https://doi.org/10.2352/ISSN.2470-1173.2017.2.VIPC-404

A fast and accurate segmentation method for medical images

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Abstract

Selecting regions of interest (ROI) of the medical images is an important task in medical image processing. Manual selection of ROIs serves as the main method for single images and it has a high accuracy. However, it will become infeasible to manually segment ROIs on a large number of images. Observing this problem, this paper proposes a fast and accurate segmentation method to obtain ROIs on a batch of medical images. Firstly, we segment the standard brain image S_t which has not been injected with tracer. Secondly, we use a B-Spline elastic registration method to get the inverse-registration parameters. Thirdly, we get the template image T_e with the registration parameters. Finally, we search the target region by template matching. Experimental results show that the proposed method performs well on medical image segmentation.

Introduction

Medical image registration is to search for a (or a series of) spatial transformation such that the corresponding points on two images can lie in the same spatial position and have the same anatomical structure. Registration results should make all the anatomical points or all the points which have diagnostic significance on the two images matched. Because of its high clinical value, medical image registration recently has become one of the hottest topics in the field of medical image research.

For medical images, traditional registration methods comprise four steps [1]. Firstly, they specify the transformation model and calculate the initial parameters. Since many tissues in the human body can be accounted for by a rigid model, a rigid transformation is often employed in medical images. Secondly, they use interpolation to generate the transformed image. Thirdly, they define the type of similarity metric. Mutual information (MI) metric is commonly used to calculate the similarity metric [2]. The last step is to choose an optimizer to optimize the transformation parameters.

In medical field, the brain nerve disease is a complicated problem. Because of unclearness of the flow process of the brain tissue fluid, clinical treatment often makes little success. Therefore, the study of tracer diffusion process in the brain gradually becomes more important [3] [4]. Quantitative analysis of diffusion property of brain extracellular space (ECS) is an important means to study its structure and physiological role [5]. Recently, a new method of using magnetic resonance imaging (MRI) tracer technique was developed to measure ECS diffusion parameters [3]. In this method, dynamic contrast-enhanced MRI time-series data of the rat brain is acquired. To measure the diffusion parameters accurately, it is needed to precisely align the pre-enhanced image with other images captured at different time. However, the time-series data is subject to unavoidable motion during the long imaging process. Therefore, a registration method is needed to align post-contrast brain section with pre-enhanced brain section [4].

Mutual information, which is a function of calculating the statistical correlation of all pixels in two images, is often used in medical image registration. But if we register entire images directly, pixel information of all tissues will be employed in the calculation of mutual information. This may have a large influence on the registration performance. Therefore, a segmentation method is needed to extract the brain tissue mask to alleviate the adverse effects of surrounding deformed tissues. To fully study the diffusion property of ECS, multiple MRI time-series, like multidimensional traffic data [6], for different rats are needed. Motivated by this, this paper presents an automatic segmentation method to segment the brain tissue that facilitates the following analysis of ROIs.

Proposed Method

In this paper, we proposed a method to segment the ROIs automatically. This method only needs to segment the rat brain section of the fixed image manually to get the standard brain image S_t. It also improves the traditional idea of medical image registration and uses the standard image as the moving image to carry out the registration. Firstly, we segment the image of standard brain S_t which has not been injected with tracer at the initial time. Secondly, to acquire the inverse transform module, we use the moving image M which is considered as the fixed image, and the fixed image F which is considered as the moving image will be mapped to the moving image M. Thirdly, we transform the standard brain image S_t with the inverse registration parameters. The result is defined to be the template image T_e. Finally, by using the method of template matching, we can get the rat brain ROI of M automatically. The process of the proposed method is shown in Fig.1. In traditional methods, ITK and VTK which have been developed into an integral technology are often used to register medical images.

In the process of traditional medical registration, a rigid transformation is commonly used to keep the distance and angle unchanged between any two points in the image. It will only generate two kinds of operations on the image: rotation and translation. However, in practice, human factors will make a different location of the rats when scanning different rats. Even when scanning one single rat, it will also generate different location at different scanning times. Since different tissues of rats have different flexibility, only applying a rigid transformation to the image of the entire rat can not register accurately. Therefore, we select B-Spline transformation which is one of the elastic transformation models [7].

In fact, rats used for our study are of the same type and have

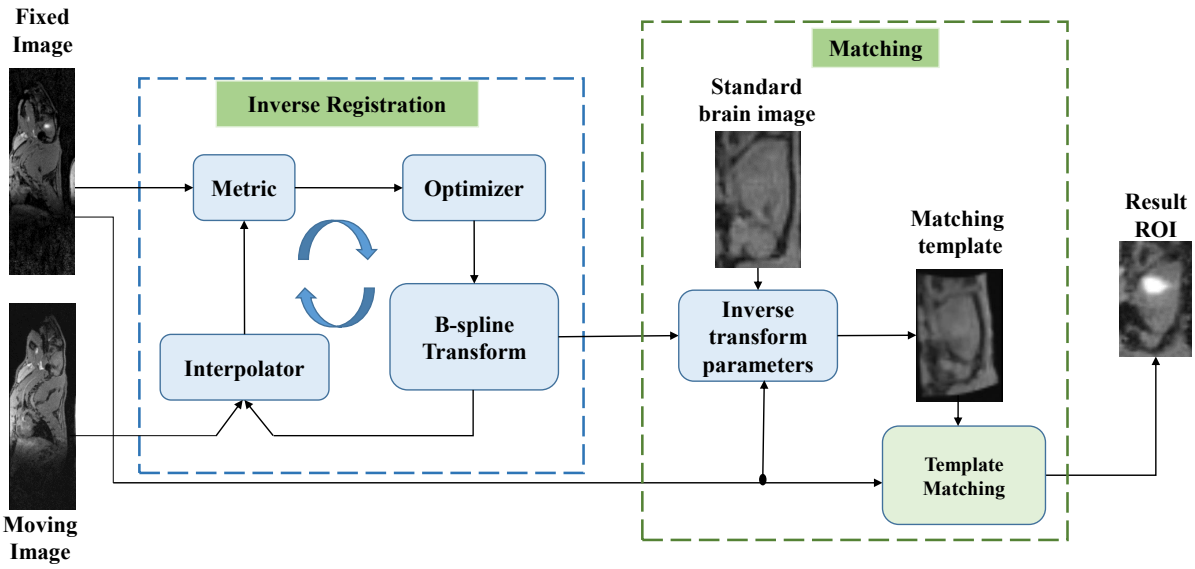
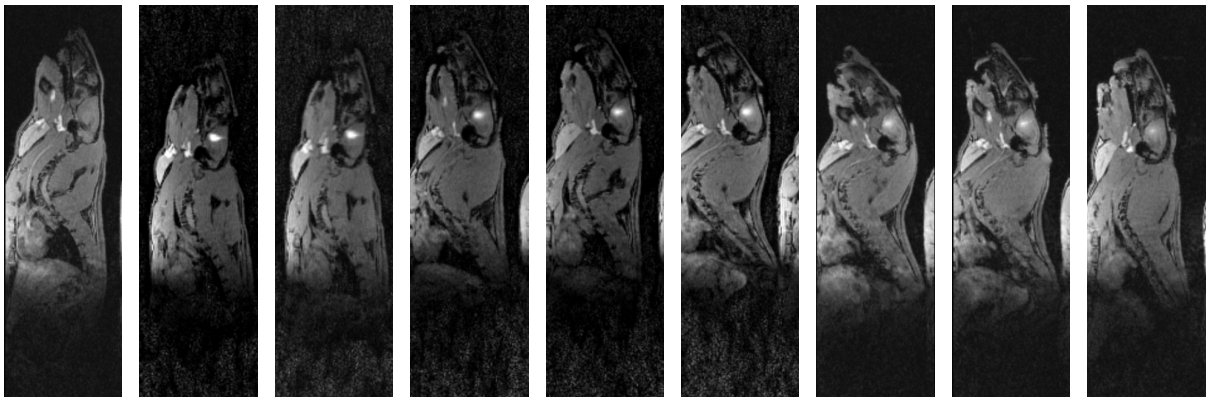


Figure 1. *Flow chart of the proposed method. The proposed method combines the B-Spline registration and template matching to segment region of interest (ROI) automatically. B-Spline transformation is employed in medical images registration, and template matching is applied to search ROIs of moving images with matching template.*



(a) (b) 35*min* (c) 50*min* (d) 80*min* (e) 110*min* (f) 140*min* (g) 170*min* (h) 200*min* (i) 230*min*

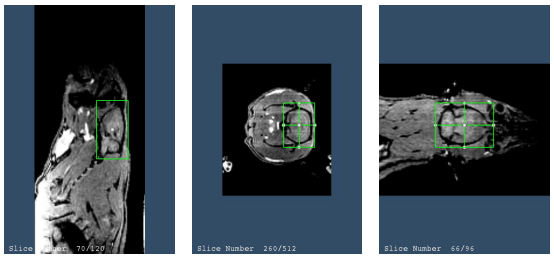
Figure 2. *(a) is the template rat image which has not been injected with tracer. (b)-(i) are the NMR scanned images which have been injected with tracer after 35, 50, 80, 110, 140, 170, 200, 230 minutes. White bright spot in the brain section is the tracer.*

similar weights. Although applying the B-Spline transformation to medical image registration, it would not cause much distortion to brain tissue. B-Spline transformation has a good partial controllability to avoid the global calculations. It also has a better approximation to partial image.

Using B-Spline curve patch as a convolution kernel, we convolve the moving image with the kernel. This type of transformation model is more complex than translation, rotation, and affine transformation. In this paper, a reverse registration module is used. With the registration parameters out of the final iteration as the transformation model, the standard brain S_t can be transformed to get the transformed image, which is defined to be template image T_e. The steps of the proposed algorithm are listed in Algorithm 1.

Acquisition of Standard Brain Images

The image datasets used in this paper are from the Peking University Third Hospital. They contain two sets of scanned images. The first set consists of twelve groups of images including one group of rat images not injected with tracer and eleven groups of rat images injected with tracer in the brain part. The sampling instances are 35, 50, 80, 110, 140, 170, 200, 230, 260, 320, and 380 minutes respectively after rat being injected with tracer. Since the tracer is substantially undetectable after 230 minutes, the latter images will not contribute to our analysis. The scanned images are shown in Fig.2. The second set of images are acquired by using another rat as the experimental subject. Dosage of tracer and scanning interval differ from that in the first one. This set consists of thirteen groups of images including one group of rat images not injected with tracer and twelve groups of rat images injected with tracer in the brain part. The sampling instances are 15, 20, 30, 70, 80, 100, 115, 130, 160, 190, 220, and 280 minutes respectively after rat being injected with tracer. And the tracer is substantially undetectable after 160 minutes. Each group of images is scanned at three directions. There are 120 layers at agittal direction, 512 layers at axial direction, and 96 layers at coronal direction.



(a) (b) (c)

Figure 3. *The image in the green frame is the standard brain image we selected. (a), (b), and (c) are images at the sagittal, axial, and coronal direction respectively.*

By using medical image algorithm libraries - ITK and VTK, we can choose the standard brain part at an initial time manually. This process is shown in Fig.3. By moving the green selection box at three directions, we can segment the desired rat brain part as the standard brain image. The box contains eight vertices with each vertex comprising three-dimensional coordinate information (x,y,z). The coordinates on each dimension represent two boundary values, x_{max}, x_{min}, y_{max}, y_{min}, z_{max}, and z_{min}. Then we can get a starting point, an ending point, length, width, and height of the standard brain part in the entire rat image. Formally, the relationship is given in equation (1).

$$\begin{aligned} Length &= x_{max} - x_{min}, \\ Width &= y_{max} - y_{min}, \\ Height &= z_{max} - z_{min}, \end{aligned} \tag{1}$$

where $(x_{min}, y_{min}, z_{min})$ is the starting point and $(x_{max}, y_{max}, z_{max})$ is the ending point. Then we can acquire the standard brain image from the entire rat image.

Algorithm 1: The steps of proposed segmentation algorithm

Input: Image at an initial time and Images to be segmented.
Output: ROIs of the images which have been injected with tracer.

1 Use the visualization technique to segment the standard brain image S_t of the initial image;
2 To segment all the images automatically, a maximum number N_t of time-series images which have been injected with tracer is needed;
3 **for** $k = 1 : N_t$ **do**
4 Consider a pair of images, one injected with tracer which serves as the fixed image, and the other one at initial time which serves as the moving image;
5 **for** *each pair* **do**
6 Apply B-Spline transformation and mutual information to register images;
7 Apply the reverse registration module to transform S_t to obtain the template image T_e with the size of $M * N$;
8 **for** *each point* (i, j) **do**
9 Compute correlation coefficient $R(i,j) = \frac{\sum_{m=1}^{M}\sum_{n=1}^{N} S^{i,j}(m,n) * T(m.n)}{\sqrt{(\sum_{m=1}^{M}\sum_{n=1}^{N}[S^{i,j}(m,n)]^2)}\sqrt{(\sum_{m=1}^{M}\sum_{n=1}^{N}[T(m,n)]^2)}}$;
10 Search $R(i,j)$ for the point (p,q) achieving the max value;
11 ROIs' starting-point is $(p - M/2, q - N/2)$, ending-point is $(p + M/2, q + N/2)$, size is $M * N$;
12 Save the ROIs of the k_{th} image injected with tracer;

Registration of Medical Images

The registration framework consists of four parts: transforming images, conducting interpolation, computing metric, and optimization. In this paper, we modify the traditional idea of medical image registration and apply a reverse registration.

Transforming images is the most important module in medical image registration. With the transformation parameters, we can map each point of the moving image to the fixed image, which then bring the moving image and the fixed image into alignment. The transformation module includes rigid transformation, B-Spline, thin-plate spline, and so on. This paper uses the B-Spline transformation.

A B-Spline curve patch $f(x,y)$ [8] is defined as:

$$f(x,y) = \sum_{n=0}^{n+1} \sum_{m=1}^{m+1} b_{i,j} \beta_{i,m}^{n}(x) \beta_{j,n}^{n}(y), \tag{2}$$

where β is the n_{th} B-Spline function, and $b_{i,j}$ is a control grid which is defined to be a B-feature grid, consisting of connection points.

Since coordinates of the transformed image may not lie exactly on integer grid points, we need to use the interpolation to compute the pixel values at non-integer points after the moving image is transformed. Interpolation methods mainly include nearest-neighbor interpolation, linear interpolation, PV interpolation, and so on. In this paper, we use B-Spline interpolation function which is expressed as [9]:

$$f(X) = \sum_{i=0}^{n} b_i \beta_3 (X - I), \tag{3}$$

where b_i is control coefficient, $X = [x,y]^T$ is the interpolation point coordinate, $I = [i,j]^T$ is the pixel coordinate of any point, $\beta_3(X-I)$ is the cubic B-Spline tensor product.

Metric is a function measuring the degree of matching between a fixed image and a moving image. Typical metrics include mutual information, normalized mutual information, mean square error, normalized cross-correlation, and so on. Mutual information (MI) measures how much information one random variable (image intensity in one image) tells about the other random variable (image intensity in the other image). The major advantage of using MI is that the actual form of the dependency does not have to be specified. Therefore, complex mapping between two images can be modeled [10]. Mutual Information is defined as:

$$I(A,B) = H(A) + H(B)H(A,B), \tag{4}$$

where $H(A) = \int p_A(a) log p_A(a) da$ is the entropy of random variable A, $H(B)$ is the entropy of random variable B, and $H(A,B) = \int p_{AB}(a,b) log p_{AB}(a,b) dadb$ is the joint entropy of A and B [10].

Image registration is actually a multi-parameter optimization problem. Therefore, the optimizer has a large influence on the precision of registration results. There are many optimization methods including Amoeba, Gradient Descent, LBFGS, LBFGS-B, One Plus One Evolutionary, Powell, L-M, and so on. Since we have chosen the B-Spline transformation, it is very suitable to use LBFGS and LBFGSB Optimizer. In order to prevent a dead loop, we set a maximum number of iterations.

Once the registration module between the moving image and the fixed image is obtained, we can directly use the registration module to transform the standard brain image by

$$T_e = T_{BSpline}(S_t), \tag{5}$$

where $T_{BSpline}$ is the transformation module after registration. The image after transformation is called the template image T_e which will be used in the template matching, as shown in Fig.4.

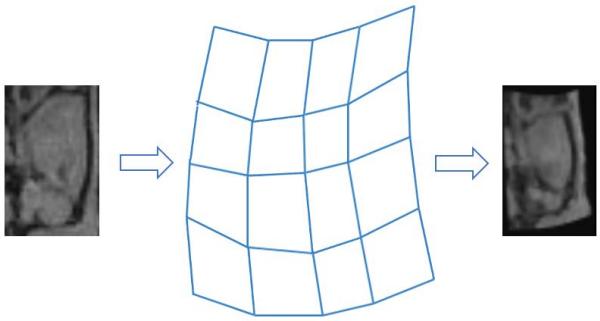


Figure 4. *The left image is the standard brain S_t. The middle grid represents the B-Spline transformation, the right image shows the template image T_e after transformation.*

Template Matching

With registration, the fixed image and moving image will correspond exactly to each other, including the brain section. Then according to the coordinates of the rat brain in the fixed image, we can find its corresponding location in the moving image which is exactly the ROI we needed. This method has a simple operation and runs fast. However, the results depend on registration excessively. When the distortion of a rat image is large, it is impossible to bring the two images completely into alignment. The rat brain selected is often too close to the boundary, or even misses some parts.

Here, we employ template matching in target recognition to segment the moving image [11]. A correlation function is defined to measure the matching degree of template image and searching sub-graph:

$$R(i,j) = \frac{\sum_{m=1}^{M} \sum_{n=1}^{N} S^{i,j}(m,n) * Te(m.n)}{\sqrt{(\sum_{m=1}^{M} \sum_{n=1}^{N} [S^{i,j}(m,n)]^2)} \sqrt{(\sum_{m=1}^{M} \sum_{n=1}^{N} [Te(m,n)]^2)}}, \tag{6}$$

where (i,j) is the point of the moving image M, $S^{i,j}$ is the sub-graph corresponding to the point (i,j), and T_e is the template image. The range of $R(i,j)$ is $[-1,1]$. $R(i,j) = 1.0$ indicates that the real-time image and the matching template match exactly. And $R(i,j) = -1.0$ indicates they completely mismatch. In our experiment, the point which has the maximum value of $R(i,j)$ is chosen. And its corresponding sub-graph in the moving image is the result. The process is shown in Fig.5.

This method is trying to search a sub-graph which has a maximum similarity to the template image. The position of ROIs in the moving image is independent of the relative position of the template image in the fixed image. The brain part segmented by this method has a high precision without important information missing, especially the region of tracer in the brain part.

Experimental Results

In order to study the process of diffusion of tracer in the rat brain, a rat is injected and then scanned at different times. Meanwhile, to obtain a complete picture of the rat brain, we scanned the rat at sagittal, coronal, and axial direction respectively. The

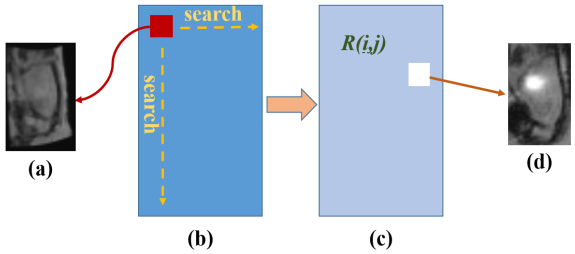


Figure 5. *(a) is the template image T_e. (b) represents the moving image M. (c) represents the $R(i,j)$ image in which each point represents the matching degree of template image and sub-graph. And (d) is the result image which is the ROI we needed.*

images used in the experiment are all nuclear magnetic resonance (NMR).

Fig.2 shows the entire rat images which were obtained at the saqittal direction. Fig.2(a) displays a fixed image in which the rat has not been injected with tracer, and Fig.2(b) - Fig.2(i) show the images taken at 35, 50, 80, 110, 140, 170, 200, 230 minutes after the rat was injected with tracer. The white bright spot in the brain part indicates the tracer. The diffusion region of the tracer is identified by the region of interest (ROI). As shown in Fig.2, the shape of the rat varies especially on the rat brain part, and the position of brain is located in different regions taken at different instances.

Fig.6 shows the ROIs which are automatically extracted using the proposed method. Fig.6(1), Fig.6(10), and Fig.6(19) show the ROIs of images which have not injected with tracer at the initial time. They are exacted manually at saqittal, coronal and axial direction respectively, and used as the standard brain in the proposed method shown in Fig.1. They are transformed into the matching templates by applying the reverse registration module. Fig.6(2) - Fig.6(9) present the ROIs of the time-series images segmented by the proposed method at the saqittal direction. Fig.6(11) - Fig.6(18) present the ROIs of the time-series images segmented by the proposed method at the coronal direction, and Fig.6(20) - Fig.6(27) present the ROIs of the time-series images segmented by the proposed method at the axial direction. Although the segmentation results in some figures are close to the boundary of brain parts, e.g. Fig.6(12) and Fig.6(18), the proposed method can also segment a relatively intact rat brain section, including the diffusion area of the tracer.

Fig.7 shows the segmentation results of the proposed method on another series of images. On Fig.7(1), Fig.7(11), and Fig.7(21), the regions of interest are delimited manually at an initial time. Varying dosage of tracer was applied to rats, which leads to different diffusion speed in rats. Also, they were scanned and sampled by different periods. Fig.7 shows that these factors do not have a great influence on the segmentation accuracy. Even if the location of rats varies and the brain part contains deformation in images, Fig.7(3) and Fig.7(4) illustrate that the proposed method can accurately segment the brain part as ROIs in such cases.

Conclusion

This paper presents an automatic method of segmenting regions of interest for medical image registration. On a large corpus of image data, extracting regions of interest manually is often infeasible. The proposed method provides a good approach to extracting regions of interest from medical images. It is used to accurately segment three-dimensional region of rat brain from MRI time-series.

Acknowledgment

This work was supported by the National Natural Science Foundation of China (Grants No., NSFC-61402046, NSFC-61471067, NSFC-81671651), Fund for Beijing University of Posts and Telecommunications (Grants No., 2013XD-04, 2015XD-02), Fund for National Great Science Specific Project (Grants No. 2014ZX03002002-004), Fund for Beijing Key Laboratory of Work Safety and Intelligent Monitoring.

References

[1] J. B. A. Maintz and M. A. Viergever, "A survey of medical image registration," *Medical Image Analysis*, vol. 2, no. 1, pp. 1–36, 1998.

[2] J. P. W. Pluim, J. B. A. Maintz, and M. A. Viergever, "Mutual-information-based registration of medical images: A survey," *IEEE Transactions on Medical Imaging*, vol. 22, no. 8, pp. 986–1004, 2003.

[3] E. Sykova and C. Nicholson, "Diffusion in brain extracellular space," *Physiological Reviews*, vol. 88, no. 4, pp. 1277–1340, 2008.

[4] B. Liu, X. Bai, F. Zhou, H. Han, and C. Hou, "Mutual information based three-dimensional registration of rat brain magnetic resonance imaging time-series," *Computers and Electrical Engineering*, vol. 39, no. 5, p. 1473V1484, 2013.

[5] H. QY, H. HB, X. FJ, Y. JH, Z. JJ, L. XG, F. Y, P. Y, C. H, H. C, and X. XJ, "Imaging and quantitative measurement of brain extracellular space using mri gd-dtpa tracer method," *Beijing Da Xue Xue Bao*, vol. 42, pp. 88–91, 2010.

[6] H. Tan, G. Feng, J. Feng, W. Wang, Y.-J. Zhang, and F. Li, "A tensor-based method for missing traffic data completion," *Transportation Research Part C: Emerging Technologies*, vol. 28, pp. 15–27, 2013.

[7] M. Gabrani and O. J. Tretiak, "Elastic transformations," in *Conference Record of the Thirtieth Asilomar*, pp. 501–505.

[8] W. Ma and J. P. Kruth, "Parameterization of randomly measured points for least squares fitting of b-spline curves and surfaces," *Computer-Aided Design*, vol. 27, no. 9, pp. 663–675, 1995.

[9] T. M. Lehmann, C. Gonner, and K. Spitzer, "Addendum: B-spline interpolation in medical image processing," *IEEE Transactions on Medical Imaging*, vol. 20, no. 7, pp. 660–665, 2001.

[10] H. J. Johnson, M. M. McCormick, L. Ibanez, and the Insight Software Consortium, "The itk software guide book 2: Design and functionality fourth edition updated for itk version 4.6."

[11] D. Pomerleau, "Ralph: rapidly adapting lateral position handler," in *Intelligent Vehicles '95 Symposium., Proceedings of the*, 1995, pp. 506–511.

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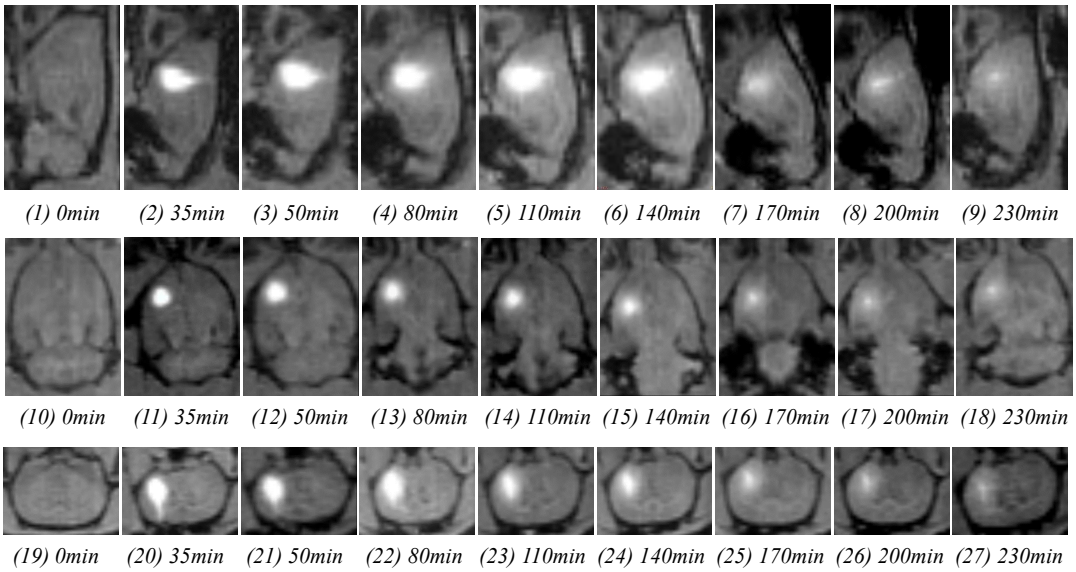

Figure 6. *(1), (10), and (19) show the standard brain images which are not injected with tracer at saqittal, coronal, and axial direction respectively. They are segmented manually. (2) - (9) present the time-series ROIs at saqittal direction which are segmented by the proposed method automatically. (11) - (18) present the time-series ROIs at coronal direction. (20) - (27) present the time-series ROIs at axial direction.*

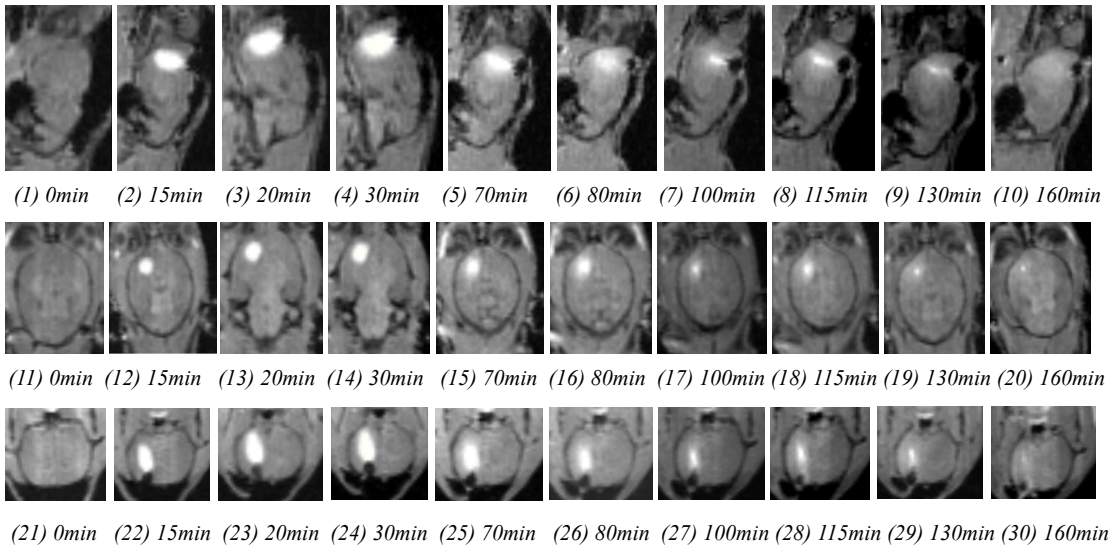

Figure 7. *(1), (11), and (21) show the standard brain images which are not injected with tracer at saqittal, coronal, and axial direction respectively. They are segmented manually. (2) - (10) present the time-series ROIs at saqittal direction which are segmented by the proposed method automatically. (12) - (20) present the time-series ROIs at coronal direction. (22) - (30) present the time-series ROIs at axial direction.*