Original Article

Computer-aided three-dimensional reconstruction of main vessels in hemangiomas

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Abstract: This study aimed to investigate three-dimensional (3-D) morphological features of the main vessel architecture of human hemangioma. Serial sections of specimens from three cases of children hemangioma were stained with hematoxylin and eosin (HE) to visualize the vessels. Serial images were taken and processed with computer-assisted 3-D reconstruction. Partial 3-D structure reconstruction of vessel morphology in hemangioma revealed strange distribution and branching, which were different from normal vessels of the human skin. The 3-5 microvascular was most common in hemangioma. We observed respective characteristics of three cases: 1 case showed uniform artery vein distribution accompanied by running trend; 1 case showed main artery distribution and less vein distribution, and there were many blood sinus in the shallow surface close to the skin; another case showed vein distribution in the middle of antrum. In conclusion, digital vascular model of 3-D structure of main vessel hemangioma provides a new way for the diagnosis and treatment of hemangioma of children.

Keywords: Hemangioma, biopsy, three-dimensional reconstruction

Introduction

Hemangioma is a common form of benign tumor in children. The treatment is still difficult for hemangiomas on important sites, such as the face, perinea and joints. Understanding vascular space distribution of hemangioma will be of great help for the diagnosis and therapy of hemangioma. 3-D image reconstruction is currently used to understand the anatomical relation between tumor and surrounding parts, as well as the origin of abnormal blood vessels [1]. However, it can not distinguish small vessels in tumor sites with skin soft tissues, such as hemangiomas and vascular malformations. Therefore, other reconstruction way have been tried to display small tissue or blood vessel. 3-D image reconstruction of serial tissue slices is able to clearly show the 3-D distribution of vascular tissues and even cell morphology [2]. In addition, 3-D reconstruction of microvessels of tumor and other tissues has been reported [3, 4]. However, the 3-D reconstruction of serial tissue slices of major blood vessels of hemangioma is rarely reported. In this study, we performed 3-D image reconstruction of serial tissue slices of intact vascular tumor following complete micro-anatomy of vascular tumors tissues from important sites, and observed the distribution of tumor blood vessels in the tissue level.

Materials and methods

Specimens

Two chest wall hemangiomas from two male patients who were 8 and 6 months old (size: 0.8 × 0.5 × 0.5; 0.6 × 0.5 × 0.5) and an abdominal wall hemangioma from a female patient who was 7 months old (size: 0.5 × 0.4 × 0.3) were taken from the Pediatric Surgery Department of Second Affiliated Hospital of Shantou University Medical College. The hemangiomas had clear boundaries with the surrounding normal skin, were located in the subcutaneous fat layer, and had an outer edge reaching the skin surface. It had semi-spherical or nodular shape with the inner edge firmly touching muscle. Complete dissection permitted diagnosis as an early reg-
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We then did conventional continuous tissue sectioning and hematoxylin and eosin (HE) staining. We also made three vertical holes on the wax block with the needle to act as reference points for the later sectioning [5]. Serial sectioning was spaced at 10 μm intervals. Water temperature and time for sectioning were controlled to be the same, reducing operation-made errors. A total of 424, 544, 202 serial sections were made.

Image acquisition and reconstruction

Images were acquired by using a real-time microscopic image acquisition system (Motic VM V1 Version 1.1). Each slice was continuously mined at 100 × magnification. 164 pictures were taken and merged by the software into a complete image.

Positioning and cutting of composite image

Using Adobe Photoshop CS6 13.0.0 (Adobe Systems, Inc.), the positioning holes for all synthetic images were overlapped; images were then uniformly cut. This process involved shifting and rotation of synthetic images as follows: 1) select a first composite image as a standard; 2) create a new blank image and record locations of two reference holes of the first compos-
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Figure 3. Three-dimensional reconstruction images of blood vessels of hemangiomas in case 1. The nine panels were rotated clockwise image of 3-D reconstruction (0°, 30°, 60°, 120°, 150°, 180°, 210°, 300°, 320°) pattern diagram. (Red: artery; Blue: vein).

Figure 4. Pathological images of hemangiomas in case 2, after alignment of the three-dimensional reconstruction software.
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Processed pictures were then imported into a computer. Main vessels that needed to be reconstructed were outlined by the software Able Software three-dimensional Doctor v4.0.20110710 (Able Software Corp.). 3-D images of the main vessels in the hemangioma were then reconstructed in the computer.

Results

Cell clusters had blurred boundaries and abundant intermediate tissues. Cells were loosely and disorderly arranged, some cells showed irregular sinus-like clusters while other cells formed dense capillary groups like honeycomb with large capillary diameters. Blood vessels in the same tumor tissue showed different stages of regression, papillary dermis mostly showed capillary-like structure and subcutaneous tissues showed dense cell mass, suggesting that the regression was developed from the dermis to the subcutaneous tissue.

The 3-D image showed that hemangioma main vessels were different from general vessels with more varied sizes and more branches. There was also traffic between the main vessels. Vessels can run through the sinus hemangioma, showing some local blind bulging tube. We observed respective characteristics of three cases: 1 case showed uniform artery vein distribution accompanied by running trend; 1 case showed main artery distribution and less vein distribution, and there were many blood sinuses in the shallow surface close to the skin;
another case showed vein distribution in the middle of antrum (Figures 1-7).

Discussion

Hemangiomas and vascular malformations are common congenital malformations found in skin and soft tissue. Angiogenesis in hemangiomas differs from that in normal and healing tissues or in chronic inflammation. The differences include the maturity of new blood vessels, the characteristics of blood supply, and the morphology, the proliferation of endothelial cells, molecular genetic alterations and angiogenesis-related diseases [6].

Currently, Mulliken’s classification is internationally accepted to divide tumors into hemangiomas and vascular malformations according to the anatomy and biological characteristics of vascular mass [7]. Tumors are further divided into artery, vein, capillary, lymphatic and mixed types based on anatomical differences. Furthermore, Jacksonn et al. proposed to divide vascular malformations into high flow vascular malformation and low flow vascular malformation [8]. We suggested that the number of blood vessels in hemangioma basically does not change based on preliminary micro-anatomical analysis and relevant literature on hemangioma imaging [10, 11]. Therefore, to study the morphology and distribution of the main vessels in hemangioma would be helpful for understanding tumor staging, the anatomical relation between tumors and surrounding tissues and the cause of malformation, and for guiding clinical treatment.

Three-dimensional image reconstruction technology has developed recently [12]. The function of three dimensional reconstruction includes. 1) Structure imaging and understand the anatomy of the visual boundaries. 2) Understand the relationship between various ele-
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1) Gather the material components [13, 14]. 3) Analyze the spatial layout for each component. 4) Quantify the spatial relationship [15].

Reconstruction is divided into the following several kinds: serial sectioning technique, Nuclear Magnetic Resonance, B ultrasound, Computed Tomography. There have been reports of three-dimensional reconstruction of computed tomography (CT) images of hemangioma, with the description of the features of main vessel of hemangioma [16]. However, CT image could not reconstruct the main vessel of very fine lesions. Therefore, in this study we used serial sections of 3-D reconstruction technology.

The continuous three-dimensional reconstruction technology improves the diagnostic accuracy and is becoming used more in the clinical, especially for cancer and brain tissues [17-23]. By using this technology in this study we found that main vessels of hemangioma are different from general vessels, having 3-5 arteries or veins and more branching. This indicates the diversity of vascular morphology in hemangioma. For the 3 cases of hemangioma, we found some common characteristics: the main vessel differed from general vascular; the shape and size of the main vessels were not the same, with many branches; traffic was connected to the main vessel through the hemangioma antrum. These observations are consistent with other reports on hemangioma imaging [16, 24]. In addition, we found respective characteristics of the 3 cases: 1 case showed uniform distribution of artery vein, accompanied by running trend; 1 case showed main distribution in artery, and there were many blood sinus in the shallow surface close to the skin; the other case had vein lumen distributed in the middle of antrum.

A rich blood supply supports the rapid growth of the tumor. We observed that main vessels in hemangioma comply with the general rule of descending from the larger to the smaller [25]. We reconstructed the 3-D morphology of main vessels in hemangioma, which provided a comprehensive platform for understanding hemangioma.

Figure 7. Three-dimensional reconstruction images of blood vessels of hemangiomas in case 3. The nine panels were rotated clockwise image of 3-D reconstruction (0°, 30°, 60°, 120°, 150°, 180°, 210°, 300°, 320°) pattern diagram. (Red: artery; Blue: vein).
gioma vessel morphology. Moreover, we could find the precise positioning of main vessels through imaging methods, and then block the main vessels in the normal skin around the tumor to cause tumor ischemia, achieving the therapeutic effect while avoiding risks of disfigurement or flap transplant.

The 3-D reconstruction process is affected by many factors. In addition to computer hardware system, algorithms and display, image positioning, compression and automatic segmentation are also important factors. Quantity and quality of images are key factors of the authenticity of 3-D reconstruction. Studies have shown that the fixation can cause tissue contraction. Formaldehyde fixation causes 30% tissue contraction. Floating on the water of tissue slices can cause deformation too. The number and type of dye also affect the structure and morphology of tissues. Therefore, we paid great attention to the process to ensure a constant temperature and same floating time, minimizing distortion effects [26]. In the process of obtaining continuous slicing, shifting and rotation will occur between slices. Therefore, in 3-D reconstruction, we must at first align serial sections. Aligning includes “hard” methods and “soft” methods [27]. In this study, we used continuous image mining followed by serial stitching to overcome the aligning errors, obtaining very nice results.

In the future, we will combine 3D reconstruction with other techniques, such as immunohistochemistry, special staining, and molecular biology to better understand morphological details of the main vessels in vascular malformation. This information will provide valuable guidance for the diagnosis, treatment and prognosis of hemangioma.

Disclosure of conflict of interest

None.

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