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BRAIN ATROPHY PROGRESS DETECTION IN MR IMAGES

Alzheimer's, Parkinson's and other dementive diseases currently pose an important social problem. High brain atrophy level is one of the most important symptoms of these disorders, but it also may result from normal ageing processes. The purpose of the presented research is to design methods that support detection of dementia symptoms in radiological images. The proposed framework consists of image registration procedure, brain extraction and tissue segmentation and the exact analysis of image series (fractal and volumetric properties).

1. INTRODUCTION

Medical imaging techniques are nowadays the main diagnostic tool for many diseases, like various pathologies, related to dementia (like Alzheimer's or Parkinson's disease) [16]. They pose an important social issue nowadays and are expected to become a more and more serious problem in the next years. A reliable diagnose of such illnesses cannot be based on image data only, however it provides valuable information on their symptoms.

Imaging techniques like CT (Computed Tomography) or MRI (Magnetic Resonance Imaging) are available even in many local hospitals. Combined Computed Tomography/Positron Emission Tomography examination is particularly interesting. However, its availability in Poland and other Eastern Europe countries is not satisfactory.

Growing amounts of image data need to be analysed by experienced radiologists, but their number is not growing up adequately. Besides, a part of useful information remains hidden inside image data and unavailable for visual inspection, unless it is uncovered with special algorithms. In case of progressive diseases, including those related to dementia, analysis of integrated images of the same patient acquired in different time (and sometimes also different place) may provide valuable content. Such profound analysis is not often performed because of time constraints and various technical problems. Because of those factors, it is desirable to design software that helps radiologists to work more efficiently.

High brain atrophy level is among the most important symptoms of dementive disorders, but it also results from normal ageing processes. That is why it is important to estimate it, its kind, and especially its time progress objectively. The authors' aim is to project, implement and test a framework that supports and automatizes detection of dementia symptoms in image series. The proposed framework consists of the following main modules:

- image registration procedure (maximization of mutual information),
- brain extraction and tissue segmentation,
- analysis of the integrated images (fractal and volumetric properties).

Generally, the implemented algorithms are known. The main problem is to select algorithms that are able to work automatically and successfully also with not always perfect images acquired during routine medical procedures. It is necessary to tune various parameters and to introduce some modifications to the algorithms.

2. MATERIALS AND METHODS

T1-weighted MR images of human head were the main point of interest (though, other MR and CT images were also used). The images used for the tests come from two sources. The first one is ELUDE

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collection (Efficient Longitudinal Upload of Depression in the Elderly) from the mBIRN Data Repository (mBDR, Project Accession Number 2007-BDR-6UHZ1) [8]. An MR scan of each subject was obtained every 2 years for up to 8 years. Multiple datasets of 30 randomly selected patients were used for the experiments. The second source was the Hospital of Ministry of Interior and Administration in Lublin (Poland). 19 subjects that were examined more than once during the last a few years were acquired from the hospital PACS (Picture Archiving and Communication System). Besides, numerous images of both normal and pathological subjects from single examinations were analysed.

In order to perform a comparative analysis of two or more 3-dimensional image datasets, it is necessary to register them. Images are registered by maximization of mutual information [9],[14] (algorithm variation by Mattes et. al [7]), using affine transformation. Because of nature of the optimization criterion (numerous local extrema) and the process (regular step gradient descent [9]), correct localization of the global extreme is never guaranteed. In order to maximize likelihood of finding the exact registration parameters and to accelerate the whole process, a number of heuristic techniques has been implemented (multi-resolution approach, multi-start, eyes' localization and preregistration [5] in order to find a reasonable starting point). The registration framework originally projected, implemented and thoroughly tested by the authors [5] has been lately redesigned and rewritten. Its general structure remains unchanged, but nowadays it is based on the Insight Toolkit (ITK) library [9].

After the registration process, it is advisable to remove non-brain tissue from the images. Presence of non-brain tissue helps to achieve correct image registration but could be disruptive for the successive analysis steps. Brain extraction is relatively easy in CT images. In case of MR images this step is not trivial. Numerous algorithms have been developed to perform it automatically. A survey of the most popular ones can be found in [1]. In the presented system, BET (Brain Extraction Tool) [11] has been utilised. It is accurate enough and fast (processing time is usually shorter than 1 min. on a standard PC for a typical head MRI dataset).

Because of fractal properties of many natural objects, fractal analysis is a reasonable choice in applications where natural objects are dealt with, including medical image processing and analysis. It is known that brain cortex images are self-similar in a way referred to as being a fractal, with a fractal dimension D = 2.60 [6] (the results vary and depend on calculation method). It is also known that value of fractal dimension corresponds to brain atrophy level [2].

Different variations of box-counting methods are the most popular for fractal dimension estimation. It is relatively easy to calculate for many reasonably regular sets. In the simplest variant, a binary image is placed on a grid of square blocks. The number of blocks N_r occupied by a part of the image is then calculated. The procedure is repeated for various grid sizes (r). It is expected that increasing the resolution of the grid, N_r should increase, too. The slope of linear regression of the $\log(N_r)$ versus $\log(1/r)$ is the fractal dimension estimation.

This approach has a relevant drawback. Images have to be binary, but MR image segmentation is not a trivial task. This process and selection of tissue to be segmented (white matter, grey matter, etc.) has a significant impact on the fractal dimension calculation result. The authors suggest using a variation of box-counting method, proposed by Sarkar and Chaudhuri (differential box-counting) [10]. It operates directly on grey scale images and does not depend on any special preprocessing scheme. An image of size $M \times M$ is scaled down to a size $s \times s$. Then $r = s/M$. The 2D image is treated as a 3D image, where (x, y) denotes 2D position and z denotes a grey level. A column of boxes $s \times s \times s'$ is obtained. If the total number of grey levels is G, then $G/s' = M/s$. If the minimum and maximum grey levels of the image in the grid (i, j) fall in the box k and l respectively, then [10]

$$n_r = l - k + 1 \tag{1}$$

is a contribution of the grid (i,j) to N_r:

$$N_r = \sum_{i,j} n_r(i,j). \tag{2}$$

N_r is calculated for various values of r as in simple box-counting. It has been confirmed that this measure can be used to classify normal and abnormal (atrophic) brain structures [3], [4].

SIENA [12], [13] is the next analysis tool (part of FSL library for MR image analysis [13][15]). It is able to perform two-time-point ("longitudinal") analysis of brain change (volumetric loss of brain tissue). In particular, it can be used for the quantitative estimation of atrophy level shift. Having performed tissue-type segmentation [17], perpendicular tissue edge displacement (between the two timepoints) is estimated at these edge points. Finally, the mean edge displacement is converted into a global estimate of percentage brain volume change between the two timepoints. SIENA (sienax tool) can be also used for total brain tissue volume estimation, from a single dataset.

3. RESULTS

The whole image processing and analysis process (image registration, brain extraction, segmentation, exact analytical procedures) is quite time-consuming. However, fractal dimension alone can be calculated very fast (less than 0.5s per single 512×512 MRI slice) using differential box-counting (described in the previous section).

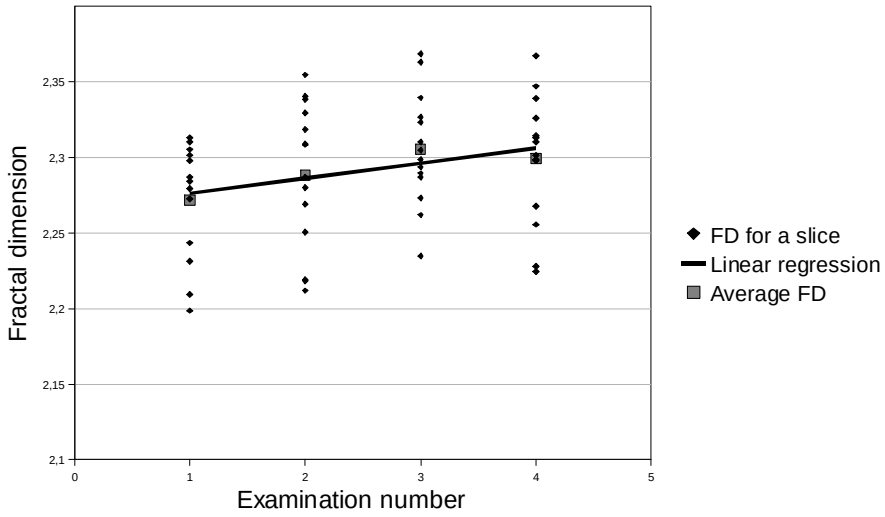

Fig. 1. Fractal dimension growth during brain atrophy progress (quadruple MR examination of the same, single patient with two-year-long intervals; 14 centrally located axial slices in the region of interest).

Fig. 1 presents results of its calculation for quadruple MR examination of the same patient (with two-year-long intervals), on 14 centrally located axial slices. The head images were not preprocessed at all. The slope of linear regression (the thick line) of fractal dimension versus time corresponds to significant (according to a radiologist's opinion) atrophy progress. Such calculations were performed for all available datasets.

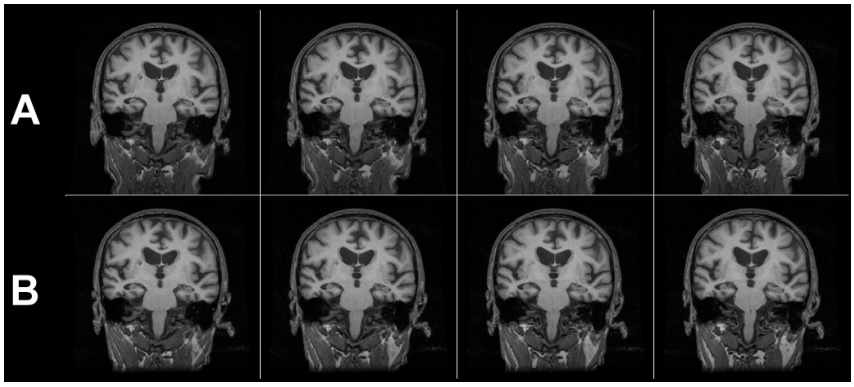

Fig. 2. MRI – MRI registration result (two examinations of the same patient).

All images from the ELUDE collection were registered successfully (regardless of the software used: either ITK-based or FSL-based program). Only 2 image pairs from Lublin hospital were problematic, due to presence of artefacts or extremely untypical (due to medical constraints) patient location inside MRI scanner. Apart from intra-modal registration (MRI T1, example presented in Fig. 2), CT-MRI registration was also executed when CT scans were available (Fig. 3).

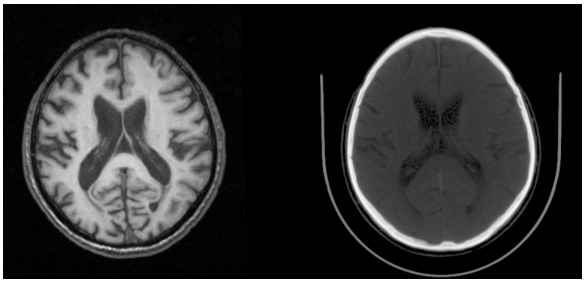

Fig. 3. MRI – CT registration result.

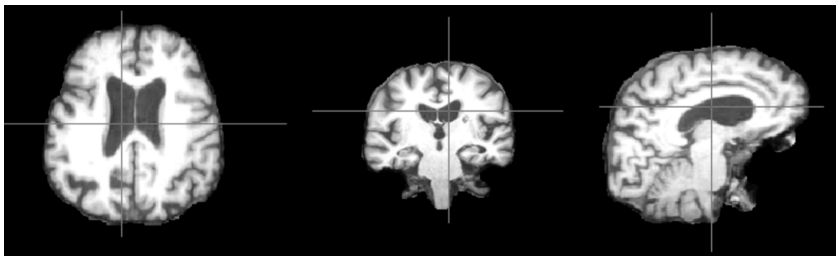

Fig. 4. Exemplary brain extraction result.

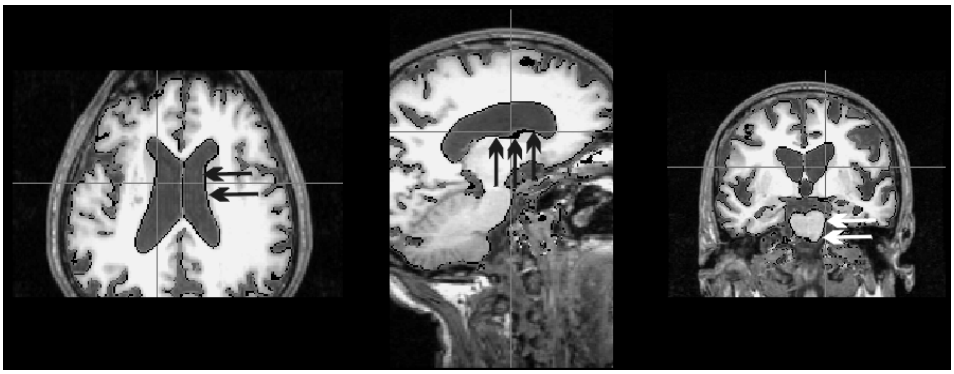

Fig. 5. Atrophic areas detected with SIENA (marked black), interesting places marked with arrows.

The brain extraction procedure was performed using BET (Brain Extraction Tool) [11]. Generally, it worked automatically (Fig. 4). In sparse cases slight manual modifications of fractional intensity threshold were necessary.

Then percentage brain volume change (PBVC) between corresponding MR T1-weighted images was calculated and places with detected atrophy were marked (Fig. 5, in this particular case estimated PBVC was about –1.4%), using SIENA package. The full processing pipeline for one image pair typically requires one hour or slightly more, using a standard PC.

4. DISCUSSION

For a doctor, it is advisable to obtain at least approximate image analysis results within a short time. Unfortunately, the complete analysis process is time-consuming. The proposed method of fractal dimension calculation seems to be a good candidate for the first analysis step. It is fast, fully automated and requires no preprocessing. It could be also used for screening assays, with large amounts of data.

Brain images can be roughly classified regarding atrophy level [3], [4]. Interestingly, it has been observed that presence of non-brain tissue does not significantly disrupt the fractal dimension calculation, so the brain extraction procedure could be skipped. Unfortunately, if two examinations of the same patient are not very time-distant and there are only subtle differences between them, this method is not sensitive enough. Then it is necessary to apply a more time-consuming, full processing scheme.

Image registration is an especially valuable, but still too seldom used tool for a doctor. Currently available algorithms (usually using various variants of maximization of mutual information and heuristics) make it possible to perform intra- or intermodal registration of standard medical datasets within a reasonable time (5 – 15 minutes). Only a small part of images can be problematic, when using a carefully tuned registration procedure [5]. Usually the problem can be solved by setting a reasonable starting point.

The Brain Extraction Tool in most cases worked correctly, however sometimes it was necessary to alter default values of the parameters. It is not useful as a standalone tool for a doctor, but is a necessary element of a head image processing system.

Atrophic changes detection performed with SIENA was especially appreciated by the radiologist. In case of the patient (with Alzheimer disease diagnosed) whose head image is presented in Fig. 2 and 5, atrophy progress (the time between two MRI examinations was only 3 months) was completely invisible when image pair was inspected visually only by an expert (even after a proper registration process, as shown in Fig. 2). SIENA not only estimates the two-timepoint percentage brain volume change, but also provides information on specific brain areas that undergo atrophy.

5. CONSLUSIONS

A vital part of information provided by medical images is hidden (and unavailable for a doctor inspecting images visually only) but can be extracted with appropriate algorithms. The presented algorithms for image registration (a necessary step for comparative analysis), brain extraction (required for further brain image analysis) and brain volume change estimation (SIENA) are mature enough to be used in clinical conditions. It is only necessary to combine them into a consistent processing system (with a suitable graphical user interface), compatible with hospital PACS. It is still advisable to improve performance, however availability of high performance computers is still growing. Fractal-dimension-based classification of radiological images is promising but still experimental. The authors are trying to construct a robust atrophy measure composed of both fractal and volumetric properties. It is also planned to use some external (not included in images) information for the classification.

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