An Age Estimation Method Using Brain Local Features for T1-Weighted Images

Chihiro Kondo*, Koichi Ito*, Kai Wu†, Kazunori Sato‡, Yasuyuki Taki‡, Hiroshi Fukuda§ and Takafumi Aoki*

***Abstract*— Previous statistical analysis studies using large-scale brain magnetic resonance (MR) image databases have examined that brain tissues have age-related morphological changes. This fact indicates that one can estimate the age of a subject from his/her brain MR image by evaluating morphological changes with healthy aging. This paper proposes an age estimation method using local features extracted from T1-weighted MR images. The brain local features are defined by volumes of brain tissues parcellated into local regions defined by the automated anatomical labeling atlas. The proposed method selects optimal local regions to improve the performance of age estimation. We evaluate performance of the proposed method using 1,146 T1-weighted images from a Japanese MR image database. We also discuss the medical implication of selected optimal local regions.**

I. Introduction

Morphological changes of a human brain have been found to follow a specific pattern of growth and atrophy in the process of brain development and healthy aging. On the other hand, neurodegenerative diseases such as Alzheimer's disease (AD) have caused the accelerated aging process, i.e., the accelerated brain atrophy. Evaluating the difference between the age estimated from the brain information and the actual age might help early identification and diagnostic support of age-related brain disorders.

Previous statistical analysis studies using magnetic resonance (MR) imaging, especially T1-weighted images, have demonstrated that age-related changes are found in gray matter (GM) volume, white matter (WM) volume and Cerebrosphinal fluid (CSF) [1], [2], [3], [4]. GM volume monotonically decreases with age from 20s to 70s, WM volume shows small changes, and CSF monotonically increases with age from 20s to 70s in contrast with GM volume [4]. Such volume changes make it possible to estimate the age of subjects from T1-weighted images.

So far, there are some studies on age estimation from T1-weighted MR images [5], [6], [7], [8], [9]. These methods employed high-order features, all the voxels or combined information to estimate the age, and hence it was difficult to give the medical implication to estimation results. In addition, experiments were not necessarily sufficient to demonstrate the effectiveness of methods in these studies, since only a few hundred MR images were used to evaluate the accuracy of age estimation methods.

Addressing the above problems, this paper proposes a novel age estimation method using local features extracted from T1-weighted images. We define local features by regional volume calculated from 90 local regions of GM, WM and CSF parcellated by the automated anatomical labeling (AAL) atlas [10]. We then construct a classifier for age estimation based on the combination of local features using relevance vector machine (RVM) [11]. The proposed method selects optimal local regions to improve the performance of age estimation. We evaluate performance of the proposed method using 1,146 T1-weighted images from a large-scale brain MR image database of normal Japanese [12], and demonstrate that the proposed method exhibits efficient performance of age estimation compared with conventional methods. We also discuss the medical implication of selected local regions.

II. Age Estimation Using Brain Local Features

This section describes the proposed age estimation method using brain local features extracted from T1-weighted images as shown in Fig. 1. The proposed method consists of 3 processes: (i) local feature extraction, (ii) local feature normalization and (iii) classifier construction. We describe the details of each process in the following.

A. Local Feature Extraction

We apply preprocessing [13] to T1-weighted images in order to extract local features of each brain tissue. This preprocessing is done using Statistical Parametric Mapping 2 (SPM2)[1] [14] and Voxel-Based Morphometry 2 (VBM2)[2]. Note that we empirically confirmed that the accuracy of age estimation with SMP2 is better than that with the newer versions of SPM such as SMP5 and SPM8.

First, T1-weighted images are transformed into the Talairach stereotactic space by registering each of the images to the T1 template, where we employ the ICBM 152 template, which approximates the Talairach space [15]. The deformation field used in this normalization process is estimated only from GM information to prevent any contribution of nonbrain voxels and perform optimal spatial normalization of brain tissues. We normalize the T1-weighted image (Fig.

* Graduate School of Information Scienves, Tohoku University, Japan
{kondo, ito}@aoki.ecei.tohoku.ac.jp
† South China University of Technology, China
‡ Institute of Development, Aging and Cancer, Tohoku University, Japan
§ Tohoku Pharmaceutical University, Japan

[1] http://www.fil.ion.ucl.ac.uk/spm/software/spm2/
[2] http://dbm.neuro.uni-jena.de/vbm/vbm2-for-spm2/

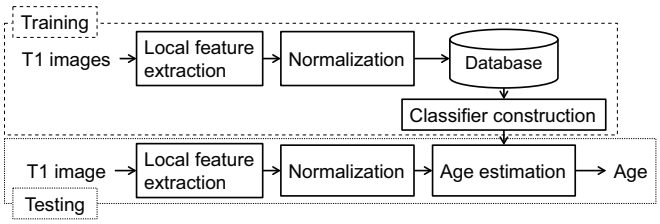

Fig. 1. Flow diagram of the proposed method.

2 (a)) using the estimated deformation field and obtain the normalized image as shown in Fig. 2 (b).

Next, the normalized images are segmented into each tissue such as GM, WM and CSF using the SMP2 default segmentation procedure, where a mixture model cluster analysis with a priori knowledge of spatial distribution of tissues is used. The segmented tissues are then modulated by the Jacobian determinants derived from spatial normalization to correct volume changes in spatial normalization. Fig. 2 (c), (d) and (e) show example of segmented GM, WM and CSF after volume modulation, respectively.

Finally, each brain tissue is parcellated into 90 regions defined by the AAL atlas [10]. We then calculate the GM volume in each parcellated local region as shown in Fig. 2 (f), and obtain the regional GM volume (RGMV). We also obtain the regional WM volume (RWMV) and the regional CSF volume (RCSFV) in the same way.

B. Local Feature Normalization

The extracted local features such as RGMV, RWMV and RCSFV include the effects from sex and total intracranial volume (TIV). These effects result in the decrease in the accuracy of age estimation. We employ a linear regression analysis to remove such effects from local features.

We now consider RGMV calculated from N subjects. The i-th RGMV can be modeled by

$$\begin{bmatrix} RGMV_1^i \\ \vdots \\ RGMV_n^i \\ \vdots \\ RGMV_N^i \end{bmatrix} = \begin{bmatrix} Sex_1 & TIV_1 \\ \vdots & \vdots \\ Sex_n & TIV_n \\ \vdots & \vdots \\ Sex_N & TIV_N \end{bmatrix} \begin{bmatrix} a_{Sex} \\ a_{TIV} \end{bmatrix} + \begin{bmatrix} e_1^i \\ \vdots \\ e_n^i \\ \vdots \\ e_N^i \end{bmatrix},$$

where i $(= 1, 2, \cdots, 90)$ is the index for local regions and n $(= 1, 2, \cdots, N)$ is the index for subjects. $RGMV_n^i$ indicates the i-th RGMV of n-th subject, a_{Sex} and a_{TIV} indicate parameters for sex and TIV, respectively, and e_n^i indicates the residual for i-th RGMV of n-th subject. Sex_n is 1 for male and 0 for female. TIV_n is the TIV calculated as the sum of GM, WM and CSF volume. Parameters a_{Sex} and a_{TIV} are estimated by using the least-square optimization method. Using the estimated parameters, we can calculate the residuals e_n^i, which do not include any effects from sex and TIV. We denote the residuals e_n^i as corrected RGMV (cRGMV) used to construct the classifier for age estimation. We also obtain cRWMV and cRCSFV by applying the above procedure to RWMV and RCSFV.

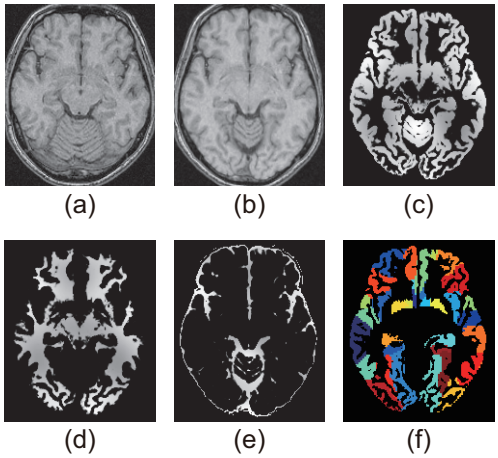

Fig. 2. Results of preprocessing: (a) T1-weighted image, (b) normalized T1-weighted image, (c) normalized, modulated GM, (d) normalized, modulated WM, (e) normalized, modulated CSF and (f) parcellated local regions of GM, where each color label indicates a segment.

C. Classifier Construction

The classifier for age estimation is constructed using the combination of cRGMV, cRWMV and cRCSFV as a feature vector. We utilize RVM [11] to make an age estimation classifier, since RVM selects a small number of support vectors to construct a classifier, and hence is robust against outliers and overlap of feature vectors compared with support vector machine (SVM) [16]. The problem of age estimation is regression estimation, since the estimated age is not a binary output but a real-valued output. We employ relevance vector regression (RVR), which is a version of RVM generalized to regression estimation [11].

We select effective local regions for age estimation by measuring the mean absolute error (MAE) of age estimation with the increase or decrease in the number of local regions, where the MAE is defined by a mean of the absolute difference between the actual and estimated age for each subject. We employ 45 local regions by making a pair of corresponding left and right local regions from 90 local regions. In the case of increasing the number of local regions, we first select the single local region, evaluate MAE using the local region, and rank the local region having the lowest MAE 1st. Next, we select one local region from the remains, combine it with 1st-ranked region, and evaluate MAE using the combined local features. We rank the local region having the lowest MAE 2nd. We repeat the above procedure until no region remains. In the case of decreasing the number of local regions, we evaluate local regions in an opposite manner. We remove one local region from 45 local regions and evaluate MAE using 44 local regions. The removed local region having the lowest MAE is ranked the last place, i.e., 45th. We remove one local region from remaining 44 local regions, evaluate MAE using 43 local regions, and rank the local region having the lowest MAE 44th. We repeat the above procedure until no region remains. Finally, we identify effective local regions in age estimation by finding the minimum of MAE obtained by changing the number of

TABLE I

CHARACTERISTICS OF THE SUBJECTS IN THE TWO PROJECTS.

Project	# of subjects	Age (mean±SD)
Aoba 1	1,156 (M: 565/F: 591)	45.6±15.7
Tsurugaya 1	176 (M: 84/F: 92)	72.1±1.7

local regions.

III. EXPERIMENTS

We describe performance evaluation of the proposed method using a large-scale T1-weighted MR image database. We also discuss the medical implication of selected local regions.

A. Experimental Condition

We use T1-weighted MR images from the Aoba Brain Imaging Project (Aoba 1) in Sendai, Japan [12] and the Tsurugaya Project (Tsrugaya 1) in Sendai, Japan. Table I shows characteristics of the subjects in both projects. T1-weighted MR images of each subject in both projects were taken using the same 0.5T MR scanner (Signa contour, GE-Yokogawa Medical Systems, Tokyo), where the image size is 256×256×124 voxels. The subjects of the two projects were all healthy and had neither present illness nor a history of neurological disease, psychiatric disease, brain tumor, or head injury. In the following, we use a combination of Aoba 1 and Tsrugaya 1 as a database for the experiment.

We select 1,146 subjects aged 20–75 years from the database, including 552 men and 594 women aged 20–75 years. We randomly select 550 subjects for the training data to construct classifiers from 1,146 subjects and also randomly select 550 subjects for the test data to evaluate the accuracy of age estimation from the remaining subjects. We perform multiple trials, where each trial includes data selection and performance evaluation, so as to prevent experimental results from depending on selected data. The number of trials is 100 for all the cases in this paper.

We employ the different types of machine learning algorithm such as linear discriminant analysis (LDA) [17] and SVM [16] in addition to RVM in order to demonstrate the effectiveness of the proposed method. The LDA-based classifier is constructed by MATLAB Statistics Toolbox, where default settings are used. The SVM-based classifier is constructed by A Library for Support Vector Machines (LIBSVM)[3], where the type of SVM is nu-SVR and parameters are optimized for each trial. The RVM-based classifier is constructed by Sparse Bayes Version 1[4], where the kernel type is set to "cauchy." We evaluate the accuracy of age estimation using the mean absolute error (MAE), the root mean squared error (RMSE) and the correlation coefficient (Corr.).

[3]http://www.csie.ntu.edu.tw/~cjlin/libsvm/

[4]http://www.miketipping.com/sparsebayes.htm

TABLE II

SUMMARY OF EXPERIMENTAL RESULTS.

	Local regions	MAE [y/o]	RMSE [y/o]	Corr.
LDA	All	7.581	9.925	0.804
	Optimal (16/90)	5.777	7.513	0.893
SVM	All	5.109	6.423	0.921
	Optimal (56/90)	4.727	5.989	0.931
RVM	All	4.630	5.812	0.936
(Proposed)	Optimal (48/90)	4.498	5.645	0.939

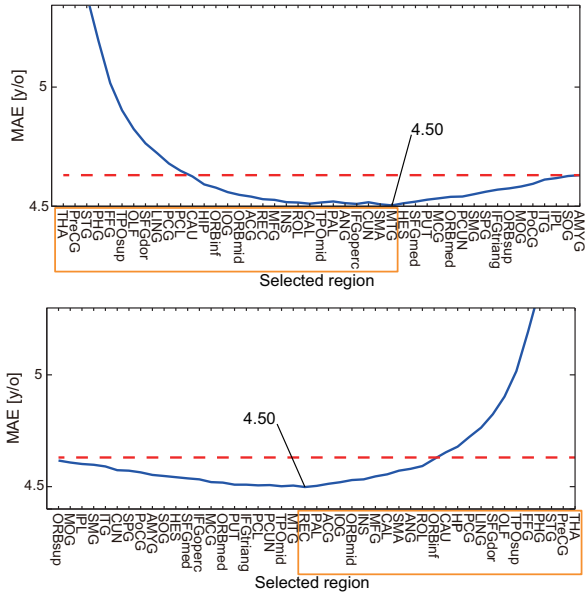

Fig. 3. MAE when changing the number of local regions (upper: increase, lower: decrease), where the dashed line indicates the MAE using all the local regions, and the orange-color box indicates the combination of local regions having the lowest MAE. We employ the same abbreviation of each local region used in [18].

B. Results

Table II shows experimental results for each classifier. The age of subjects can be estimated with an MAE of 4.498 years when using the RVM-based classifier with the optimal local regions. The classifier constructed by the proposed method can estimate reliable age from T1-weighted MR images, since there is strong correlation between the real and estimated age. Fig. 3 shows experimental results of MAE variations both for increasing and decreasing the number of local regions in the case of the proposed method.

Fig. 4 shows selected regions having the lowest MAE which are visualized by BrainNet Viewer[5]. Effective local regions are concentrated in the frontal association area, the Wernicke's area, the angularis gyrus and the primary motor cortex. The frontal association area takes on the function of behavioral decision and working memory. The functions of the Wernicke's area include language comprehension, semantic processing, language recognition and language interpretation. The angularis gyrus takes on the functions related to language, spatial cognition, memory retrieval, attention and theory of mind. The above regions take on the high-order function compared with other regions, and hence are

[5]https://www.nitrc.org/projects/bnv/

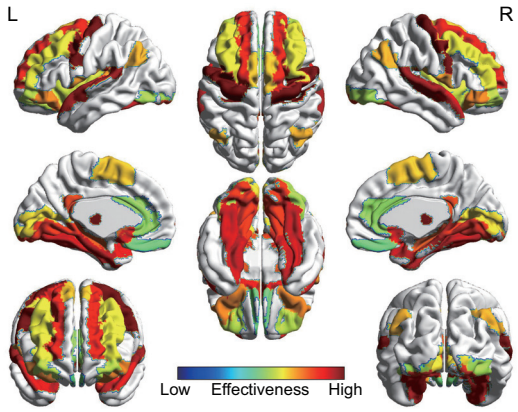

Fig. 4. Visualized optimal local regions for age estimation.

TABLE III
COMPARISON AMONG CONVENTIONAL AND PROPOSED METHODS.

Method	# of subjects (Age range)	MRI	MAE [y/o]	Corr.
Lao et al.[5]	153 (56∼85)	1.5T	—	—
Neeb et al.[6]	44 (23∼74)	1.5T	6.3	0.69
Franke et al.[7]	547 (19∼86)	1.5T, 3T	4.61	0.94
B. Wang et al.[8]	20 (50∼86)	1.5T	2.41	—
J. Wang et al.[9]	360 (20∼82)	1.5T, 3T	4.57	0.94
	303 (7∼22)	∼3T	1.38	0.79
Proposed	1,146 (20∼75)	0.5T	4.50	0.94

impaired with aging. The primary motor cortex exhibits high effectiveness in age estimation, although this region takes on the low-order function. The location of the primary motor cortex is close to that of the central sulcus. The central sulcus becomes dilated by atrophying the frontal area and the primary motor cortex also becomes dilated which looks like atrophy. On the other hand, ineffective local regions are concentrated in the parietal lobe and the occipital lobe. These regions take on the low-order function and hence are robust against aging. The above result corresponds to the statistical analysis of age-related morphological changes [4].

Table III shows comparison among conventional and proposed age estimation methods. The proposed method is evaluated using much more subjects and wider age range than the conventional methods. The MAE of the proposed method is lower than that of most conventional methods. The proposed age estimation method is more reliable than the conventional methods, since the proposed method indicates low MAE and high correlation coefficient.

IV. CONCLUSION

This paper proposed a novel age estimation method using brain local features extracted from T1-weighted MR images. Through a set of experiments using a large-scale MR image database, we demonstrated that the proposed method exhibits efficient performance in age estimation compared with the conventional methods. We also discuss the medical implication of selected local regions. We verified that the selected local regions suggested by the proposed method correspond to the previous statistical analysis study. We will develop a system using the proposed method to help early identification and diagnostic support of age-related brain disorders.

REFERENCES

[1] T.L. Jernigan, S.L. Archibald, C. Fennema-Notestine, A.C. Gamst, J.C. Stout, J. Bonner, and J.R. Hesselink, "Effects of age on tissues and regions of the cerebrum and cerebellum," *Neurobiol. Aging*, vol. 22, pp. 581–594, 2001.

[2] J.S. Allen, J. Bruss, C.K. Brown, and H. Damasio, "Normal neuroanatomical variation due to age: The major lobes and a parcellation of the temporal region," *Neurobiol. Aging*, vol. 26, pp. 1245–1260, 2005.

[3] D. Terribilli, M.S. Ṣchaufelberger, F.L.S. Duran, M.V. Zanetti, P.K. Curiati, P.R. Menezes, M.S. Scazufca, E. Amaro Jr., C.C. Leite, and G.F. Busatto, "Age-related gray matter volume changes in the brain during non-elderly adulthood," *Neurobiol. Aging*, vol. 32, pp. 354–368, 2011.

[4] Y. Taki, B. Thyreau, S. Kinomura, K. Sato, R. Goto, R. Kawashima, and H. Fukuda, "Correlations among brain gray matter volumes, age, gender, and hemisphere in healthy individuals.," *PLoS One*, vol. 6, no. 7, pp. e22734–1–e22734–13, Apr. 2011.

[5] Z. Lao, D. Shen, Z. Xue, B. Karacali, S. M. Resnick, and C. Davatzikos, "Morphological classification of brains via high-dimensional shape transformations and machine learning methods," *NeuroImage*, vol. 21, no. 1, pp. 46–57, Jan. 2004.

[6] H. Neeb, K. Zilles, and N. J. Shah, "Fully-automated detection of cerebral water content changes: Study of age- and gender-related H2O patterns with quantitative MRI," *NeuroImage*, vol. 29, no. 3, pp. 910–922, Feb. 2006.

[7] K. Franke, G. Ziegler, S. Kloppel, and C. Gaser, "Estimating the age of healthy subjects from T1-weighted MRI scans using kernel methods: Exploring the influence of various parameters," *NeuroImage*, vol. 50, no. 3, pp. 883–892, Apr. 2010.

[8] B. Wang and T. D. Pham, "MRI-based age prediction using hidden Markov models," *J. Neurosci. Methods*, vol. 199, no. 1, pp. 140–145, July 2011.

[9] J. Wang, W. Li, W. Miao, D. Dai, J. Hua, and H. He, "Age estimation using cortical surface pattern combining thickness with curvatures," *Med. Biol. Eng. Comput.*, vol. 52, no. 4, pp. 331–341, Apr. 2014.

[10] N. Tzourio-Mazoyer, B. Landeau, D. Papathanassiou, F. Crivello, O. Etard, N. Delcroix, B. Mazoyer, and M. Joliot, "Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI single-subject brain," *NeuroImage*, vol. 15, no. 1, pp. 273–289, Jan. 2002.

[11] M. E. Tipping, "Sparse Bayesian learning and the relevance vector machine," *J. Machine Learning Research*, vol. 1, pp. 211–244, 2001.

[12] K. Sato, Y. Taki, H. Fukuda, and R. Kawashima, "Neuroanatomical database of normal Japanese brains," *Neural Networks*, vol. 16, no. 9, pp. 1301–1310, Nov. 2003.

[13] C. D. Good, I. S. Johnsrude, J. Ashburner, R. N. A. Henson, and K. J. Friston, "A voxel-based morphometric study of ageing in 465 normal adult human brains," *NeuroImage*, vol. 14, no. 1, pp. 21–36, July 2001.

[14] K. J. Friston, A. P. Holmes, K. J. Worsley, J-P. Poline, C. D. Frith, and R. S. J. Frackowiak, "Statistical parametric maps in functional imaging: A general linear approach," *Hum. Brain Mapp.*, vol. 2, pp. 189–210, 1995.

[15] J. Talairach and P. Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*, George Thieme Verlag, 1988.

[16] C. Cortes and V. Vapnik, "Support-vector networks," *Machine Learning*, vol. 20, no. 3, pp. 273–297, Sept. 1995.

[17] C.M. Bishop, *Pattern Recognition and Machine Leaning*, Springer, 2006.

[18] K. Wu, Y. Taki, K. Sato, S. Kinomura, R. Goto, K. Okada, R. Kawashima, Y. He, A. C. Evans, and H. Fukuda, "Age-related changes in topological organization of structural brain networks in healthy individuals," *Hum. Brain Mapp.*, vol. 33, no. 3, pp. 552–568, Mar. 2011.