicate the likelihood of abnormality by measuring the difference of the patient activity from the estimated mean of normal database [17, 18]. The purpose of this subject was to develop a new CAD system with anatomical standardization of torso FDG-PET scans as a normal model of FDG accumulations in torso regions and to evaluate the radiologists' performance when the output from the automated detection system was used [19]. In addition, the observer performance study was performed in terms of "without" and "with" the system output for detecting temporal changes on images because radiologists often compare the changes of lesions' activities between previous and current examinations for the evaluation of chemotherapy prognosis.

Proposed model: The CAD scheme developed consists of the following 6 steps: (1) anatomical standardization of normal FDG-PET scans, (2) normal model construction from the normal FDG-PET scans, (3) Z-score mapping based on the statistical image analysis, (4) automated detection of abnormal regions, (5) comparison of the detected regions between previous and current scans, and (6) image subtraction of previous and current scans. The first step of the anatomical standardization requires a data collection of normal cases. The normal cases were collected from a medical checkup institution for cancer screening by using FDG-PET scans in Japan. All of the normal cases are deformed into a standard body surface at the second step after the organ locations of liver, bladder, shoulder, and body surface are recognized on the basis of the image recognition methods for anatomical standardization. **Fig. 3** shows examples of recognized surface regions of the liver in **Fig. 3** (a) and bladders in **Fig. 3** (b). The points are spread throughout entire body surface, as shown in **Fig. 3** (c) and (d), which are used as the landmarks in image deformation by using a thin-plate spline (TPS) technique. The image deformation of many normal cases into one body structure can create two data of the mean (M) and the standard deviation (SD) of pixel values in each pixel.

Experiment and Evaluation: The original SUVs can be converted into statistical values by the M and SD. Z-score mapping based on the statistical image analysis provides a statistical index of FDG accumulation as a result of model application. The index as Z-score can be recognized as a severity of abnormal region by comparing the normal accumulation range obtained from the normal database. The detection performances of a single examination database (63 abnormal cases) was 82.6% in sensitivity with 12.4 false-positive (FP) marks per case [19].

The image deformation for constructing normal model was also applied to the temporal subtraction technique [20]. The subtraction images can be easily obtained by the anatomical standardization results because all of the patients' scans were deformed into standard body shape [17, 18]. An observer study was performed without and with CAD to evaluate the usefulness of the scheme by ROC (receiver operating characteristic) analysis. Readers were asked to determine their confidence levels from absolutely no change to definitely change between two scans on a continuous scale. The recognition performance of the computer for activity changes among 43 pairs of previous and current scans was 96.0% in sensitivity with 31.1 FP marks per scan. The average of area-under-the-ROC-curve (AUC) from 4 readers was increased from 0.85 without CAD to 0.90 with CAD ($p=0.0389$, DBM-MRMC). The average interpretation time was decreased from 42.11 to 40.04 seconds per case ($p=0.625$, Wilcoxon test) [21]. We conclude that the CAD system for torso FDG-PET scans with temporal subtraction technique might improve the diagnostic accuracy of radiologists for cancer therapy evaluation.

D) Inferior border segmentation of mandible on dental panoramic radiographs

Background/Purpose: A large number of dental panoramic radiographs (DPRs) are obtained annually to examine dental diseases in dental clinics over the world. On DPRs, not only the dental region but also nasal cavity and cervical regions are included. However, general dentists are apt to focus only on dental diseases when reading DPRs. Therefore, we have been investigating the CAD systems for detection of extra findings on DPRs: measurement of mandibular cortical width (MCW) [22, 23] for diagnosis of osteoporosis, detection of carotid artery calcifications (CACs) [24] for a possible risk of arteriosclerosis, and detection of maxillary sinusitis [25]. Finding these extra signs on DPRs may bring a supplemental benefit to asymptomatic patients with these diseases.

Detection of inferior border of mandible is essential for the measurement of MCW. It is also used in the determination of regions of interest for CAC detection and maxillary sinus areas. Therefore an accurate detection of the border is the first step for our computerized analysis of DPRs.

Proposed Model: Although overall shapes of mandible border are similar, local variations and size variations must be taken care of. Therefore, our border detection procedure consists of a similar model selection and model fitting. **Fig. 4** illustrates the contour detection process. The models used in this

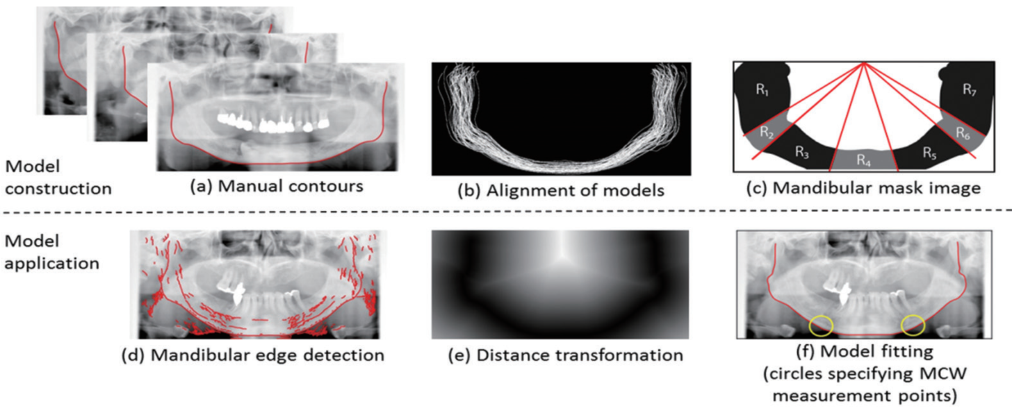

Fig. 4 Mandible contour detection process.

study are the manual mandible contours of 100 training cases obtained by an experienced dental radiologist [**Fig. 4**(a)]. These contours serve as initial models and are also used for creating a mask for the direction-specific edge detection. In the creation of the mask, 100 model contours are overlaid [**Fig. 4** (b)], and the margin is added by morphological dilation. The lines are drawn from the center of the upper edge for division of the mask into 7 regions with different directions of interest [**Fig. 4** (c)].

Experiment and Evaluation: In border detection for a test case, Kirsch's method for the Canny edge detector is applied to detect region-specific edges using the mask [**Fig. 4** (d)]. After potential edges are detected, the most similar contour model is selected by similarity measures based on the distance transformation [**Fig. 4** (e)]. Finally, the selected model is fitted to the mandible contour of the test case by the active contour model [**Fig. 4** (f)]. By leave-one-out cross validation test, the detection was generally successful in all cases with a small number of partial failures in mandibular angle regions.

3. Summary

Our recent progresses for anatomical model construction and applications based on multimodality medical images were described.

- We were able to improve our universal solution for automatic organ segmentation and confirm its usefulness and efficiency by applying to 5 kinds of organ regions based in 100 CT cases. This work may be beneficial to the further anatomical model constructions by providing a possible way to extract a large number of anatomical structures quickly and automatically from the CT images.
- For other structures with characteristic shapes and a large inter-patient variation, such as muscles, the development of an automated detection scheme based on the simplified mathematical shape models was described. By use of the virtual unfolding technique, the effect of the body difference could be reduced, so it was effective for automatic recognition of the skeletal muscles.
- A whole body probabilistic model to show the metabolic activities of glucose in the normal organs and tissues on FDG-PET images was described. This work showed the possibility of detecting the lesions by using statistical comparison methods of the patient image with a normal human body model. The clinical application to detect temporal changes as a CAD scheme was demonstrated and the effectiveness of the proposed CAD scheme was confirmed by the observer performance study.
- More specific application of the similar-model based approach was described in the mandible contour detection, which showed the encouraging results.

As shown in this article, the models for universal anatomical structure recognitions, muscle recognitions, multi-lesion detections, and mandible contour detection have been proposed by our group for solving the problem of the multi-lesion detection in multi-organs. Our models have been also applied to many CAD systems and their good performances and usefulness have been confirmed.

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