Construction of a registration and fusion of unreformed thin-sectional high-resolution sectional anatomical image (Chinese Visible Human images) and CT and MRI images based on B-spline and mutual information and its application in segmenting nasopharyngeal structures in Treatment Planning System (TPS)

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Research
Abstract

Background

To help radiotherapy doctors recognize and segment the nasopharyngeal organs in risk of Nasopharyngeal carcinoma (NPC) and make radiotherapy plan.

Materials/Methods:

Based on the continuous thin-layer, high-precision, high-resolution and true-color sectional anatomical data (Chinese Visible Human (CVH) images), we used B-spline and mutual information to transform, register and fuse the CVH images with the patient’s personalized CT images, and integrated them into the Treatment Planning System (TPS). Consequently, Three-Dimensional Visualization Treatment Planning System (3DV + TPS) was created. To verify it, 3DV + TPS was deployed to identify and segment the nasopharyngeal organs in risk of NPC, and a questionnaire was filled out by radiotherapy doctors.

Results

Result shows that 3DV + TPS can finish registration and fusion of 4 sets of sectional anatomical images and individual CT images of patients in approximately 3 minutes and 50 seconds.

Conclusion

The registered and fused images can accurately reflect the position, outline and adjacent space of the nasopharyngeal structure which is not clear in the CT images. Thus, it is helpful for recognizing and segmenting neural, muscular and glandular structures. Through automatically registering and fusing of color images and CT gray images, 3DV + TPS improves the accuracy and efficiency of recognizing nasopharyngeal structures in making radiotherapy plan, and it is useful to improve the teaching quality of tumor radiotherapy for medical students and interns as well.

1 Background

In China, nasopharyngeal carcinoma (NPC) has become the main cancer and cause of death in otorhinolaryngologic malignancies [1–2]. It is more common in young and middle-aged patients, and it is more common in southern China, with a current trend of metastasis to the north [3–4]. The etiology of NPC may be related to genetic, environmental and EB viral infection factors [5–7]. The incidence area is usually the top anterior wall and pharyngeal recess of the nasopharynx [8]. The treatment plan for NPC mainly includes radiotherapy, drug therapy and operation therapy, among which radiotherapy is most commonly used; it has a significant effect on improving the survival rate of patients and can even achieve a complete cure [9–10]. However, recognition of the pharyngeal organs at risk in NPC radiotherapy,
such as the pharyngeal constrictor, optic chiasm, brainstem and diencephalon and other neural structures, are very limited due to the low resolution of CT and MRI grayscale images[11]. Especially for junior doctors, it takes much time and energy, and the accuracy of the segmentation is not high.

The Chinese Visible Human dataset has the characteristics of high precision, true color, high resolution and thin layer thickness, and it has a very high recognition ability for the structure of the nasopharynx[12–13]. In this paper, the CVH image was deformably registered according to the CT and MRI images of patients by B-spline and mutual information and then fused with them and integrated into the TPS radiotherapy system of Xudong Company; this technique was attempted by radiotherapy doctors in a clinic to explore and study the practical help effects of the registration and fusion method of CVH images and medical images based on B-spline and mutual information to improve the accuracy and efficiency of the radiotherapy doctors in segmenting the target area[14].

2 Materials And Methods

2.1 Image selection of the structure area of the nasopharynx in the CVH dataset

All materials needed in this experiment were from the intangible and high-precision head and neck sectional anatomical images from the CVH dataset that were frozen and thin-layer-milled in the teaching and research section of digital medicine of Army Medical University, including 4 cases of CVH1, CVH2, CVH4, and CVH5. The image area was from the top of the head to the lower edge of the thyroid gland; the lowest layer thickness of the image was 0.2 mm, the highest image resolution was 4064 × 2704, and the smallest pixel size was 0.12 × 0.12 mm. The collection steps of the dataset selected in the experiment were all performed in a low-temperature laboratory below -25℃. The milling ice surface did not fog, which made the clarity and accuracy of the dataset image much higher than those of the existing datasets in the world. Moreover, the milling data collected in the low-temperature laboratory could avoid small structures falling off from the milling surface and maintain the integrity of the image data. In addition, the dataset adopted continuous sections of the whole human body without segmental data loss. The main parameters of the dataset selected in this experiment are shown in Table 1.

2.2 CT and MRI image selection of NPC volunteers

We selected CT and MRI data of the head and neck of 8 patients with normal nasopharyngeal structures or early NPC from Southwest Hospital and Xinqiao Hospital Affiliated with Army Medical University. The study was approved by the volunteers and their families with informed consent and by the institutional review committee of Army Medical University. It is followed with Chinese ethics and laws.

2.3 Image registration and fusion of the multimodal nasopharyngeal structure based on B-spline and mutual information

Through B-spline and mutual information, CVH head and neck tomograms were registered and fused to CT and MRI images of patients or volunteers to add true-color tomographic anatomy information to the
original grayscale images. The method consists of the following steps: (1) image preprocessing; (2) registration using the spatial transformation model bicubic B-spline surface; (3) measuring the degree of similarity between two images in the registration process by mutual information to evaluate the result of image registration; (4) optimizing the problem-solving process by a gradient descent algorithm and searching for the optimal registration parameters that maximize the similarity measure; (5) matching CVH images with CT and MRI images using the obtained optimal parameters and displaying the fused images.

2.4.1 Integrating CVH nasopharynx data, B-spline and mutual information algorithm into TPS software

The CVH color sectional anatomical image and its fused registration image with the CT image were integrated into 3DV+TPS software from Xudong Company. Through this software, radiotherapy doctors can obtain a fused registration image of a color CVH sectional anatomical image with CT and MRI images of patients or volunteers, observe the structure of the nasopharynx, and recognize the anatomical structure of the nasopharynx, which is difficult to recognize on CT and MRI images (shown in Figure 1).

2.4.2 According to the CVH image after registration and fusion, the radiotherapy doctors identified and segmented some structures of the nasopharynx on CT/MRI, including the temporal lobe, parotid gland, optic nerve, brainstem, cerebellum and pharyngeal constrictor.

2.4.3 CT and MRI images of the same volunteer were selected. The CVH5 image was registered and fused to the cross-sectional MRI and CT images of this volunteer according to the B-spline and mutual information algorithm. The opacity of the deformed CVH image as the image mask was adjusted. The nasopharyngeal structure in the CVH image and that on the CT image were observed and compared; meanwhile, MRI and CT images were registered and fused for comparison (shown in Figure 2).

2.4.4 The radiotherapy doctor looked for the organs in risk of NPC on CVH, CT and MRI and made a comparative analysis.

A questionnaire survey (Appendix 1) of radiotherapy doctors was designed to evaluate the effect of recognition and segmenting on CVH, CT and MRI of the organs in risk of NPC. Twenty-two radiotherapy doctors in the Xinqiao Hospital completed the questionnaire. The effect which recognized and segmented effect the eyeball, lens, brainstem, spinal cord, inner ear, pharyngeal constrictor, parotid gland, temporal lobe, optic nerve and optic chiasm on CT, MRI and CVH were compared and analyzed (shown in Table 2).

3 Results

3.1 Creation of B-spline and mutual information algorithm

A B-spline and mutual information algorithm was created, and it could achieve the registration and fusion of CVH, CT and MRI. The image registration and fusion were achieved mainly using the method of image fusion registration of the multimodal nasopharyngeal structure and spatial transformation of the cubic B-spline surface.
3.2 Completing the registration and fusion of the temporal lobe, parotid gland and optic chiasm

The temporal lobe, parotid gland, optic chiasm, pharynx muscle (shown in Figure 3) and other structures that could not be recognized on CT/MRI could be identified after integrating the registered and fused CVH image with the CT/MRI images of volunteers into TPS software of Xudong Company, and the fused image could show the corresponding structures clearly.

Several important NPC-endangered organs in radiotherapy, such as the temporal lobe, parotid gland and optic chiasm, were chosen as representatives for registration, fusion and structure recognition.

3.3 Design and complete the questionnaire

There were 22 effective questionnaires. Of the 22 doctors surveyed, all were doctors or physicians from the oncology department of Xinqiao Hospital. Eleven of them had only a bachelor's degree, 7 had a master's degree, and 4 had a doctoral degree. The data of each problem were statistically analyzed (shown in Table 2).

According to the analysis of the survey results, the nonrigid registration method of B-spline and mutual information and the registration fusion based on CVH and the patient's personalized CT image could help radiotherapy doctors to identify structures that are difficult to recognize. It was generally believed that the CVH image was superior to the CT image in identifying the critical structures; 3DV+TPS could assist radiotherapy doctors in making the operation plan and applying it to clinical operation.

3.4 Statistical verification of the survey questionnaire

The clinicians generally thought that the CVH image was better than the CT image in recognizing the organs in risk of NPC (Table 2).

Among the 11 structures surveyed in the questionnaire, the recognition of the eyeball and lens structures was not as good as the CT or MRI images in terms of the enhancement effect of segmentation recognition of the corresponding structures after registration and fusion of CVH image into CT or MRI images; the enhancement effect of the spinal cord, inner ear, pharyngeal cavity, optic nerve and other structures was quite obvious; the enhancement effect of the brainstem, pharyngeal constrictor, parotid gland, temporal lobe, optic chiasm and other structures was very obvious. The CVH images can help clinicians complete the task of target area segmentation, successfully deliver the precise radiotherapy, and meet the needs of clinical application.

4 Discussion

In this paper, the thin-layer high-precision and high-resolution true-color sectional anatomy images (CVH) were fused with the volunteers’ personalized CT and MRI after nonrigid registration based on B-spline and mutual information research methods using a CVH dataset, and the images were integrated into TPS software. This integration is the first to fuse the true-color and high-precision sectional anatomical
images into the radiotherapy contour segmentation process. Using this method, radiotherapy doctors can recognize the human body structures that are difficult to recognize on CT images through the sectional anatomical images after deformable registration in TPS software, such as the brainstem, cerebellum, thalamus, optic nerve, optic chiasm and other nerve tissue structures; the pharyngeal constrictor and other muscle structures; and the parotid gland, submandibular gland and other gland structures. On CT images, the structures of nerves, muscles and glands are difficult to recognize and segment precisely because of the close CT value, whereas in the color sectional anatomical images of CVH, the structures of the nasopharynx can be prepared for recognition and segmentation according to their natural colors. Compared with the TPS System of Varian and medical Kodak, etc. 3DV + TPS has the unique function in referring to the high-precision true-color anatomical images suitable for an individual patient's CT morphology to guide the contour segmentation of organs at risk on CT images more accurately. It is of great significance for clinicians to accurately segment the target area and organs at risk through radiotherapy, and it can help radiotherapy doctors improve the precision of segmenting at-risk organs, shorten the segmentation time, and improve segmentation efficiency. It can help radiotherapy doctors, especially junior radiotherapy doctors, make and optimize the radiotherapy plan.

B-spline uses polygons and weight functions to define curves, which can be registered and adjusted for free-form curves and surfaces, while mutual information is used as a similarity measure to evaluate registration results such that registration has a good local deformation effect. A method of similarity measure based on the unified image grayscale level is proposed to solve the problem where similarity measures based on the grayscale level can’t easily express the relationship between the two images accurately due to the inconsistent grayscale range of images. Therefore, this paper is based on the nonrigid registration method of B-spline and mutual information. Currently, we constructed 8 CVH atlases of different sexes, ages, and body weights. We will try to match the atlas with the closest head shape to the patient to maximize the atlas registration accuracy, which can fit the patient’s nasopharyngeal structures to a greater extent. In this way, we hope to further improve the segmentation accuracy of the head structures. In future research, we will also consider using multiple CVH atlases to improve the segmentation accuracy.

5 Limitation

From a methodology perspective, our method uses a fully automated registration strategy. However, there are some limitations in our study. First, the automatic method only maximizes the mutual information between the atlas and the patient image, which can’t guarantee precise alignment of fine-scale structures such as nerves, vessels, etc. Because the CVH volunteer and NPC patient have different bodies, and they do not match very precisely. Second, the 3DV + TPS registration method mainly aims at the integral registration of the local structure of the human body, which cannot meet the personalized accurate registration of a single anatomical structure. Third, the B-spline and mutual information algorithm can’t achieve the manual registration of images. Our future research will also try to combine the mutual information metric with user intervention of the anatomical landmark definition to allow doctors to control the registration accuracy of local fine-scale structures. Function optimization technology can be
used to solve the problem of feature extraction and registration in addition to the transformation of model parameters and optimization of the algorithm to improve the accuracy of automatic registration[28–29].

6 Conclusion

In this paper, 4 cases of head and neck sectional anatomical images of a CVH dataset were selected, and the CVH image and patient's personalized CT image were automatically registered and fused by the nonrigid registration method of B-spline and mutual information and integrated into the TPS system such that the radiotherapy doctors could identify and segment the organs in risk of NPC based on the CVH color sectional anatomical image. The radiotherapy doctors could accurately identify the position, shape contour and spatial adjacent relationship of the structure of the nasopharynx on the CT images according to the registration and fusion image of the CVH and patient's individualized CT and segment them[30]. The research is helpful for the recognition and segmentation of the structures that are difficult to recognize on CT images, such as the muscles, nerves and glands of the nasopharynx. This method achieved the automatic registration and fusion of the color image and CT gray image, improved the accuracy and efficiency of segmentation, is helpful for radiotherapy doctors to make accurate and detailed radiotherapy plans, and helps to improve the teaching quality of tumor radiotherapy for medical students and interns.

Declarations

Ethics approval and consent to participate

The study was approved by the volunteers and their families with informed consent and by the institutional review committee of Army Medical University (Third Military Medical University).

Consent for publication

Written informed consent for publication was obtained from all participants.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

Funding
The authors are grateful to The National Key Research and Development Project (grant No. 2016YFC0106402), the National Natural Science Foundation of China (grant No. 31671251), the National Natural Science Foundation of China (grant No. 31771324), and the Technological Innovation and Application Demonstration of Chongqing CSTC of China (No. cstc2018jscx-msybX0073), Graduate Education Teaching Reform Research Project in Army Medical University (No. 2018yjgA009).

Authors’ Contributions

JY: Data analysis; manuscript writing. XZ: Designed the experiments. ZX and XH: Provision of materials and literature search. BY and HL: Designing and collecting the questionnaire. LQ: Data collection. HW, JS and YW: Conceived and designed the experiments.

Acknowledgements

The authors thank Professor Yi Wu, Professor Jianguo Sun and Professor Shaoxiang Zhang for their constructive comments during the manuscript writing. We are grateful Professor Liang Qiao, Professor Hongkai Wang for data analyses. Thanks also go to Miss Xiaoqin Zhang, Mr Bangyu Luo and Dr Hongjun Liu for their help in the field.

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**Tables**

Table 1. The main parameters of the Chinese Visible Human dataset

|                  | CVH-1   | CVH-2   | CVH-4   | CVH-5   |
|------------------|---------|---------|---------|---------|
| Age (y)          | 35      | 22      | 25      | 25      |
| Sex              | male    | female  | female  | female  |
| Height (mm)      | 1700    | 1620    | 1620    | 1700    |
| Weight (kg)      | 65      | 54      | 57.5    | 59      |
| Layer thickness (mm) | 0.1, 0.5, 1.0 | 0.25, 0.5 | 0.25, 0.5, 1.0 | 0.2 |
| Number of faults | 2518    | 3640    | 3060    | 8510    |
| Image resolution | 3072×2048 | 3072×2048 | 4064×2704 | 4064×2704 |
| Pixel size (mm)  | 0.15×0.15 | 0.15×0.15 | 0.12×0.12 | 0.12×0.12 |

Table 2. Comparison and analysis of clarity of CT and CVH recognition structure
| Structure          | Recognition definition of structure on CT | Recognition definition of structure on CVH | CT versus CVH |
|--------------------|-------------------------------------------|------------------------------------------|----------------|
| Eyeball            | 4.27±0.88                                 | 2.68±1.29                                | <0.001        |
| Lens               | 4.32±1.04                                 | 2.73±1.29                                | <0.001        |
| Brainstem          | 3.45±1.01                                 | 3.95±0.72                                | 0.102         |
| Spinal cord        | 3.73±1.08                                 | 3.68±0.84                                | 0.896         |
| Inner ear          | 2.72±1.08                                 | 4.36±0.58                                | <0.001        |
| Pharyngeal cavity  | 3.18±1.01                                 | 4.22±0.43                                | <0.001        |
| Pharyngeal constrictor | 2.32±1.17                                  | 4.27±0.70                                | <0.001        |
| Parotid gland      | 2.82±1.29                                 | 4.32±0.72                                | <0.001        |
| Temporal lobe      | 2.45±1.22                                 | 4.41±0.67                                | <0.001        |
| Optic nerve        | 3.64±1.05                                 | 4.18±0.73                                | 0.09          |
| Optic chiasm       | 2.00±1.19                                 | 4.45±0.74                                | <0.001        |

**Figures**
Figure 1

A CVH image is integrated into 3DV+TPS software after registration and fusion according to the CT image, and its multimodal image is displayed in the software with 3D visualization. A. the CT image of a patient and volunteer; B. the CVH image of a patient and volunteer; C. fused registration image of the CVH and CT image of a patient and volunteer; D. CVH nasopharynx image after deformation based on the CT image; F. segmenting the CVH images after the registration fusion of the CVH and CT images; E. the registration fusion of the CT images help radiotherapy doctors recognize and segment.
Figure 2

Registered and fused CVH image and MRI and CT images of a volunteer. Br: brainstem; E: eyeball; TL: temporal lobe; OPN: optic nerve; NS: nasal septum; CB: cerebellum; OPC: optic chiasma. A. volunteer's CT image; B. volunteer's MRI image; C. the deformed CVH images of a volunteer; D. registration and fusion of volunteer's CVH and CT image; E. registration and fusion of CVH image and MRI; F. registration and fusion of CVH image and CT; F. 3D reconstruction of CVH5.
Figure 3

Registration fusion and segmentation of the temporal lobe, parotid gland, optic chiasm, pharynx muscle. A. the temporal lobe on the CVH image after registration was recognized and segmented; B. the temporal lobe structure on CT could be clearly recognized and segmented through temporal lobe segmentation of the CVH image; C. the parotid gland was recognized and segmented through the CVH image after deformable registration; D. the parotid gland structure on CT could be clearly recognized and segmented through segmentation of the parotid gland on the CVH image; E. the optic chiasm was recognized and segmented through the CVH image after deformable registration; F. the structure of the optic chiasm on CT could be clearly recognized and segmented through segmentation of the CVH image; J. the pharynx muscle was recognized and segmented through the CVH image after deformable registration; H. the structure of the pharynx muscle on CT could be clearly recognized and segmented through segmentation of the CVH image; T-P. the number i to p is enlarged the corresponding position of the number a to h.
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