

Automated analysis of whole skeletal muscle for muscular atrophy detection of ALS in whole-body CT images: Preliminary study

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) causes functional disorders such as difficulty in breathing and swallowing through the atrophy of voluntary muscles. ALS in its early stages is difficult to diagnose because of the difficulty in differentiating it from other muscular diseases. In addition, image inspection methods for aggressive diagnosis for ALS have not yet been established. The purpose of this study is to develop an automatic analysis system of the whole skeletal muscle to support the early differential diagnosis of ALS using whole-body CT images. In this study, the muscular atrophy parts including ALS patients are automatically identified by recognizing and segmenting whole skeletal muscle in the preliminary steps. First, the skeleton is identified by its gray value information. Second, the initial area of the body cavity is recognized by the deformation of the thoracic cavity based on the anatomical segmented skeleton. Third, the abdominal cavity boundary is recognized using ABM for precisely recognizing the body cavity. The body cavity is precisely recognized by non-rigid registration method based on the reference points of the abdominal cavity boundary. Fourth, the whole skeletal muscle is recognized by excluding the skeleton, the body cavity, and the subcutaneous fat. Additionally, the areas of muscular atrophy including ALS patients are automatically identified by comparison of the muscle mass. The experiments were carried out for ten cases with abnormality in the skeletal muscle. Global recognition and segmentation of the whole skeletal muscle were well realized in eight cases. Moreover, the areas of muscular atrophy including ALS patients were well identified in the lower limbs. As a result, this study indicated the basic technology to detect the muscle atrophy including ALS. In the future, it will be necessary to consider methods to differentiate other kinds of muscular atrophy as well as the clinical application of this detection method for early ALS detection and examine a large number of cases with stage and disease type.

Keywords: Amyotrophic lateral sclerosis, Muscular atrophy, Computer-aided diagnosis, Body cavity

1. PURPOSE

Amyotrophic lateral sclerosis (ALS) causes functional disorders such as difficulty in breathing and swallowing through atrophy of the voluntary muscles. Although the fundamental treatment method for ALS has not been developed, it is possible to inhibit the progression by the medicinal therapy. Because ALS is also a problem in Japan, new medication was approved in 2015 for the progressive inhibition of ALS. On the other hand, while there are a wide variety of

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inspection methods for ALS, the inspection methods employ invasive diagnosis by exclusion. In addition, the image inspection methods for aggressive diagnosis of ALS have not yet been established [1]. Therefore, the development of new non-invasive image inspection methods for the differential diagnosis of early ALS is awaited.

A related study has detected the lingual fascicular contraction for ALS in ultrasonic images [2]. However, since we have whole-body CT images including ALS patients, it is possible to analyze the condition of whole skeletal muscle.

In this study, we develop an automatic analysis system of whole skeletal muscle using whole-body CT images including ALS patients. By automatically recognizing whole skeletal muscle, it is possible to grasp the muscle mass and the change of muscle shape. Additionally, this study automatically identifies muscular atrophy parts for ALS patients. It is expected to identify the areas where ALS has developed and differentiate early ALS by analyzing the areas of muscular atrophy. In the preceding study, we recognized the individual parts of deep skeletal muscle such as the psoas major muscle successfully [3]. In this study, we automatically identify the areas of muscular atrophy parts including ALS patients by recognizing and segmenting the whole skeletal muscle on the surface.

2. METHODS

We describe the recognition methods of whole skeletal muscle using the anatomical segmented skeleton and the method of identifying the areas of muscular atrophy including ALS patients in the whole-body CT images. The input images are whole-body CT images without contrast. First, the skeleton is recognized by the information from the gray values. Second, the skeleton is segmented into 22 areas by the anatomical positions. Third, the body cavity is recognized because it includes many organ areas. Therefore, the thoracic cavity is recognized using the lungs and ribs. The initial area of the body cavity is recognized by the deformation of the thoracic cavity based on the four points of the pelvis. In addition, the abdominal cavity boundary is recognized for the purpose of precise recognition of the body cavity using ABM. The body cavity is then precisely recognized using a flexible registration method based on the reference points for the abdominal cavity boundary. Fourth, it is realized that whole skeletal muscle is recognized by excluding the skeleton, the body cavity, and the subcutaneous fat. Finally, the whole skeletal muscle is segmented using the segmented skeleton. The areas of muscular atrophy including ALS patients are automatically identified by comparison of the muscle mass.

2.1 Recognition and segmentation of the skeleton

The initial area of the skeleton is recognized by emphasizing the boundary of the skeleton using a Sobel filter. The skeleton is recognized using the region growing method, which is controlled by the gray value information. Finally, the recognized skeleton is segmented into 22 areas by the anatomical skeleton position. The skeleton segmented in this section is used for the recognition of the body cavity and the segmentation of whole skeletal muscle.

2.2 Recognition of the initial area of the body cavity

Using only the information from the gray values of the lungs is unsuitable for recognizing the lower thoracic cavity, which includes other organ areas. Therefore, the thoracic cavity is recognized using the information from the lungs for the upper thoracic cavity, and the information from the ribs. First, the lungs are recognized by gray values. The upper thoracic cavity is recognized by connecting the endpoints of the lungs on the right and left. Figure 1 shows the lungs in green and the area enclosed by the connected line in blue. Second, the curve which passes through the center of gravity of the ribs, sternums, and thoracic vertebrae is drawn using a spline curve interpolation. The insides of the red curve in Figure 1 are regarded as the lower thoracic cavity. Additionally, the initial area of the body cavity is recognized by deforming the thoracic cavity using Thin-Plate Splines (TPS) [4]. The reference points that are necessary to deform the thoracic cavity are based on the four points of the pelvis. Figure 2 (a) shows the four reference points that are on the front of the body, the lowest part of the pelvis, and the iliac crest on the right and left, respectively. The thoracic cavity is deformed by approaching the grid control points that surround the lower thoracic cavity to the four points of the pelvis using TPS. The deformed body cavity is regarded as the initial area of the body cavity as shown in Figure 2 (b).

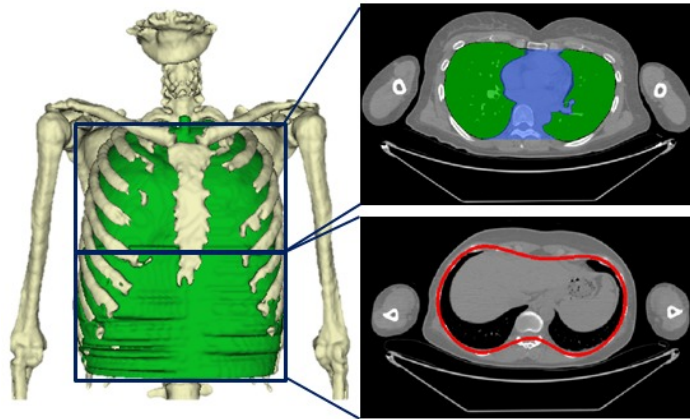
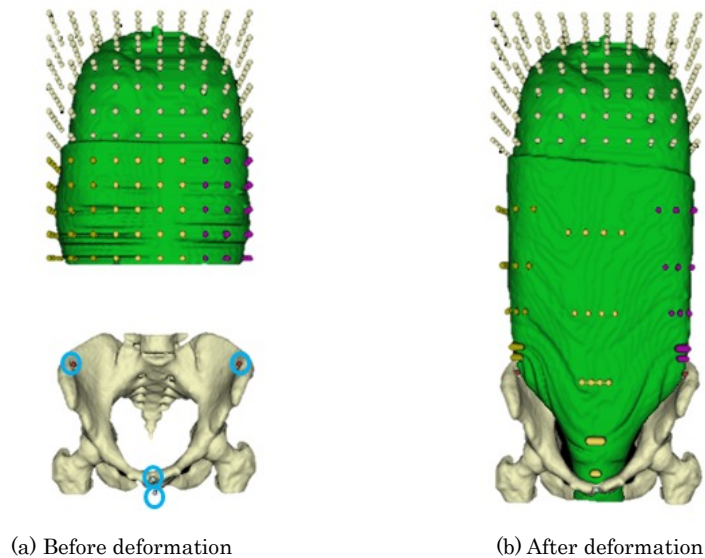


Figure 1. Thoracic cavity recognition

2.3 Recognition of the abdominal cavity using the Active Balloon Model (ABM)

The abdominal cavity boundary is recognized for the purpose of precise recognition of the body cavity. The abdominal cavity boundary is recognized using the Active Balloon Model (ABM) [5]. ABM is composed of three-dimensional models which include the Snakes methods [6]. It is possible to construct the surface shape of the object from the discrete coordinate points by energy minimization. In this study, the abdominal cavity boundary is constructed from the feature points of the visceral fat areas using ABM. Because it is unnecessary for the abdominal cavity to be precisely recognized to define the direction of the body axis, the abdominal cavity is recognized using the global segmented abdomen.

First, the skin and the upper limbs are excluded so as to recognize the visceral fat areas. Second, the skeletal muscles and the organ areas of the abdomen are recognized by the discriminant analysis method. The closed curves that surround the skeletal muscles of the abdomen are constructed using the Snakes methods on axial slices of the abdomen. Third, the visceral fat areas are recognized by excluding the skeletal muscles and the organ areas of the abdomen from the inside of the closed curve. Fourth, only the visceral fat areas cause excessive contraction for ABM. Therefore, we set the curves to control excessive ABM shrinkage by excluding 30 [pixels] from the surface of skeletal muscles of the abdomen empirically. Figure 3(a) shows the feature points of the visceral fat areas in light blue and the control curves of excessive shrinkage by ABM in red. The shape model of ABM in this study is constructed from pentagons or hexagons based on the



(a) Before deformation (b) After deformation
Figure 2. Initial area recognition of the body cavity

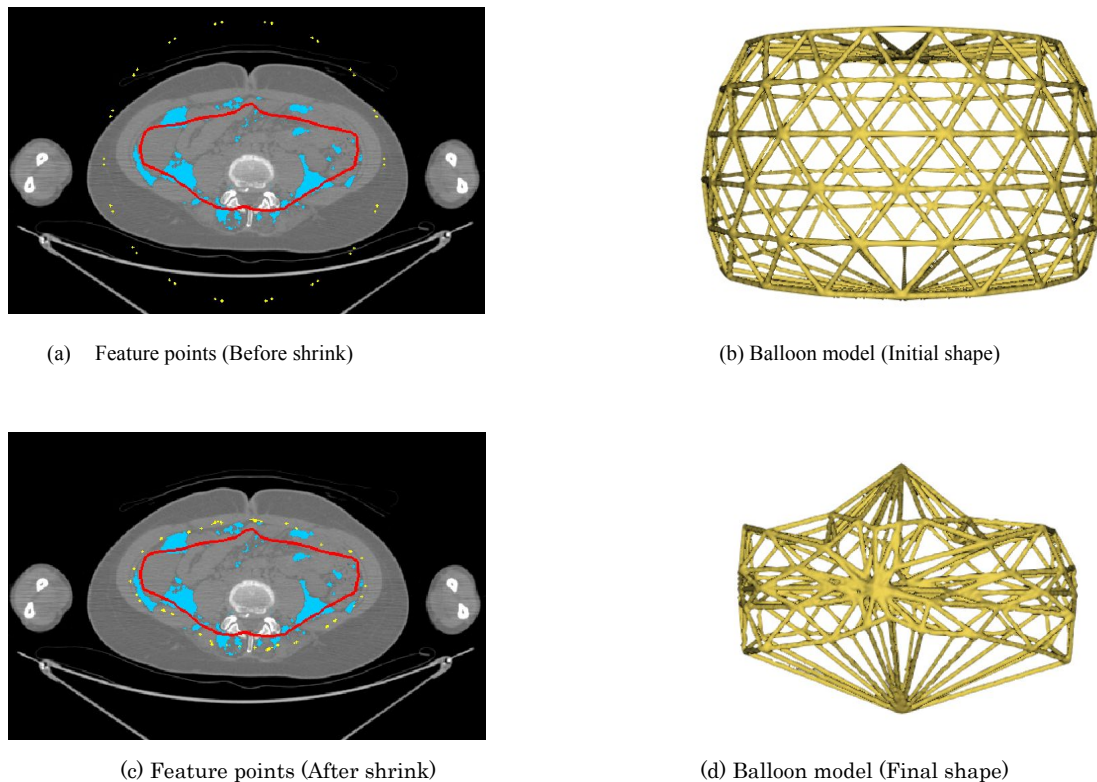


Figure 3. Abdominal cavity recognition using ABM

sphere which encloses the feature points of the visceral fat areas, as shown in Figure 3(b). The surfaces of the balloon model are constructed from the patches of triangles. The abdominal cavity boundary is recognized by shrinking the balloon model by the energy minimization of each node of the patches. Additionally, because it is not necessary to precisely recognize the abdominal cavity to define the direction of the body axis, the balloon model is shrunk such that it is fixed on two points that are up and down on the body axis so as to shorten the computation time.

In this study, $E(p)$ is the energy minimization of each node p . $E(p)$ is constituted by the sum of the internal energy $E_{int}(p)$ and the external energy $E_{ext}(p)$. $E(p)$ is defined by $E(p) = E_{int}(p) + kE_{ext}(p)$. The internal energy $E_{int}(p)$ is the sum of the areas of the triangle patches S_i for pentagons or hexagons defined by $E_{int}(p) = \sum_i S_i^2$. The external energy $E_{ext}(p)$ is defined by $E_{ext}(p) = \sum_s -G_\sigma(s - p)$. In the above expression, G_σ is Gaussian function of variance, and σ^2 and s are feature points of the visceral fat areas, respectively. The balloon model is shrunk by the minimization of these energies. In addition, the energy is calculated based on the condition of the neighboring 27 positions of $p'=(x\pm 3, y\pm 3, z\pm 3)$ for node $p=(x, y, z)$. Figure 4 shows the shape of the balloon model before and after shrinking in yellow.

After the balloon model is shrunk, the roundest axial slice is selected in the abdominal cavity boundary. The movement points based on the selected slice are set for TPS while, the fixed points on the thorax and the lowest part of the pelvis are set so as to control the deformation.

2.4 Recognition and segmentation of the whole skeletal muscle and atrophy parts detection

First, the skeletal muscles and organ areas of the abdomen (excepting the skeleton) are recognized by the discriminant analysis method for CT images. Second, the whole skeletal muscle on the surface is recognized by excluding the body cavity. Finally, the whole skeletal muscle is segmented into 22 areas using the segmented skeleton. The muscle mass in every axial slice is measured for the segmented whole skeletal muscle. The muscular atrophy parts are identified by

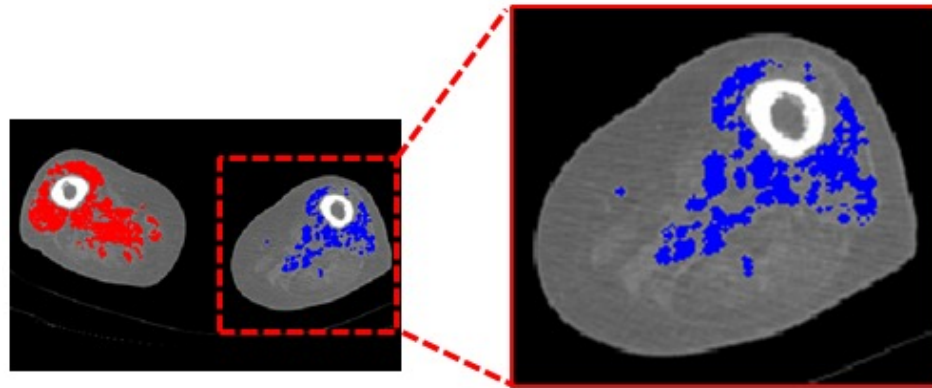


Figure 4. Detection of the muscular atrophy region in ALS patients

selecting the axial slice which has the maximum muscle mass on the right and the left. Figure 4 shows the areas of muscular atrophy successfully identified in the lower limbs.

3. EXPERIMENT AND RESULTS

The experiments were carried out using ten cases without contrast and with abnormality present. There are six ALS cases in the data. The number of pixels and slices are 512×512 pixels and 1929-2433 slices, respectively. The spatial resolution is 0.625-0.977 mm. We evaluated the recognition accuracy of the muscular region visually.

As a result, we globally recognized and segmented the whole skeletal muscle in eight cases well. In addition, the automatic identification of the areas of muscular atrophy in ALS patients was realized in the lower limbs. The global recognition and segmentation of the whole skeletal muscle were successfully realized for eight cases. Although the recognition accuracy of the pelvic cavity presented a problem, it scarcely affected the analysis of the whole skeletal muscle. The two cases of failure represented a lack of accuracy. In one case, a cardiac pacemaker was implanted, and in the other case, the intestine was abnormally expanded by the gas inside it. Therefore, this method is useful for automatic recognition of the whole skeletal muscle distinguished by the comparative differences between the left and the right sides. In addition, automatic identification of the areas of muscular atrophy parts including ALS patients was realized in the lower limbs. Using this system, it is possible to quantitatively analyze the areas of muscular atrophy including ALS patients. However, it is necessary to examine a large number of cases with stage and disease types.

4. CONCLUSION

This study developed an automatic analysis method of the whole skeletal muscle using whole-body CT images including ALS patients. The global recognition and segmentation of the whole skeletal muscle were performed successfully in eight cases. Additionally, the automatic identification of areas of muscular atrophy including ALS patients was accomplished for the lower limbs. In this study, we developed the basic methodology to detect muscular atrophy including ALS cases. In the future, it is planned to recognize more precise muscle regions by increasing the precision of the pelvic cavity recognition process. In addition, it is necessary to consider both the methods for differentiating more kinds of muscular atrophy and the clinical application of ALS detection by analyzing the muscular regions and the identified areas of muscular atrophy. Needless to say, it is also necessary to examine a large number of cases with stage and disease type.

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REFERENCES

- [1] Kiernan, MC., Vucic, S., Cheah, BC., Turner, MR., Eisen, A., Hardiman, O., Burrell, JR. and Zoing, MC., "Amyotrophic lateral sclerosis," *Lancet*, 377(9769), 942-955 (2011).
- [2] Misawa, S., Noto, Y., Shibuya, K., Iose, S., Sekiguchi, Y., Nasu, S. and Kuwabara, S., "Ultrasonographic detection of fasciculations markedly increases diagnostic sensitivity of ALS," *Neurology*, 77(16), 1532-1537 (2011).
- [3] Kamiya, N., Zhou, X., Chen, H., Muramatsu, C., Hara, T., Yokoyama, R., Kanematsu, M., Hoshi, H. and Fujita, H., "Automated segmentation of psoas major muscle in X-ray CT images by use of a shape model: Preliminary study," *Radiological Physics and Technology*, 5(1), 5-14 (2012).
- [4] Bookstein, FL., "Principal warps: Thin-plate splines and the decomposition of deformations," *IEEE Trans. on Pattern Analysis and Machine Intelligence*, 11, 567-585 (1989).
- [5] Sekita, Y., Matsuda, I. and Itoh, S., "Reproduction of Surface Shapes from Characteristic Points in 3D Space using the Active Balloon Model," *IEICE*, 99(445), 17-24 (1999).
- [6] Kass, M., Witkin, A. and Terzopoulos, D., "Snakes: Active contour models," *Int. J. of Computer Vision*, 1(4), 321-331 (1988).