An atlas based approach to segment the hippocampus from MRI of human head scans for the diagnosis of Alzheimer's disease

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***Abstract*-The Hippocampus in a human brain is the focus of neuro imaging research for the recent years due to its important role in memory processes and the significance in neurological and psychiatric disorders. Hence the segmentation of hippocampus from MRI is inevitable to identify the diagnosis and the disease progression. But, the extraction of hippocampus is a tedious task since it is smaller in size and has a vague boundary. To facilitate the segmentation, in this paper we propose a method to segment Hc from MRI of human head scans. This segmentation method constitutes two phases. In the first phase, the approximate location of Hc in the input image is identified by atlas based approach. From that location, an enclosed rectangle called region of interest (ROI) is derived. In the second phase the ROI is processed by applying conservative smoothing and top-hat filter to preserve the edges of hippocampus. The filtered image is then binarized using Riddler Calvard method to differentiate the hippocampus from other irrelevant structures. Finally, hippocampus alone is segmented by Connected Component Analysis (CCA).**

Keywords-hippocampus, segmentation, conservative smoothing, connected component analysis

I. INTRODUCTION

The Hippocampus (Hc) is a part of limbic system situated in the Medial Temporal Lobe (MTL) of a human brain. The Hc plays a vital role in spatial memory, integrating external with internal signals to form a spatial and temporal orientation of oneself in the environment [1]. The dysfunction of Hc leads to various neurodegenerative diseases such as Alzheimer's Disease (AD), post-traumatic stress disorder, major depression and schizophrenia [2].

Structural neuro imaging provided potential way in predicting the onset of AD in mild cognitive impairment (MCI) subjects [3] [4]. In the beginning of 1980's, the Magnetic Resonance Imaging (MRI) technique provided a tool for examining the alterations in brain anatomy [5]. It is the non-invasive and non-ionizing imaging modality to image the human anatomy. Nowadays, MRI is used extensively in identifying anatomical origins of Alzheimer's disease [6].

The segmentation of Hc by manual is considered to be a gold standard for volumetric assessment [7]. But, the manual segmentation causes low inter, intra-rater variability and time consumption (30-60 min per Hc) [8]. To address these drawbacks, automatic segmentation methods have been developed. However, developing automatic methods to segment Hc is still a challenging task due to its anatomically varying smaller size ($\approx$ 35 x 15 x 7 mm3) and the lack of clearly defined edges [9]. Some of the automatic and semi-automatic methods to segment hippocampus from MRI of human head scans are described below.

The atlas based method is a commonly used segmentation technique. J. M. P. Lotjonen et.al, [10] presented a segmentation method in which the atlas is randomly selected from a database. The similarity of intensity is then measured between atlas image and the target image. R. A. Heckemann et.al, [11] and Rohlfing et. al, [12] performed multiple registrations from all the atlases to the target and fusing the results to generate the target segmentation. Chupin et.al, [13] developed a hybrid segmentation method that uses probabilistic atlas built from 16 young controls and registered using Statistic Parametric Mapping (SPM). Pablo Mesejo et.al, [14] describe the parameters of an empirically-derived deformable model of the hippocampus which maximize its overlap with the corresponding anatomical structure in histological brain images. Baillard et.al, [15] describe a level set formalism in which a closed 3D surface propagates towards the desired boundaries through the iterative evolution of a 4D implicit function.

The segmentation method is proposed by Shiyan Hu et. al, [16] which combines level set and active appearance models. An approach to segment hippocampus is presented by Courtney A. Bishop et. al, [17] using the Sethian Fast Marching technique to grow a hippocampal ROI from an automatically-defined seed point. A method that uses manually labelled image data to provide anatomical training information is proposed by Brian Patenaude et. al, [18] uses Active Shape and appearance models. An automatic method is proposed by Juan Zhou et. al, [19] in which a fuzzy templates are created based on intensity, spatial location, and relative spatial relationship among structures from a set of training images by defining the fuzzy membership functions.

In this paper, we propose a technique to segment hippocampal from MRI of human head scans using atlas based technique. The remaining part of the paper is organized as follows. In section II, the proposed method is explained. The materials used are given in section III. In section IV, results and discussions are given. In section V, the conclusion is given.

II. PROPOSED METHOD

In the proposed method, an atlas image is generated using ITK-SNAP [20]. By using the atlas image, the region of interest (ROI) for the given input image is derived. The conservative smoothing and morphological top-hat filter are applied to the ROI to distinguish the boundary of Hc. The filtered image is then binarized using Riddler Calvard thresholding technique. Finally, the hippocampus alone is segmented using CCA. The flow chart of the proposed method is shown in Figure. 1.

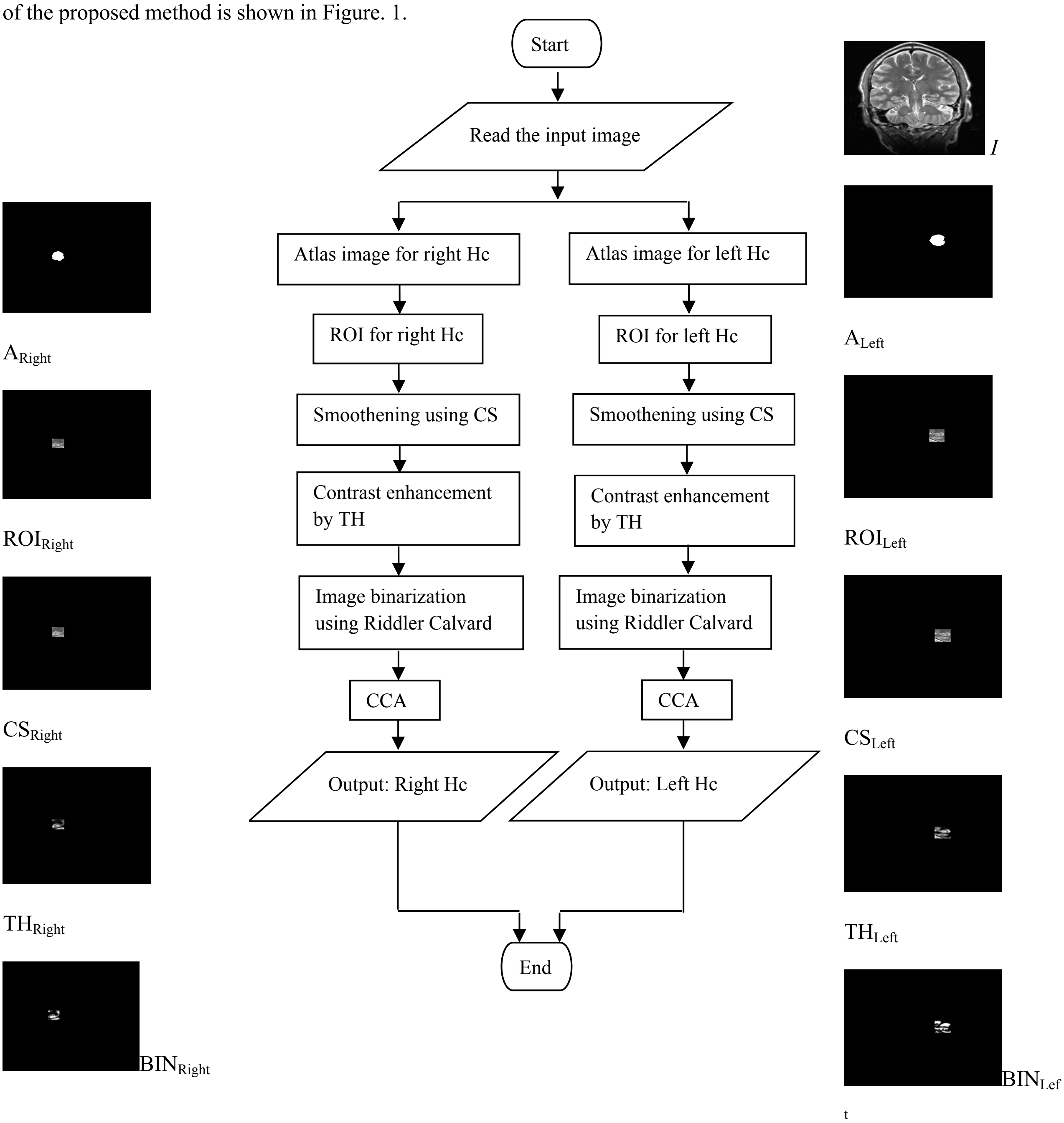


Figure 1. Flow chart of the proposed method

B. Phase 1: Generating an atlas image for Hc

In preprocessing, accurate location of Hc is found. It will help to segment Hc easier. To achieve this, we take n number of segmented Hc portions using ITK-SNAP and generate an atlas image A by taking the union of all the Hc as:

$$A = \bigcup_{i=0}^{n-1} Hc_i \tag{1}$$

where, Hc_i is the ith hippocampal image segmented by ITK-SNAP. From eqn. 1, the atlas image for right Hc (A_{Right}) and left Hc (A_{Left}) are generated. The block diagram for obtaining the A_{Right} is shown in Figure. 2.

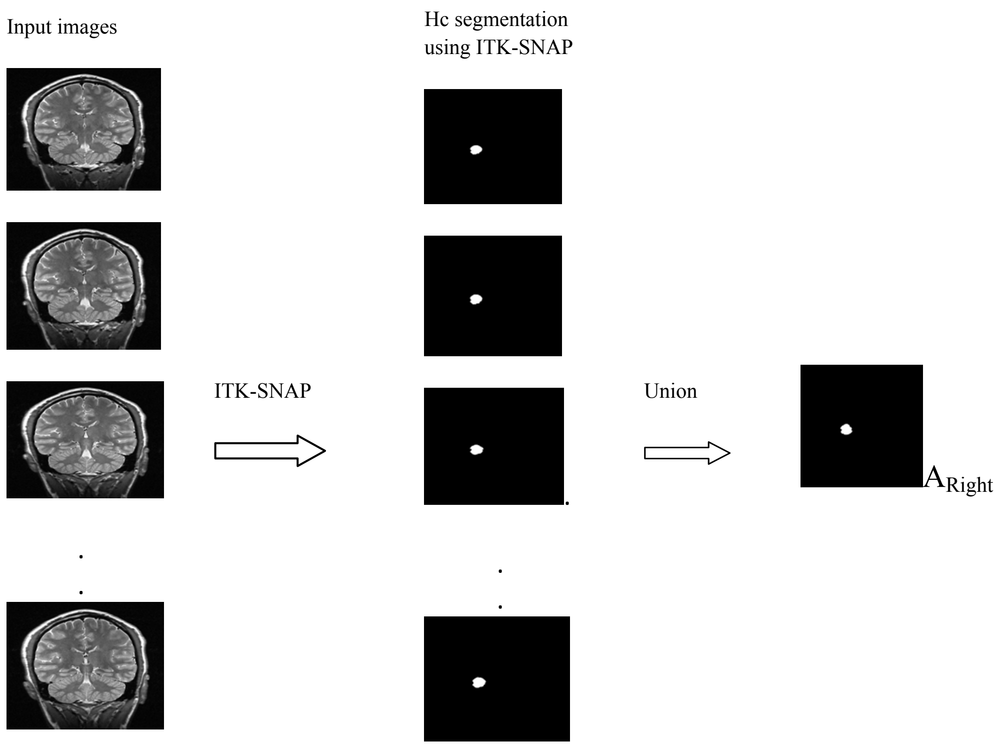
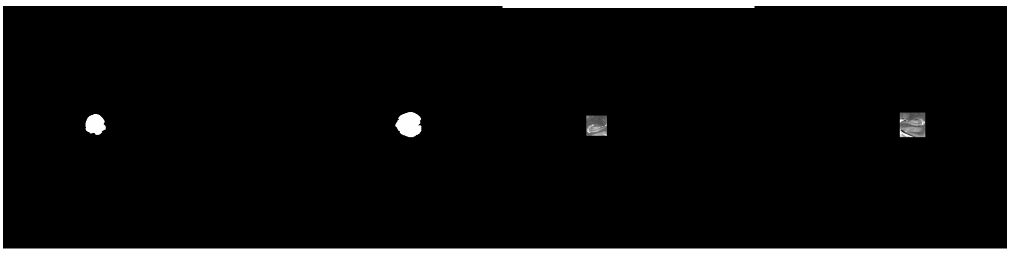


Figure 2. Block diagram of generating an atlas image for right Hc

C. Obtaining ROI from the atlas image

The computation is made from top-left to bottom-right of an atlas images. At some region, the occurrence of non-zero pixel begins at one point and ends at another point both in horizontal and vertical directions. From these points, an enclosed rectangle is formed from A_{Right} and A_{Left}. They are shown in Figure. 3. Hereafter, these enclosed rectangles are termed as ROI_{Right} and ROI_{Left}. Now, the total number of pixels to be processed is reduced.

The boundary of Hc is not clear in both the ROIs. To get rid of the false boundaries and to enhance the contrast, Conservative Smoothing (CS) and top-hat filtering are applied on two ROIs. The refined ROIs are then binarized using Riddler Calvard thresholding technique.



(a) (b) (c) (d)

Figure 3. ROI (a) A_{Right} (b) A_{Left} (c) ROI_{Right} (d) ROI_{Left}

D. *Conservative smoothing and top-hat filtering*

Conservative smoothing [21] is a simple, fast filtering algorithm that suppresses noise in an image. It is applied to the ROIs to get refined edges. The conservative smoothing (CS) finds the minimum and maximum intensity values in a windowed region (3x3). If the intensity of a central pixel is greater than the maximum value, it is set equal to the maximum value and if the central pixel intensity is less than the minimum value, it is set equal to the minimum value. The output pixel will remain unchanged if the central pixel lies within the intensity range (> minimum < maximum). Figure. 4. shows the process of applying CS. The algorithm of CS is given as:

Step 1: Arrange the elements (excluding center pixel) in the mask in ascending order.

Step 2: Find the maximum (max) and minimum (min) values from the list.

Step 3: Apply smoothing as:

$$
\begin{aligned}
CSRight\,(x,y) &= \max \text{ if } ROI_{Right}\,(x_i) > \max \\
&= \min \text{ if } ROI_{Right}\,(x_i) < \min \\
&= x_i \text{ otherwise.}
\end{aligned}
$$

where, xi is the center pixel in 3x3 mask. The CS is also applied to ROI_{Left} to get $CS_{Left.}$

69	77	90
61	~~95~~	70
75	89	79

95
90

Figure 4. Conservative smoothing process$_t$

After applying conservative smoothing, the new smoothed images called CS_{Right} and CS_{Left} are obtained. Now, the boundary becomes clear and free from false edges. Then the contrast of these smoothed images is enhanced by top-hat filter (TH) to differentiate Hc and non Hc pixels. The top hat filtering process is given as:

$$TH_{Right} = CS_{Right} - (CS_{Right} \circ B) \tag{2}$$

where, CS_{Right} is the smoothed image, $CS_{Right} \circ B$ is a morphological opening of the smoothed image CS_{Right} with 3x3 structuring element B. The TH is also applied to CSLeft. After top hat filtering, we get new images TH_{Right} and TH_{Left}. The Riddler Calvard technique is then applied to both TH_{Right} and TH_{Left} to get a binary image.The Riddler Calvard is an iterative method [22] where the initial threshold T1 is computed as:

$$T_1 = \sum_{i=0}^{n-1} x_i / N \tag{3}$$

where, x_i is the intensity of i^{th} pixel varies from 0 to 255 and N is the total number of pixels in TH_{Right}. By using eqn. (3), the TH_{Right} is separated in to two modes M1 and M2 as:

$$
\begin{aligned}
TH_{Right}\,(x, y) &= M1 \text{ if } x_i >= T1 \\
&= M2 \text{ otherwise}
\end{aligned} \tag{4}
$$

Now, the new threshold T is computed as:

$$T = \left(\left(\sum_{0}^{c_1-1} M_1/C_1\right) + \left(\sum_{0}^{c_2-1} M_2/C_2\right)\right)/2 \tag{5}$$

where, C1 is the number of pixels in M1 and C2 is the number of pixels in M2. The eqn. 4 and eqn. 5 are iteratively computed until T and T1 get closer. The THRight (x, y) is then converted to a binary image g using the optimum threshold T as:

$Bin_{Righ}t\ (x, y) = 1$ if $TH_{Right}\ (x, y) >= T$

$= 0$ otherwise (6)

Similarly, TH_{Left} is also converted to a binary image. From the binarization, two new images called Bin_{Right} and Bin_{Left} are obtained. Finally by using CCA, the right Hc (Hc_{Right}) and left Hc (Hc_{Left}) are segmented from Bin_{Right} and Bin_{Left} respectively. The CCA is computed as follows:

Step 1: The image is scanned from left to right, top to bottom. If the current pixel is 1, then

a. If only one of the upper or left pixels has a label, copy this label to the current pixel.

b. If both have the same label, copy this label.

c. If they have different labels, copy one label and mark these two labels as equivalent.

d. If there are no labeled neighbors, assign it with a new label.

Step 2: The labeled image is scanned and replaces all equivalent labels with a common label.

From the labels computed by CCA, the label for the hippocampus is taken as a mask and is segmented from the original image.

III. MATERIALS USED

To validate the robustness of the proposed method, we have used T2 weighted coronal dataset collected from Neuro imaging Informatics Tools and Resources Clearinghouse (NITRC). This dataset consists of 10 volumes and each volume has 24 images with manual segmented slices. Out of 24 slices, only 18 contain the portion of hippocampus. The resolution of an image is 504 x 512 pixels.

IV. RESULTS AND DISCUSSIONS

To evaluate the proposed method quantitatively, the parameters such as Dice, Sensitivity, Specificity, Precision and Recall are computed using Eqs. (7)-(11). The results are compared with existing single atlas and multi-atlas segmentation methods [23]. The result generated by the proposed method is shown in Figure. 5. The Dice coefficient (D) [24] is given as:

$$D(A,B) = 2\frac{|A \cap B|}{|A|+|B|} \tag{7}$$

where, A is the manual segmented Hc and B is the Hc segmented by the proposed method. The similarity index D gives a value zero if the segmentations are not overlapping and the value one for the perfect overlap.

The sensitivity (S), [25] is the percentage of ROI voxels recognized by an algorithm and specificity (Sp) is the recognition of the pixels as Non-ROI by the proposed method. They are given as:

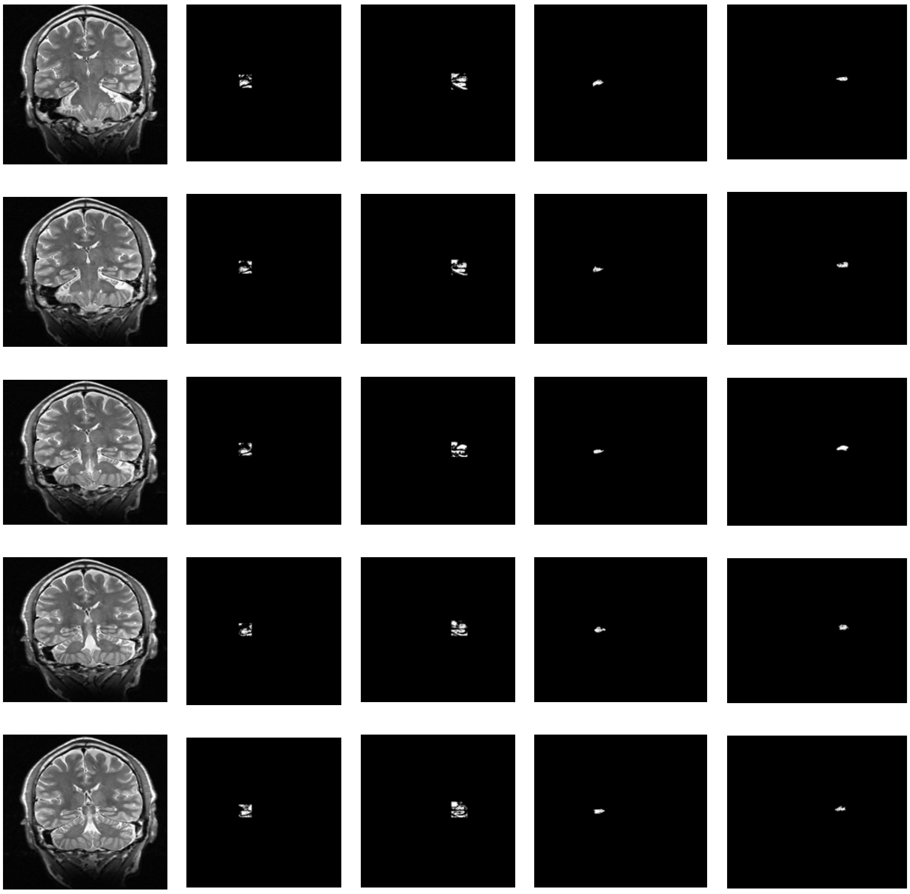
$$S = \frac{TP}{TP+FN} \tag{8}$$

$$Sp = \frac{TN}{TN+FP} \tag{9}$$

where, True Positive (TP) and False Positive (FP) are the total number of pixels correctly and incorrectly classified by the proposed method. True Negative (TN) and False Negative (FN) are defined as the total pixels correctly and incorrectly classified pixels by the proposed method. The Precision (P) and Recall (R) [26] represent the measure of relevance. They are given as:

$$P = \frac{A \cap B}{B} \tag{10}$$

$$R = \frac{A \cap B}{A} \tag{11}$$



(a) (b) (c) (d) (e)

Figure 5. Segmented Hippocampus. (a) Original slices (b) BinRight (c) BinLeft (d) HcRight (e) HcLeft

The average Dice coefficient, precision and recall values computed using the proposed method and other existing methods are given in Table I. The average S, Sp value of the proposed method are 99.94, 93.89 while it is 99.50, 98.89 for knowledge based localization method [27].

TABLE I. THE AVERAGE VALUES OF D, P, R CO-EFFICIENT COMPUTED USING PROPOSED METHOD AND OTHER EXISTING METHODS

Method	No. of Datasets	D	P	R
Proposed	10	0.82	0.77	0.88
Multi-atlas + Expectation Maximization	30	0.81	0.76	0.87
Single atlas	17 images	0.66	0.69	0.76

V. CONCLUSION

We have developed a new method to segment the hippocampus from MRI of human brain. The proposed method uses atlas based approach to define the ROI. The conservative smoothing and trimmed mean filters are used to remove false boundary and to enhance the contrast of ROI. The Riddler Calvard method is applied to convert ROI into a binary one. Finally, the CCA is used to segment the Hc alone from ROI. Experimental results obtained by the proposed scheme show that it performs better than the existing single atlas and multi-atlas segmentation methods. The average value for Sensitivity and Specificity is 99.94 and 93.89. Similarly, the average value for Dice, Precision and Recall is 0.82, 0.77 and 0.88 for the proposed method while it is 0.81, 0.76 and 0.87 for the Multi-atlas based method and 0.66, 0.69 and 0.76 for the single atlas based method. The number of dataset used in the proposed method is 10 whereas it is 30 and 17 images in Multi-atlas and single atlas based methods.

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