Virtualized Angioscopy of the Thoracic Aorta in a Rabbit Model of Atherosclerosis

Katsuya Yoshida, MD; Masahiro Endo, Ph D; Kensaku Mori, Ph D*;
Kazuhiro Katada, MD**; Makiko Ueda, MD***;
Jun-Ichiro Toriwaki, Ph D*; Yukio Tateno, MD

The purpose of this study was to apply virtual reality technology to spiral computed tomographic (CT) angiogram images in a rabbit model of atherosclerosis and to correlate the images with histopathologic evaluation of the aorta. Image data were transferred to the virtual endoscope system in a graphics workstation. "Virtualized angioscopy" includes an interactive graphic user interface, which controls the viewpoint, the direction of the observation, and rendering and navigation functions. The virtual angioscopy system demonstrated irregularities of the luminal surface of the ascending aorta and a smooth luminal surface in the descending aorta. These observations were correlated with histopathologic findings. The results of this study indicate that the potential and real benefits of virtualized angioscopy far outweigh several technical limitations. (*Jpn Circ J* 1998; 62: 198–200)

Key Words: Virtual reality; Spiral computed tomography; Angiography; Rabbit; Atherosclerosis

In recent years, the application of virtual reality technology to the medical field has developed rapidly. Virtual endoscopy using volumetric data sets of computed tomography (CT) and magnetic resonance (MR) images is one of the applications!^{1–5} We have recently described a "virtualized endoscope system" that applies virtual reality technology to the production of simulated bronchoscopic images using spiral CT images!¹ As an extension of that work, we now describe "virtualized angioscopy" using spiral CT angiogram images. To provide a basic study before human trials, we chose an animal model so that the correlation between the images and histopathologic evaluation of the aorta could be investigated in an atherosclerotic rabbit.

Methods

A male New Zealand White rabbit, weighing 3.7 kg, was fed a rabbit chow diet supplemented with cholesterol (1% w/w, Oriental Yeast, Tokyo, Japan) for 11 weeks and given water ad libitum. The animal was anesthetized by an intramuscular (before imaging) or intravenous (during imaging) administration of a mixture of ketamine (37.5 mg/kg) and xylazine (5 mg/kg).

CT scans were performed using a Toshiba CT X-force/SH (Toshiba Medical, Tokyo, Japan) scanner with the spiral CT option. The table speed was 2 mm/sec, with 2 mm collimation. The scan duration was 45 sec. The total scan length (cranio-caudal) was 9.0 cm. Spiral CT scans were performed at 150 mA and 120 kV peak (kVp).

The reconstructed pitch was 1 mm, 512×512 matrix, and 180 mm field of view.

The rabbit was positioned in a left recumbent position within the CT scanner. After a CT scout image and a non-contrast scan of the thorax were acquired, 800 mg of iodine per kilogram of iodinated contrast media (Iopamiron-300, 300 mgI/ml, Schering, Germany) was infused manually through an ear vein at a rate of approximately 1 ml/3 sec. Immediately after the start of contrast media infusion, spiral CT scanning began at the level of the aortic arch and continued caudally through the diaphragm.

The rabbit was killed with an intravenous injection of potassium chloride. The aorta and heart were removed and fixed in buffered formalin. The ascending aorta, aortic arch, and thoracic aorta were serially sliced at 3-mm intervals. Slices were processed routinely, embedded in paraffin, sectioned at 5 μ m thickness, and stained with Weigert's elastic van Gieson stain. The experiment was carried out in accordance with the Recommendations for Handling of Laboratory Animals for Biomedical Research, compiled by the Committee on the Safety and Handling Regulations for Laboratory Animal Experiments of the NIRS.

Image data were transferred to the virtualized endoscope system, which was implemented on graphics workstations (SGI Power ONYX Reality Engine 2, and INDIGO 2, Silicon Graphics, Mountain View, CA, USA) in the Department of Information Engineering, Graduate School of Engineering, Nagoya University. The data consisted of a 3-dimensional (3D) volumetric set, in which each voxel contained a CT value. Vessels were segmented automatically using an image recognition algorithm (thresholding and region growing). Manual correction was also performed as needed. The segmented data were stored as binary voxel data, which were converted to surface data using the marching cubes algorithm modified to generate smoother surfaces based upon CT values of the original data. "Virtualized

(Received, June 12, 1997; revised manuscript received September 8, 1997; accepted September 17, 1997)

National Institute of Radiological Sciences, Chiba, *Faculty of Engineering, Nagoya University Graduate School, Nagoya, **School of Health Sciences, Fujita Health University, Toyoake-shi, and ***Department of Pathology, Osaka City University Medical School, Osaka, Japan

Mailing address: Katsuya Yoshida MD, Division of Advanced Technology for Medical Imaging, National Institute of Radiological Sciences, 4-9-1, Anagawa, Inage-ku, Chiba-shi, Chiba 263, Japan

Fig 1. Virtualized angioscopy of the ascending aorta. (a) One of the original axial CT images. The cross-mark shows the view point. (b) Outside view (arrow shows the view direction). (c) An inside, "angioscopic" view shows the irregular shape of the vessel. (d) Histologic section of the ascending aorta shows the vessel wall and the superimposed atherosclerotic changes (magnification $17\times$, Weigert's elastic van Gieson stain). BC, brachiocephalic artery; AA, aortic arch.

Fig 2. Virtualized angioscopy of the descending aorta. (a) One of the original axial CT images. The cross-mark shows the view point. (b) Outside view (arrow shows the view direction). (c) An inside, "angioscopic" view shows the smooth and round shape of the descending aorta. (d) Histologic section of the descending aorta revealed no intimal thickening (magnification $17\times$, Weigert's elastic van Gieson stain).

angioscopy" includes an interactive graphic user interface, which controls the viewpoint, the direction of the observation, and rendering and navigation functions.

Results

Representative images are shown in Figs 1 and 2. Outside and inside views depicted the irregular shape of the ascending aorta (Fig 1b and c) and the smooth, round shape of the descending aorta (Fig 2b and c). Histologic sections of the ascending aorta showed intimal thickening with lipid-laden foam cells and extracellular lipid deposits (Fig 1d). Sections of the descending aorta, however, revealed no intimal thickening (Fig 2d).

Discussion

Virtualized endoscopy is a relatively new technique that is under development by a number of investigators¹⁻⁵. However, this is the first report to demonstrate "virtualized angioscopy" of the entire thoracic aorta and correlate the radiographic findings with histopathology in an animal model. Although the rabbit aorta is much smaller than that in humans, the results were satisfactory. The virtual perspective and interactive features of this system provided improved visualization and allowed a broader range of geometric measurements. These functions may be useful in the evaluation of patients with vascular diseases, such as aortic aneurysms.

The virtualized angioscopy system demonstrated irregularities of the luminal surface of the ascending aorta, and a smooth luminal surface in the descending aorta. These observations were correlated with histopathologic findings⁶, although precise correlation with histopathologic examination was somewhat limited.

The clinical application of virtual angioscopy still poses several technical problems. If the entire thoracic vasculature is to be examined in humans using spiral CT, it could only be done by decreasing the longitudinal resolution or by additional scanning⁷. It is not practicable to acquire volumetric data sets of the vasculature in humans with near-isotropic voxels. Electron-beam⁸ and cone-beam CT^{9,10} can image a wider area than spiral CT and have the potential to study the entire thoracic vasculature with a single injection of contrast material and a single breath hold. Segmentation is also more difficult for the contrast-enhanced vasculature than for the bronchus in CT imaging, because CT values of the vasculature have a wider range than those of the bronchus. Thus, segmentation, including the manual procedure, took approximately 1 h in the study. To achieve aortic enhancement efficient for 3D rendering in clinical applications, further studies are needed to capture the proper rate and timing of contrast infusion. This

limitation may be overcome by a new blood pool agent that remains in the vascular system for a longer period¹¹. Additionally, some useful information in CT numbers, such as tissue calcification, may be lost. Caution must be exercised in evaluating the ascending aorta as artifacts may be generated by transmitted cardiac pulsation⁷. MR angiography is also available for 3D vascular imaging^{2,4,5}. It does not require the administration of contrast material and does not expose the patient to radiation, although more time is required.

In spite of these limitations, virtualized angioscopy could have important implications in diagnostic imaging and may enable non-invasive angioscopy.

Acknowledgments

The authors thank Hiroshi Satoh, RT, for his expert technical assistance. The authors also thank Akira Takami, MD, Shinobu Kitsukawa, MD, Kazuhiro Shimada, MD, Yoshiaki Masuda, MD, University of Chiba Medical School, and Hiroyuki Tadokoro, MD, Nihon Medical School, for helpful discussion and suggestion. This study was supported in part by the Special Coordinating Funds for Promoting Science and Technology from the Science and Technology Agency, Japan.

References

1. Mori K, Urano A, Hasegawa J, Toriwaki J, Anno H, Katada K: Virtualized endoscope system. An application of virtual reality technology to diagnostic aid. *IEICE Trans Inf Syst* 1996; **E79-D**: 809-819
2. Rubin GD, Beaulieu CF, Argiro V, Ringl H, Norbash AM, Feller JF, et al: Perspective volume rendering of CT and MRI images: applications for endoscopic imaging. *Radiology* 1996; **199**: 321-330
3. Hayashi H, Kobayashi H, Takagi R, Kawamata H, Kumazaki T: Three-dimensional CT angiographic assessment of aorto-arterial pathology with the use of various postprocessing techniques. *Radiology* 1995; **197(P)**: 516
4. Ladd ME, Gohde SC, Steiner P, Pfammatter T, McKinnon GC, Debatin JF: Virtual MR angioscopy of the pulmonary artery tree. *J Comput Assist Tomogr* 1996; **20**: 782-785
5. Davis CP, Ladd ME, Romanowski BJ, Wildermuth S, Knoplioch JF, Debatin JF: Human aorta: preliminary results with virtual endoscopy based on three-dimensional MRI imaging data sets. *Radiology* 1996; **199**: 37-40
6. Clarkson TB, Lehner M, Bullock BG: Diet-induced atherosclerosis of rabbits. In: Weisbroth SH, Flatt RE, Kraus A, editors. *The biology of the laboratory rabbit*. San Diego; Academic Press: 1974: 156-165
7. Rubin GD, Dake MD, Semba CP: Current status of three-dimensional spiral CT scanning for imaging the vasculature. *Radiol Clin North Am* 1995; **33**: 51-70
8. Galvin JR, Gingrich ED, Hoffman E, Kao SCS, Stern EJ, Stanford W: Ultrafast computed tomography of the chest. *Radiol Clin North Am* 1994; **32**: 775-793
9. Kumazaki T, Kobayashi H, Ishio M, Iida E: Diagnostic 3D imaging of vascular system using a new cone-beam CT. *Eur Radiol* 1995; **5**: S338
10. Endo M, Yoshida K, Kamagata N, Satoh K, Okazaki T, Hattori Y, et al: Development of a 3D CT-scanner using cone beam and video-fluoroscopic system. *Radiat Med* (in press)
11. Milos M: Contrast media: a journey almost sentimental. *Invest Radiol* 1994; **29**: S4-S14