Combining Static and Dynamic Features to Improve Longitudinal Image Retrieval for Alzheimer's Disease

Katarina Trojachanec Dineva[1][0000-0002-7050-4947], Ivan Kitanovski[1], Ivica Dimitrovski[1], Suzana Loshkovska[1], for the Alzheimer's Disease Neuroimaging Initiative*

[1] Ss. Cyril and Methodius University
Faculty of Computer Science and Engineering, Skopje
Rugjer Boshkovik 16, PO Box 393, Skopje, Macedonia
{katarina.trojacanec, ivan.kitanovski,ivica.dimitrovski,
suzana.loshkovska}@finki.ukim.mk

Abstract. The aim of this paper is to enhance medical case retrieval for Alzheimer's disease on the basis of the domain knowledge. We approached the problem in a longitudinal manner, and we represented the medical cases by using different kind of information extracted from Magnetic Resonance Images (MRI) aiming to improve the semantic relevance, precision and efficiency of the retrieval. More particularly, we evaluated the combination of the static, dynamic features and the index reflecting the spatial pattern of abnormality (SPARE-AD) for representing the longitudinal images. According to the obtained results, the combination of the static features representing the volumetric measures along with the cortical thickness measures of the brain structures at the later time point/s together with the dynamic features such as percent change with respect to the value obtained from the linear fit at baseline and symmetrized percent change of the volumetric measures, as well as the index of abnormality provided the best overall retrieval results. The dimensionality of the feature vector was 31-33 features in most of the cases which is significantly lower than in the case of the traditional approach (thousands features in the cases when the whole brain is considered). The approach based on a combination of different kinds of features extracted from the longitudinal data, suggested in this paper, corresponds directly to the nature of the application domain and provides powerful results, yet effective and efficient way for MRI retrieval for AD.

Keywords: Medical Cases, Medical Images, MRI, Image Retrieval, Longitudinal Data, Static Features, Dynamic Features, SPARE-AD, Alzheimer's Disease.

* "Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report (http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf)"

1 Introduction

Alzheimer's Disease (AD) accounts for estimated 60-80% of dementia cases [1]. Therefore, it is considered as one of the most common forms of dementia in older adults nowadays [2-3]. It is a progressive, irreversible, neurodegenerative disease that usually starts as a long asymptomatic stage, called preclinical AD. Then, a symptomatic stage called appears, known as mild cognitive impairment (MCI). This stage may be followed by the third possible phase, dementia, which may vary from mild to severe [2, 4-6].

The early and accurate detection of AD, monitoring the progression of the disease and the condition of the patient in general, finding powerful diagnostic or prognosis biomarkers, detecting patients who are most likely to develop AD, as well as reaction to the therapy, are still open questions. Our research is part of AD-related data organization and usage [7-19]. It provides a good basis for the other research directions related to AD, including (1) defining risk factors and the information usage to develop recommendations for prevention [20-21], (2) diagnosis and prognosis - finding diagnostic biomarkers and biomarkers for prognosis (biomarkers from cerebrospinal fluid and blood, as well as imaging markers) [10, 20, 22-26], treatment reaction analysis [20, 27-28]. It should be noted that there is no sharp border between the aforementioned research directions, and they are not mutually exclusive.

In fact, due to the rapid development of the technology and medicine, large amount of data is continuously and rapidly generated as part of the medical cases related to AD. In this regard, blood and cerebrospinal fluid biomarkers, genetic markers, neuroimages, and cognitive tests results, are produced and commonly examined and analysed by the physicians in the process of diagnosis or, slightly wider, in the period of monitoring the patient's condition. Then, they usually remain unused in the clinical databases until the need for their removal. Hence, it is essential to provide a way for efficient storage, organization and representation of these data in an appropriate manner that will enable quick and easy access to the medical cases, as well as clinically relevant, but also, precise and efficient retrieval, providing a way for powerful knowledge discovery from these continuously growing data. The computer science development undoubtedly facilitates and enables information extraction from this kind of data, their analysis, visualization and knowledge discovery. Longitudinal images (images acquired at multiple consecutive time points) play crucial role in this domain and reflect the disease progression. Thus, taking into consideration the progressive nature of the disease, the longitudinal approach to the problem of brain image retrieval for AD is essential to make the retrieval more accurate and clinically relevant.

Several studies focus on brain MRI retrieval for AD. Some of them use the traditional approach for feature extraction and base the descriptors directly on the visual image content. For instance, general-purpose image feature algorithms are evaluated for the purpose of a similar retrieval process in [14]. The main idea is that they might be beneficial because of their simplicity (they consider only one 2D slice). This makes their approach appropriate for large scale systems. Authors in [15] proposed a hybrid features extraction technique. They extracted contrast feature, morphological operated features, and texture-based features from brain MRI. Those features are then hybridized by applying fusion technique. The research in [16] is based on evaluation of texture

features extracted by using Gray Level Co-occurrence Matrix algorithm, Law Texture Energy Measure and a combination of the features extracted with these two methods. Gray-level cooccurrence matrix is also evaluated in [17], together with local binary pattern and colour cooccurrence matrix. On the other hand, authors in [18] used estimated volumes of the brain structures, and cortical thickness measures to generate image descriptors for patients' representation in the multistage classifier. In fact, they incorporate this classifier in the process of AD prediction and retrieval. Finally, with the aim to increase the early detection performance for AD, authors in [19] used pre-trained 3D-autoencoder, 3D Capsule Network, and 3D-Convolutional Neural Network.

Several challenges can be identified considering the existing research related to image retrieval for AD. One important challenge is gaining the semantically relevant retrieval results. Another critical part might be the size of the feature vector, tending to be high dimensional. Despite the power and accuracy, the deep neural networks bring, the difficulty to understand and interpret their way of decision making makes them challenge to be adapted for medical applications [29]. The main challenge that should also be mentioned is whether the problem is approached cross-sectionally or longitudinally. Common limitation in the existing studies is that images are processed and included in the research cross-sectionally, thus loosing potentially crucial information.

Taking this into consideration, our research is aimed to provide better longitudinal image representation that will reflect the early stage of the disease, the patient's condition at one moment (static state of the brain / current brain degeneration) but will also represent the brain changes caused by the disease over time (dynamic aspect / disease progression). For that purpose, this research aims to evaluate a representation containing a combination of static and dynamic features, together with the SPARE-AD index, namely the Spatial Pattern of Abnormality for Recognition of Early Alzheimer's disease. In fact, we suggest using a combination of the best descriptors, investigated and evaluated in the previous research, namely static [11] and dynamic features [12] along with the value of SPARE-AD [13]. Therefore, the different type of information that each of them separately carries, will be utilized and incorporated into one feature vector. For this purpose, we identified four scenarios and then and then we evaluated them to find out if they are complementary and will contribute to better retrieval results.

Providing efficient and precise medical case retrieval based on MRI for Alzheimer's disease may have multiple benefits from different perspective. One is in the direction of decision support in a way of providing clinicians with powerful and relevant information at the right moment by giving the medical cases of other examined patients that are the most similar to the query patient. This is valuable assistance in the clinical environment. The knowledge that can be discovered from the retrieved medical cases, enables a deeper understanding of the disease in general, as well as, specifically, of the condition of the query patient, thus contributing to the completion of the clinical picture of the query patient. This way, the knowledge gained from the retrieval result supports the decision-making process and determination of an adequate treatment/therapy. Pattern discovery and understanding is another important benefit. Retrieved images and cases they belong to, contain valuable information. This information can provide new insights about the disease, biomarkers identification, and exploration of the disease pro-

gression. Assessing response to a treatment is another, very important benefit. The information gathered from the other relevant cases, especially if they are treated in a longitudinal manner provide information about the brain changes due to disease. They give insight of the disease progress that might be used to analyze and assess the reaction to a given treatment. Finally, providing a reliable retrieval system is very beneficial for educational purposes. The possibility of searching through the large medical databases is crucial for educational and research purposes. Medical cases of patients with similar structural brain characteristics, anatomical changes or treatment reaction to the query, provide valuable knowledge for students and scientists.

The paper is organized as follows. The materials and methods are covered in Section 2. Here we present data used in our study as well as the general approach and evaluation methodology. The experimental results and discussion are presented in Section 3. Section 4 contains the concluding remarks.

2 Materials and Methods

2.1 Participants and Inclusion Criteria

Our research is based on the scans and data provided by ADNI (Alzheimer's Disease Neuroimaging Initiative) database [30]. The aim of ADNI is to enable research that will provide an answer to the question whether imaging techniques such as MRI and positron emission tomography (PET), other biological markers, including APOE status, cerebrospinal fluid (CSF) markers, and full-genome genotyping, along with neuro-psychological and clinical assessments, may indicate the presence and allow assessment of the progression of MCI and AD.

For this research, we used the standardized list from ADNI-1, containing images acquired at multiple time points. We selected the subjects that have available scans at four time points (TP 1-4), namely, at baseline, and the 6-, 12-, and 24-month follow-ups and belong to AD or normal control (NL) group. Thus, we obtained a total of 267 patients from the standardized list, 168 in AD group, and 99 in NL group. Patients' demographics information and the timing of scans by clinical group for each time point can be found in [12].

We used this selection criteria because of the following reasons: (1) more time points (ex. 36-month follow-up) is not available for the AD group of patients and, additionally, the total number of patients for whom all the scans are available is reduced by more than 12%; (2) a smaller number of time points would not give enough space for investigation and an opportunity to have a good insight into the problem (3) with the selected time points, we have an opportunity to analyze the problem in the case of equally and unequally spaced available time pointes (depending of which time point is missing).

2.2 Longitudinal Image Retrieval for AD

The image retrieval process consists of generating a representation of the query image and all the images previously stored in the database using the same feature extraction technique. After that, the feature vector (descriptor/representation) of the query image

is compared to the feature vector of all other images. All the images in the database are then sorted by similarity to the query image, so that the most similar one is at the top. This sorted list of the database images is the result of the retrieval process. In this research, for a given medical case of a patient for whom MRI was acquired at multiple consecutive time points, the set of images (longitudinal images) is given as a query to the system. The retrieval system provides a sorted list of all other patients in the medical database according to their similarity to the query.

To evaluate the proposed scenarios in this research, we used the standard evaluation metric MAP (Mean Average Precision) for quantitative measurement of the retrieval performance. We also calculated precision at first (top) x returned cases (Px), where $x \in \{1, 5, 10, 20, 30\}$, and the precision at first (top) R returned case (RP). In this case, R is the total number of relevant images/cases.

In our research, the retrieved case is considered as relevant if the clinical group (AD/NL) of that patient is the same with the clinical group of the query patient. The precision value is the higher the relevant cases are located higher in the result list. Additionally, we used leave-one-out strategy because of the small number of patients used in the evaluation. This means that the descriptor of each patient was used as a query against all other patients' descriptors stored in the database.

2.3 MRI Processing

MRI processing is a critical and very complex task due to the specific characteristics of neurological images. For this research, we used the fully automated software pipelines from the package FreeSurfer [31]. We selected this software package because it has been shown that its processing and morphometric techniques are robust and stable regardless of the manufacturer of the scanner and the strength of the magnetic field [32-33]. We approached the problem longitudinally, considering that AD tends to progress over time, and applied the fully automated longitudinal pipeline provided by FreeSurfer. Fig. 1 depicts the main steps of the processing flow [33] that we applied to all images in the dataset.

2.4 Representation of longitudinal images

After the fully automated longitudinal processing with FreeSurfer, several types of measurements can be calculated for the brain regions and used for analysis. These include volume of the cortical and subcortical regions, cortical thickness, calculated for parts of the cerebral cortex, surface area, etc. (static features). Considering these features, research has shown that the quantitative measurements like volume or cortical thickness are more reliable and superior imaging markers related to AD in comparison with surface area [34-36]. Additionally, longitudinal changes of the volume of the cortical and sub-cortical regions as well as longitudinal change of the cortical thickness can be estimated as a single statistic (e.g. annualized atrophy rate or percent change) for each subject (dynamic features).

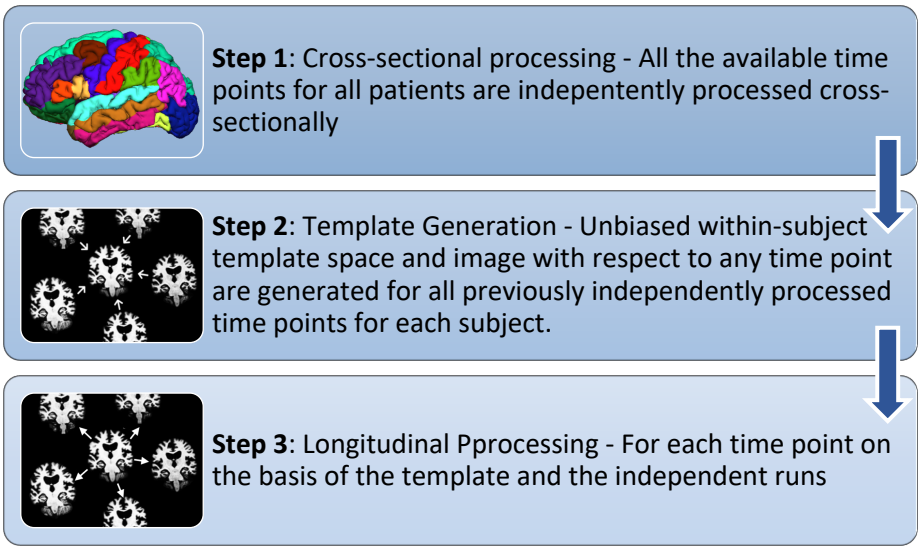

Fig. 1. Main step of the processing flow using the longitudinal stream in FreeSurfer

Both types of features were part of our previous research for image retrieval for AD [11-12]. For completeness, we provide a short description for them in the following subsections. Considering that they bring different kind of information related to the disease, we propose to use the advantage of all of them, combine the information they carry into a single descriptor for each patient and evaluate whether they are complementary and lead to better retrieval performance. Additionally, according to our previous research [13], the SPARE-AD index provides very powerful image representation and is very successful in capturing and representing the atrophy caused by AD. We included the SPARE-AD index in this research as part of the combined descriptor.

Static Features. Static features are related to the volumetric measures of the brain regions and cortical thickness of the cerebral cortex regions, calculated at different time points [11]. They represent the current state of the patient's brain at a given moment of time, in fact, when the scan is acquired, so they are called static features. On the basis of this kind of features, we have identified the following scenarios:

1. A representation composed of volumetric measures, cortical thickness measures or a combination of volumes and cortical thickness extracted from the scan at each time point TP_Y, $Y \in \{1, 2, \ldots, N\}$ separately, where Y is the total number of the available time points for a patient, and in this research is 4. In this respect, a total of Y scenarios is possible.
2. A representation containing a combination of the representations extracted from the scans of the available time points (a combination of the representations obtained according to the strategy descripted in 1).

Considering this, we defined 15 scenarios with static features:

1. L-TP_1 (volume, cortical thickness and a combination of them at time point TP_1)
2. L-TP_2 (volume, cortical thickness and a combination of them at time point TP_2)
3. L-TP_3 (volume, cortical thickness and a combination of them at time point TP_3)
4. L-TP_4 (volume, cortical thickness and a combination of them at time point TP_4)
5. L-TP_1 + TP_2 (concatenated descriptors of TP_1 and TP_2),
6. L-TP_1 + TP_3 (concatenated descriptors of TP_1 and TP_3),
7. L-TP_1 + TP_4 (concatenated descriptors of TP_1 and TP_4),
8. L-TP_2 + TP_3 (concatenated descriptors of TP_2 and TP_3),
9. L-TP_2 + TP_4 (concatenated descriptors of TP_2 and TP_4),
10. L-TP_3 + TP_4 (concatenated descriptors of TP_3 and TP_4)
11. L-TP_1 + TP_2 + TP_3 (concatenated descriptors of TP_1, TP_2 and TP_3),
12. L-TP_1 + TP_2 + TP_4 (concatenated descriptors of TP_1, TP_2 and TP_4),
13. L-TP_1 + TP_3 + TP_4 (concatenated descriptors of TP_1, TP_3 and TP_4),
14. L-TP_2 + TP_3 + TP_4 (concatenated descriptors of TP_2, TP_3 and TP_4),
15. L-TP_1 + TP_2 + TP_3 + TP_4 (concatenated descriptors of TP_1, TP_2, TP_3 and TP_4).

Regarding the volumetric measures, there are 123 measures in total, while in terms of cortical thickness, we used 70 features in total. Ten of these scenarios were evaluated and the results reported in [11]. For completeness, here we provide results of the evaluation of all 15 scenarios (Table 1). Moreover, according to [37], the quality control (QC) of the processed data might influence the performance of the retrieval process, thus it is recommended to be applied. After the automated processing of the images, we detected failures in in at least one time point for some of the cases. In order to ensure a complete automatic processing and taking into account that in our research we did not have the possibility to involve a medical expert, we considered only the cases without global or regional failures in all time points (153 patients in total, 41 AD and 112 NL). In [37], the QC is not applied. Hence, for the evaluation of the scenarios for this research, we also included this step. Moreover, we applied Correlation-based Feature Selection (CFS) algorithm [38] to be able to select the most relevant features and, in the same time, to reduce the dimension of the descriptor.

Considering the separate descriptors in Table 1, volume measurements at all time points generally led to better retrieval precision. Regarding the combined descriptors, concatenation of the descriptors of the volume and cortical thickness resulted in improved results in comparison with the separate descriptors. We obtained the best results with a concatenation of volume and cortical thickness measures in the third and fourth time points. The MAP value in this case is 0.864. These results are very reasonable from clinical perspective. In fact, Anatomical changes in the relevant brain structures become more prominent in AD patients as the disease progresses. Hence, the static features extracted from scans acquired at later time points are more powerful.

Considering the dimension of the feature vector, when the information from the specific time point is used separately, the descriptor usually has between 16 and 21 features of the volume measures, from 6 to 13 for the descriptors containing cortical thickness measures, 22-25 characteristics in the concatenated vector in most cases after the ap-

plication of the feature selection. Considering the combined vectors, the descriptor dimension is reduced to 27-30 features, when the information from the volumes and cortical thickness measures from two time points are used, 31-33 considering the information from three time points, and usually 33 characteristics when combining descriptors from all time points. As a result, it should be noted that a significant reduction in descriptor length is actually achieved.

Table 1. Evaluation of static features obtained by longitudinal processing.

Scenario	MAP		
	Volumes	Cortical thickness	Volumes + Cortical thickness
L-TP_1	0.798	0.771	0.811
L-TP_2	0.819	0.801	0.830
L-TP_1+TP_2	0.818	0.799	0.823
L-TP_3	0.830	0.812	0.836
L-TP_1+TP_3	0.834	0.807	0.834
L-TP_2+TP_2	0.834	0.806	0.837
L-TP_1+TP_2+TP_3	0.830	0.806	0.838
L-TP_4	0.854	0.826	0.862
L-TP_1+TP_4	0.849	0.824	0.863
L-TP_2+TP_4	**0.855**	**0.827**	0.861
L-TP_3+TP_4	**0.855**	0.826	**0.864**
L-TP_1+TP_2+TP_4	0.846	**0.827**	0.861
L-TP_1+TP_3+TP_4	0.854	0.824	0.863
L-TP_2+TP_3+TP_4	0.853	0.823	0.862
L-TP_1+TP_2+TP_3+TP_4	0.849	0.822	0.862

Dynamic Features. Unlike static features, the dynamic features are aimed to reflect the disease progression, in fact, the speed and severity of degeneration. The dynamic features are calculated as a single statistic reduced from the temporal data for a particular measure (volume or cortical thickness of each region) taking into account all the available scans for each patient. Based on the dynamic features, the research in [12] evaluates descriptors comprised of the following statistics: rate of change (RC), percent change with respect to the value obtained from the linear fit at baseline (PC1/fit), and symmetrized percent change (SPC). Moreover, the statistics were derived from the templates generated on the bases of different number and differently spaced time points [12], as follows:

- T_123 – template based on baseline scan and the 6- and 12-month follow-ups
- T_134 – template based on baseline scan and the 12- and 24-month follow-ups
- T_234 – template based on 6-, 12- and 24-month follow-ups
- T_1234 – template based on baseline scan and the 6-, 12 and 24-month follow-ups.

According to the results reported in [12], the best value of MAP was 0.84. This value was gained in two cases, based on T1234_VolumesPCfit (descriptor comprised of PCfit changes of the volumetric measures estimated on the bases of the template generated

when considering all the available scans) and T1234_VolumesSPC (descriptor comprised of SPC changes of the volumetric measures estimated on the bases of the template generated from all four time points). In this evaluation, the QC phase was also included. Regarding the feature vector dimension, in most of the cases, 19–21 features were selected.

SPARE-AD index. The SPARE-AD index [39-41] tends to reflect the extent to which atrophy occurred in specific brain regions. It is calculated and publicly available in ADNI database.

According to our previous work and the evaluation performed in [13], the best retrieval results from the evaluated scenarios were achieved when the descriptor was composed only of the SPARE-AD. The MAP in this case was 0.81.

Combination of static, dynamic features and SPARE-AD index. Static and dynamic features carry different kinds of information extracted from the brain images. While static features represent the patient's condition at a given moment, the dynamic reflect the progress of the disease. However, none of these aspects should be overlooked. In order to determine whether they complement each other, we propose to evaluate combination of the most powerful and efficient descriptors from the scenarios based on the static and dynamic features separately. Therefore, we concatenated the appropriate feature vectors from those scenarios that led to the best retrieval results in the experiments that are based only on the static or dynamic features separately. Additionally, taking into consideration the powerful information that the SPARE-AD index carries, we also evaluated scenarios in which this index is included in the descriptor. Thus, we propose 4 scenarios based on the combination of static and dynamic features as well as SPARE-AD index:

1. SD1-Vol34 + CT34 + VolPC - concatenated measures of volume and cortical thickness of the third and fourth time point (best static features) and volume percent change (best dynamic features);
2. SD2-Vol34 + CT34 + VolSPC - concatenated measures of volume and cortical thickness from the third and fourth time point ((best static features)) and volume symmetrized percent change (best dynamic features);
3. SD3-Vol34 + CT34 + VolPC + SPARE-AD - concatenated measures of volume and cortical thickness from the third and fourth time point, the volume percent change and the SPARE-AD index;
4. SD4-Vol34 + CT34 + VolsSPC + SPARE-AD - concatenated measures of volume and cortical thickness from the third and fourth time point, volume symmetrized percent change and the SPARE-AD index;

3 Experimental Results and Discussion

Results of the retrieval based on the combined descriptors of static, dynamic measures and the SPARE-AD index are given in Table 2. This table contains the MAP value,

whereas the detailed results for R-precision and precision at the fixed level are presented in Table 3. According to the results obtained from the evaluation, it can be concluded that the combination led to improvement in all cases. The best precision was obtained in the case of a combination of static measures of volume and cortical thickness from the last two time points (third and fourth), percent change or symmetrized percent change of the volume and the SPARE-AD index. The MAP in this case is 0.88 (scenario 3 and 4). Hence, the proposed scenarios outperform the scenarios based solely on static, dynamic features and SPARE-AD index. Due to the diversity of the datasets or the inclusion criteria of the subjects, we cannot perform an objective comparison with other research [14-18] focused on brain MRI retrieval for AD, although the retrieval performance improvement based on our strategy is evident.

Table 2. Evaluation of the combined descriptors.

Descriptor	MAP
SD1-Vol34 + CT34 + VolPC	0.87
SD2-Vol34 + CT34 + VolSPC	0.87
SD3-Vol34 + CT34 + VolPC + SPARE-AD	0.88
SD4-Vol34 + CT34 + VolsSPC + SPARE-AD	0.88

Table 3. Evaluation of the combined descriptors – detailed results.

Descriptor	RP	P1	P5	P10	P15	P20	P25	P30
SD1-Vol34 + CT34 + VolPC	0.83	0.90	0.91	0.90	0.89	0.89	0.88	0.87
SD2-Vol34 + CT34 + VolSPC	0.83	0.90	0.90	0.90	0.89	0.88	0.88	0.87
SD3-Vol34 + CT34 + VolPC + SPARE-AD	0.83	0.90	0.91	0.91	0.90	0.90	0.89	0.88
SD4-Vol34 + CT34 + VolsSPC + SPARE-AD	0.83	0.91	0.91	0.90	0.90	0.89	0.89	0.88

Additionally, we calculated the frequency of the selection of the features in the best two scenarios SD3 and SD4. The graphical representation of the features selected more than 50% for the retrieval based on the descriptor SD3-Vol34 + CT34 + VolPC + SPARE-AD is given in fig. 2. Regarding the case of descriptor SD4-Vol34 + CT34 + VolsSPC + SPARE-AD, the most frequently selected measures are shown in fig. 3. It is interesting to note that besides the known AD markers, the SPARE-AD is selected in all cases in both scenarios. In addition, most of the static and dynamic characteristics with the highest frequency of selection are from the left hemisphere. The dimension of the descriptors in most of the cases was 31-33 in both scenarios.

We believe that the improvement in longitudinal image retrieval obtained by the combination of the static and dynamic features and the SPARE-AD index occurs as a result of the different types of information these features carry. Namely, the SPARE-AD index efficiently and accurately describes the structural change in the patient's brain caused by the disease obtained on the basis of the first scan acquired for the patient. In fact, this index reflects the early stage of the disease. Then, the combination of static

volumetric and cortical thickness measurements of the brain structures (which we showed to be complementary) extracted from the scans at the third and fourth time points describe the changes in the brain at fixed time points (static state) when AD is in an advanced stage. Finally, the complete progression of the disease and the degree to which it has developed (dynamic aspect) is described by the percentage change (or symmetrical percent change) of the volume of the brain structures that have been proven to be superior dynamic indicators during the retrieval.

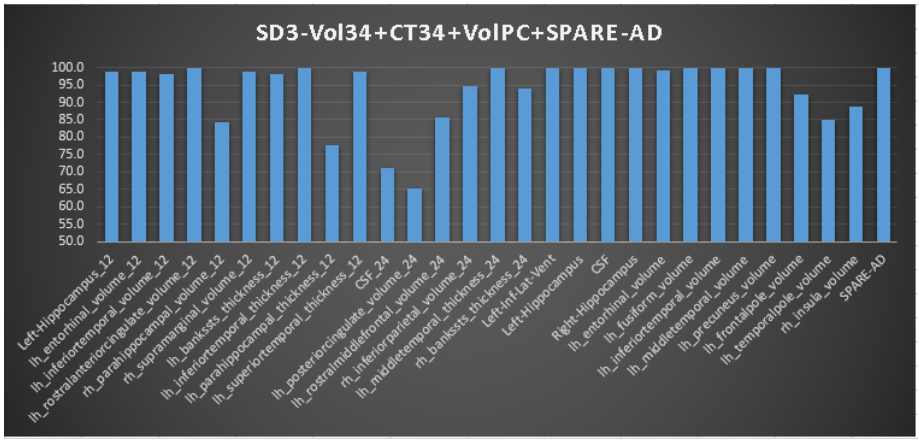

Fig. 2. The most frequently selected features (more than 50% of the cases) during the retrieval on the bases of the descriptor SD3-Vol34 + CT34 + VolPC + SPARE-AD.

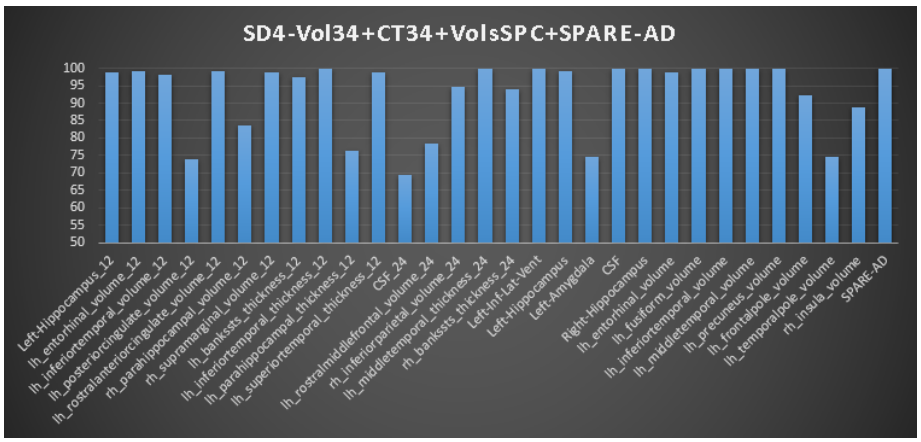

Fig. 3. The most frequently selected features (more than 50% of the cases) during the retrieval on the bases of the descriptor SD3-Vol34 + CT34 + VolPC + SPARE-AD.

Combining all these aspects into one descriptor makes it comprehensive and powerful in describing the medical case based on MR images and thus leads to the best retrieval results. Such a descriptor actually allows the retrieval to be reduced to retrieve cases

that have the most similar pattern of atrophy of structures affected by the disease in its early stage, the most similar anatomical condition of the brain during the development of the disease (at later time points) and the most similar dynamics of disease progression (change in brain structure / disease severity) with the case being given as a query. This is very beneficial from the medical perspective because the retrieved top similar cases bring rich clinical information to the physicians regarding the patient's current conditions, disease progression and prognosis, and/or response to the therapy.

4 Conclusion

We focused our research on improvement of the representation of longitudinal MRI for Alzheimer's disease that will properly reflect the current state and the severity of the disease and will provide semantically relevant retrieval results. For that purpose, we proposed and evaluate four scenarios based on the combination of the most powerful static and dynamic features from the previous research together with the SPARE-AD index. In fact, with the combination of the volume of cortical and subcortical regions and cortical thickness of the regions in the cerebral cortex at the later time points together with the volume percent change or symmetrized percent change, along with SPARE-AD score we superior, outperforming the scenarios based solely on static, dynamic features or the SPARE-AD index. In this case, the value of the MAP was 0.88. The number of features in the descriptor in this case was 31-33 features in most of the cases which is significantly lower than in the case of the traditional approach.

Our future work is directed towards dealing with converters, i.e., patients who converted the diagnosis during the period of examination.

Acknowledgement. Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012).

References

1. Alzheimer's Association, 2022. 2022 Alzheimer's disease facts and figures. [https://www.alz.org/media/documents/alzheimers-facts-and-figures.pdf] Last accessed: 30.06.2022.
2. Porsteinsson, A.P., Isaacson, R.S., Knox, S., Sabbagh, M.N. and Rubino, I. Diagnosis of early alzheimer's disease: Clinical practice in 2021. The Journal of Prevention of Alzheimer's Disease, 8(3), 371-386 (2021).
3. Winblad, B., Amouyel, P., Andrieu, S., Ballard, C., Brayne, C., Brodaty, H., Cedazo-Minguez, A., Dubois, B., Edvardsson, D., Feldman, H. and Fratiglioni, Defeating Alzheimer's disease and other dementias: a priority for European science and society. The Lancet Neurology, 15(5), 455-532 (2016).
4. Beason-Held, L.L., Goh, J.O., An, Y., Kraut, M.A., O'Brien, R.J., Ferrucci, L. and Resnick, S.M. Changes in brain function occur years before the onset of cognitive impairment. Journal of Neuroscience, 33(46), 18008-18014 (2013).

5. Sperling, Reisa A., Paul S. Aisen, Laurel A. Beckett, David A. Bennett, Suzanne Craft, Anne M. Fagan, Takeshi Iwatsubo et al. Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's & dementia 7, no. 7(3), 280-292 (2011).
6. Wilson, R.S., Leurgans, S.E., Boyle, P.A. and Bennett, D.A. Cognitive decline in prodromal Alzheimer disease and mild cognitive impairment. Archives of neurology, 68(3), 351-356 (2011).
7. Agarwal, M. and Mostafa, J. Content-based image retrieval for Alzheimer's disease detection. In Content-Based Multimedia Indexing (CBMI), 2011 9th International Workshop on. 13-18. IEEE. (2011)
8. Cai, W., Liu, S., Wen, L., Eberl, S., Fulham, M.J. and Feng, D. 3D neurological image retrieval with localized pathology-centric CMRGlc patterns. In Image Processing (ICIP), 2010 17th IEEE International Conference on. 3201-3204. IEEE. (2010)
9. Mizotin, M., Benois-Pineau, J., Allard, M. and Catheline, G. September. Feature-based brain MRI retrieval for Alzheimer disease diagnosis. In Image Processing (ICIP), 2012 19th IEEE International Conference on. 1241-1244. IEEE (2012)
10. Liu, X., Chen, K., Wu, T., Weidman, D., Lure, F. and Li, J. Use of multimodality imaging and artificial intelligence for diagnosis and prognosis of early stages of Alzheimer's disease. Translational Research, 194, 56-67 (2018).
11. Trojacanec, K., Kitanovski, I., Dimitrovski, I. and Loshkovska, S. October. Medical image retrieval for Alzheimer's disease using data from multiple time points. In International Conference on ICT Innovations, pp. 215-224. Springer, Cham (2015).
12. Trojachanec, K., Kitanovski, I., Dimitrovski, I. and Loshkovska, S. Longitudinal brain MRI retrieval for Alzheimer's disease using different temporal information. IEEE Access, 6, 9703-9712 (2017).
13. Trojacanec, K., Kalajdziski, S., Kitanovski, I., Dimitrovski, I., Loshkovska, S. and Alzheimer's Disease Neuroimaging Initiative. Image Retrieval for Alzheimer's Disease Based on Brain Atrophy Pattern. In International Conference on ICT Innovations, pp. 165-175. Springer, Cham (2017).
14. Leon, R.A.M., Puentes, J., González, F.A. and Hoyos, M.H. Empirical evaluation of general-purpose image features for pathology-oriented image retrieval of Alzheimer Disease cases. In CARS 2016: 30th International Congress on Computer Assisted Radiology and Surgery In: International Journal of Computer Assisted Radiology and Surgery (Vol. 11, pp. S39-S40). Springer (2016).
15. Chethan, K. and Bhandarkar, R. Hybrid Feature Extraction Technique on Brain MRI Images for Content-Based Image Retrieval of Alzheimer's Disease. In Advances in Communication, Signal Processing, VLSI, and Embedded Systems, 127-141. Springer, Singapore. (2020)
16. Vinutha, N., Sandeep, S., Kulkarni, A.N., Shenoy, P.D. and Venugopal, K.R. A Texture based Image Retrieval for Different Stages of Alzheimer's Disease. In 2019 IEEE 5th International Conference for Convergence in Technology (I2CT) (pp. 1-5). IEEE (2019).
17. Sagayam, K.M., Bruntha, P.M., Sridevi, M., Sam, M.R., Kose, U. and Deperlioglu, O., 2021. A cognitive perception on content-based image retrieval using an advanced soft computing paradigm. In Advanced Machine Vision Paradigms for Medical Image Analysis, 189-211, Academic Press (2021).
18. Kruthika, K.R., Maheshappa, H.D. and Alzheimer's Disease Neuroimaging Initiative Multistage classifier-based approach for Alzheimer's disease prediction and retrieval. Informatics in Medicine Unlocked, 14,34-42 (2019)

19. Kruthika, K.R., Maheshappa, H.D. and Alzheimer's Disease Neuroimaging Initiative. CBIR system using Capsule Networks and 3D CNN for Alzheimer's disease diagnosis. Informatics in Medicine Unlocked, 14, 59-68 (2019).
20. Veitch, D.P., Weiner, M.W., Aisen, P.S., Beckett, L.A., Cairns, N.J., Green, R.C., Harvey, D., Jack Jr, C.R., Jagust, W., Morris, J.C. and Petersen, R.C. Understanding disease progression and improving Alzheimer's disease clinical trials: Recent highlights from the Alzheimer's Disease Neuroimaging Initiative. Alzheimer's & Dementia, 15(1), 106-152 (2019).
21. Imtiaz, B., Tolppanen, A.M., Kivipelto, M. Soininen, H. Future directions in Alzhei-mer's disease from risk factors to prevention. Biochemical pharmacology, 88(4), 661-670 (2014).
22. Chatterjee, P., Pedrini, S., Ashton, N.J., Tegg, M., Goozee, K., Singh, A.K., Karikari, T.K., Simrén, J., Vanmechelen, E., Armstrong, N.J. and Hone, E. Diagnostic and prognostic plasma biomarkers for preclinical Alzheimer's disease. Alzheimer's & Dementia, 18(6), 1141-1154 (2022).
23. Simrén, J., Leuzy, A., Karikari, T.K., Hye, A., Benedet, A.L., Lantero-Rodriguez, J., Mattsson-Carlgren, N., Schöll, M., Mecocci, P., Vellas, B. and Tsolaki, M. The diagnostic and prognostic capabilities of plasma biomarkers in Alzheimer's disease. Alzheimer's & Dementia, 17(7), 1145-1156 (2021).
24. Nanni, L., Interlenghi, M., Brahnam, S., Salvatore, C., Papa, S., Nemni, R., Castiglioni, I. and Alzheimer's Disease Neuroimaging Initiative. Comparison of transfer learning and conventional machine learning applied to structural brain MRI for the early diagnosis and prognosis of Alzheimer's disease. Frontiers in neurology, 11, 576194 (2020).
25. Wang, Y., Xu, C., Park, J.H., Lee, S., Stern, Y., Yoo, S., Kim, J.H., Kim, H.S., Cha, J. and Alzheimer's Disease Neuroimaging Initiative. Diagnosis and prognosis of Alzheimer's disease using brain morphometry and white matter connectomes. NeuroImage: Clinical, 23, 101859 (2019).
26. Salvatore, C. and Castiglioni, I. A wrapped multi-label classifier for the automatic diagnosis and prognosis of Alzheimer's disease. Journal of neuroscience methods, 302, 58-65 (2018).
27. Soininen, H., Solomon, A., Visser, P.J., Hendrix, S.B., Blennow, K., Kivipelto, M., Hartmann, T. and LipiDiDiet Clinical Study Group. 36-month LipiDiDiet multinutrient clinical trial in prodromal Alzheimer's disease. Alzheimer's & Dementia, 17(1), 29-40 (2021).
28. Meyer, P.F., Tremblay-Mercier, J., Leoutsakos, J., Madjar, C., Lafaille-Maignan, M.É., Savard, M., Rosa-Neto, P., Poirier, J., Etienne, P., Breitner, J. and PREVENT-AD research group. INTREPAD: A randomized trial of naproxen to slow progress of presymptomatic Alzheimer disease. Neurology, 92(18), e2070-e2080 (2019).
29. Rebsamen, M., Suter, Y., Wiest, R., Reyes, M. and Rummel, C. Brain morphometry estimation: From hours to seconds using deep learning. Frontiers in neurology, 11, 244 (2020).
30. Alzheimer's Disease Neuroimaging Initiative: ADNI, 2017. [https://adni.loni.usc.edu/] Last accessed: 30.06.2022.
31. FreeSurfer. [https://surfer.nmr.mgh.harvard.edu/]. Last accessed: 17.06.2022.
32. Han, X., Jovicich, J., Salat, D., van der Kouwe, A., Quinn, B., Czanner, S., Busa, E., Pacheco, J., Albert, M., Killiany, R. and Maguire, P. Reliability of MRI-derived measurements of human cerebral cortical thickness: the effects of field strength, scanner upgrade and manufactur-er. Neuroimage, 32(1), 180-194 (2006).
33. Reuter, M., Schmansky, N.J., Rosas, H.D. and Fischl, B. Within-subject template estimation for unbiased longitudinal image analysis. Neuroimage, 61(4), 1402-1418 (2012).
34. Zhao, W., Luo, Y., Zhao, L., Mok, V., Su, L., Yin, C., Sun, Y., Lu, J., Shi, L. and Han, Y. Automated brain MRI volumetry differentiates early stages of Alzheimer's disease from normal aging. Journal of Geriatric Psychiatry and Neurology, 32(6), 354-364 (2019).

35. Schwarz, C.G., Gunter, J.L., Wiste, H.J., Przybelski, S.A., Weigand, S.D., Ward, C.P., Senjem, M.L., Vemuri, P., Murray, M.E., Dickson, D.W. and Parisi, J.E.. A large-scale comparison of cortical thickness and volume methods for measuring Alzheimer's disease severity. NeuroImage: Clinical, 11, 802-812 (2016).
36. Voevodskaya, O., Simmons, A., Nordenskjöld, R., Kullberg, J., Ahlström, H., Lind, L., Wahlund, L.O., Larsson, E.M., Westman, E. and Alzheimer's Disease Neuroimaging Initiative, 2014. The effects of intracranial volume adjustment approaches on multiple regional MRI volumes in healthy aging and Alzheimer's disease. Frontiers in aging neuroscience, 6, 264 (2014).
37. Trojacanec, K., Kitanovski, I., Dimitrovski, I. and Loshkovska, S. The Influence of Quality Control on the Image Retrieval: Application to Longitudinal Images for Alzheimer's Disease. In Proceedings of the 14th International Conference for Informatics and Information Technology, pp. 37-42 (2017).
38. Hall, M.A., Holmes, G. Benchmarking attribute selection techniques for discrete class data mining. IEEE Transactions on Knowledge and Data engineering, 15(6), 1437-1447 (2003).
39. Toledo, J.B., Da, X., Bhatt, P., Wolk, D.A., Arnold, S.E., Shaw, L.M., Trojanowski, J.Q. and Davatzikos, C. Relationship between plasma analytes and SPARE-AD defined brain atrophy patterns in ADNI. PloS one, 8(2), e55531 (2013).
40. Davatzikos, C., Xu, F., An, Y., Fan, Y. and Resnick, S.M. Longitudinal progression of Alzheimer's-like patterns of atrophy in normal older adults: the SPARE-AD index. Brain, 132(8), 2026-2035 (2009).
41. Habes, M., Erus, G., Toledo, J.B., Zhang, T., Bryan, N., Launer, L.J., Rosseel, Y., Janowitz, D., Doshi, J., Van der Auwera, S. and Von Sarnowski, B. White matter hyperintensities and imaging patterns of brain ageing in the general population. Brain, 139(4), 1164-1179 (2016).