In Vivo Validation of Cardiac Spiral Computed Tomography Using Retrospective Gating

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Background. **Cardiac functional assessment represents the basis for diagnostics and cardiac operation planning. Spiral computed tomography (CT) combines the advantages of three-dimensional imaging and high temporal resolution when using gating techniques. However, in vivo validation data of this novel imaging technology are lacking. The purpose of this study was to validate in vivo the new imaging method using retrospective gating and to evaluate the clinical usefulness of the achieved temporal resolution.**

Methods. **In domestic pigs (n = 10, weight 35 to 40 kg) a flowmeter was placed surgically on the ascending aorta. Flow velocity integrated over systole served as the gold standard for left ventricular (LV) stroke volume (LVSV-FM). CT signal, projection data, pacemaker signal, and flow velocity were recorded simultaneously at constant heart rate (pacemaker, 90 beats per minute). End-systolic and end-diastolic frames were calculated by retrospective gating. LV volumes were traced, the difference representing CT stroke volume (LVSV-CT). Image data were three-dimensionally reconstructed using ray-tracing.**

Results. **Temporal resolution was 170 ms. Correlation of stroke volumes was high (r = 0.94, mean difference 1.75 mL). Intraobserver (0.49 mL for LVEDV, 0.31 for LVESV) and interobserver variability (p = 0.21 and p = 0.06, respectively) were low. Postprocessing resulted in four-dimensional beating-heart models useful for operation planning.**

Conclusions. **Spiral CT using retrospective gating was validated in vivo. Clinically acceptable temporal resolution and accuracy in determining cardiac stroke volumes were found. As a true volumetric imaging modality the method may now play an important role in computer-assisted diagnostics and surgery.**

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Computer-assisted technology plays an important role in aiding surgical and interventional procedures. Based on true three-dimensional imaging and image processing, navigational and volumetric tasks may be performed with high spatial accuracy. In cardiology and cardiac surgery the three-dimensional approach has led to better quantitation of intracardiac volumes by overcoming the need for geometric assumptions on two-dimensional image data [1]. For functional imaging, however, high temporal resolution is needed in addition.

Imaging today only fits in part the needs of cardiac surgery. The main three-dimensional imaging modalities available in the clinical routine are magnetic resonance imaging (MRI), computed tomography (CT), and three-dimensional echocardiography. Whereas three-dimensional echocardiography provides no true tomographic data, MRI and CT provide the raw data for tomographic slice reconstructions. With the advent of fast gradients MRI is a candidate for the diagnostic "one-stop shop," for example it provides the whole diagnostic information on morphology and function. However, MRI scanners with the needed hardware are not widely available. In contrast, CT scanning is widely used for morphologic diagnostics. However, radiation exposure and poor temporal resolution excluded the method in the past from functional cardiac imaging. In particular, electron beam CT scanning turned out to use high-dose radiation, resulting in high temporal but comparatively poor spatial resolution [2].

Validation data of retrospectively gated CT scanning in order to image the heart with clinically acceptable temporal resolution are missing. The purpose of the present study was therefore to validate in vivo the new functional cardiac imaging method using retrospective gating on conventional CT hardware.

Material and Methods

Animals and Validation Setup

Domestic pigs (n = 10, weight 35 to 40 kg) were used for in vivo experiments. Animals received care according the ethical guidelines set by the Deutsche Forschungsgemeinschaft (German Research Association). Premedication was performed using an intramuscular injection of ketamine at 20 mg/kg body weight in combination with azaperone at 1 mg/kg body weight, analgetic and narcotic medication during the operation using fentanyl at 1 mg/h and propofol (50 mg initially, 5 mg/kg body weight continuously) initially into a peripheral vein, after sufficient analgesia. The V. jugularis was cannulated by a central vein catheter. After intubation animals were ven-

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tilated (Servo ventilator 900 B [Siemens, Erlangen, Germany]). Median sternotomy was performed. After median pericardial incision, ascending aorta was prepared for perivascular placement of Doppler flowmeter (Transonic 105 [Transonic Systems Inc, Ithaca, NY]). The existence of intracardiac shunts and mitral valve insufficiency was ruled out by transesophageal Doppler examination before the CT scanning. Unipolar pacemaker leads were placed on the epicardium of the right ventricle and in the pericardium, and constant ventricular pacing was performed during the whole experiment using VVI-mode at a frequency of 90/min. Intravenous sotalol was administered (2 mg/kg body weight) to enable constant pacing. No type of additional cardiac surgery was performed. The thoracotomy was closed before CT examination.

Data Acquisition

Image acquistion was performed using a conventional subsecond spiral CT scanner (SOMATOM Plus 4; Siemens Medical Solutions, Erlangen, Germany). For synchronization with the heart beat, the pacemaker signal was digitized simultaneously to the roentgenogram-on signal from the CT scanner using a personal computer (PC) equipped with an analog-to-digital converter (ComputerBoards, Middleboro, MA). The roentgenogram-on signal indicates the start of the data acquisition of the CT scanner. A computer program was developed that automatically detects the R waves in the electrocardiographic (ECG) signal and puts out the time points relative to the start of the CT scan. The raw projection data from the CT scanner were transferred to a standard PC through a local network. The heart was covered using a slice thickness of 2 mm and a table feed of 1 mm per rotation, which corresponds to the minimum pitch the scanner supports. Each pig contributed to one CT examination. Total scan time was 80 seconds. Digital data acquisition was performed using synchronous AD conversion of the flowmeter data (flow velocity), the pacemaker signals (voltage), and the roentgenogram-on signal (5V-signal). Electronic hardware used was one laptop computer (Pentium 200) and an AD-conversion card (PCMCIA DAQ-Card 1200, National Instruments [National Instruments Corp, Austin, TX]). The CT scanner was connected to the AD-board through an optical coupler. Software consisted of LabView (National Instruments) for data acquisition, and MatLab (The MathWorks Inc, Natick, MA) for integration of flow velocity measurements over time.

Image Reconstruction

Retrospective gating and image reconstruction was performed on a standard PC with algorithms developed using Visual C++ (Microsoft, Redmond, Washington). The process of raw data sorting works as follows. Using the information from the ECG analysis, each measured projection was assigned a time within the cardiac cycle where it was acquired. When several rotations are performed, the same projection angle is available at different heart phases. In order to find an estimate for a projection at a certain time point within the cardiac cycle, from the available projections the one with the least distance in time is selected. For each ray in the sinogram of parallel projections, two available are selected, one from each side of the reconstruction position within a selectable range of rotations. Between these two values, linear interpolation with respect to the spatial distance to the reconstruction slice is performed. Temporal resolution depends on the range used [4]. In this study a range of two rotations was used, which is a compromise between slice profile and temporal resolution. With a scanner period of 1,000 ms and a heart period of 664 ms, this results in a temporal resolution of 170 ms. Images were reconstructed at an interval of 0.5 mm with a pixel size of 0.5 by 0.5 mm, resulting in an isotropic data set.

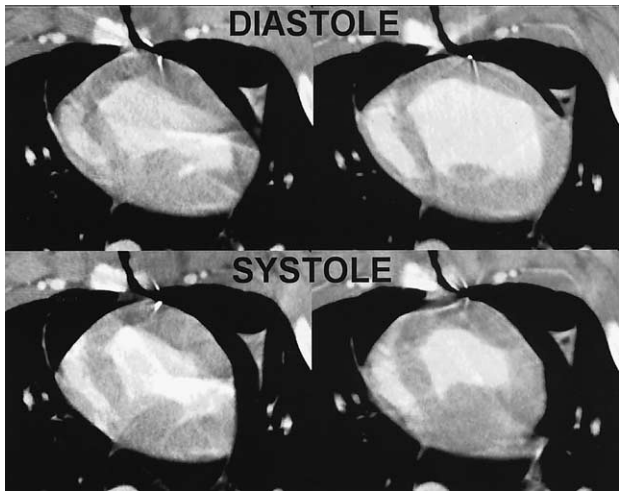

Fig 1. Reduction of motion artifacts by retrospective gating. End-diastolic (upper row) and end-systolic frames (bottom row) are depicted both without gating (left) and using retrospective gating (right). Images were acquired from the same animal.

Image Analysis

After CT image reconstruction, the beginning and end of each ventricular systolic period were determined using the aortic flow curves together with the epicardial ECG curves. The end of the left ventricular isovolumetric period (beginning of ventricular systole) was defined as the onset of the aortic flow curve; the beginning of isovolumetric relaxation coincident with the closure of the aortic valve (end of ventricular systole) was defined as the negative turn of the aortic flow curve or the end point of the T wave in the epicardial ECG. Endocardial borders were traced manually in order to define ventricular volumes at predefined end-diastolic and end-systolic CT frames. The number of pixels (n_p) in the segmented two-dimensional areas was calculated. Volume of every slice $_i$ (V_i)was calculated according to $V_i = n_p \cdot 0.05 \cdot 0.05 \cdot 0.05$ (value in mL).

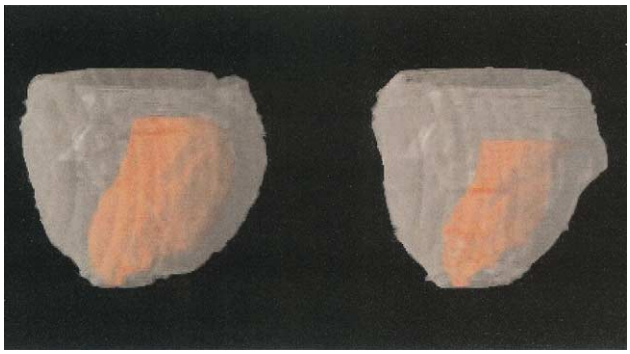

Fig 2. Three-dimensional reconstruction of functional computed tomography (CT) image data. Postprocessing of CT image data using ray-tracing resulted in illustrative views of end-diastolic (left) and end-systolic (right) rotating cardiac volumes (red). *This may be advantageous for future diagnostic routine (frame taken from three-dimensional movie).*

Statistics

Volume data samples were compared using the calculation of mean and standard deviation. Statistical analysis used linear model of correlation. Level of significance was determined to p less than 0.05 and 97.5% confidence intervals were used. As an indicator for clinical suitability, Bland-Altman plots were performed. Three calculations of intracardiac volumes were carried out by observer 1 for determination of intraobserver variability. Two additional calculations of intracardiac volumes were carried out by observer 2 for both determination of interobserver variability and additional determination of a second individual intraobserver variability.

Table 1. Resulting Cardiac Volumes

Pig No.	LVEDV-CT	LVESV-CT	LVSV-CT	LVSV-FM
1	33.40 ± 0.6	17.70 ± 0.2	15.70	22.00
2	44.87 ± 0.15	20.67 ± 0.06	24.20	27.00
3	36.27 ± 0.55	14.80 ± 0.1	21.47	20.00
4	53.20 ± 0.44	18.63 ± 0.31	34.57	46.40
5	34.80 ± 0.26	9.53 ± 0.12	25.27	24.80
6	59.40 ± 0.61	21.03 ± 0.25	38.37	38.50
7	49.83 ± 0.15	12.33 ± 0.25	37.50	34.60
8	40.80 ± 1.04	11.57 ± 0.65	29.23	29.60
9	56.20 ± 0.4	48.40 ± 0.36	7.80	8.00
10	56.13 ± 0.72	49.87 ± 0.78	6.27	6.90
Mean	46.49 ± 0.49	22.45 ± 0.31	24.04	25.78

Values of intracardiac volumes are represented as mean ± SD resulting from three measurements (intraobserver variability). Values of stroke volume were calculated from intracardiac volumes (CT) or taken from the flowmeter gold standard (FM).

LVEDV-CT = left ventricular end-diastolic volume calculated from CT image data; LVESV-CT = left ventricular end-systolic volume calculated from CT image data; LVSV-CT = left ventricular stroke volume calculated from LVEDV-CT and LVESV-CT; LVSV-FM = left ventricular stroke volume calculated from digital integration of flowmeter data (gold standard).

Results

The reconstruction time of retrospectively gated image data was 1 minute per slice. Three-dimensional reconstruction including segmentation and ray-tracing took several hours of postprocessing time. Effective radiation dose was 2 mSv.

The temporal resolution of the reconstructed image data was 170 ms. This was sufficient to clearly resolve diastolic as well as systolic heart phases. Motion artifacts were markedly reduced compared with conventional partial scan reconstructions. An example of image quality for standard as well as multiphase ECG-gated reconstruction is shown in Figure 1. Moreover, postprocessing resulted in three-dimensional beating-heart models (see Fig 2).

Left ventricular end-diastolic (LVEDV-CT) and end-systolic volumes (LVESV-CT) were determined on CT images, and stroke volumes (LVSV-CT) were calculated as the difference of both values. Comparison of those values was performed with flowmeter values (LVSV-FM) determined by integration of measured flow velocity over systolic period. LVEDV-CT was 46.49 ± 0.49 mL and LVESV-CT was 22.45 ± 0.31 mL (mean ± SD). Therefore, mean LVSV-CT in this experimental series was 24.04 mL compared with LVSV-FM of 25.78 mL (see Table 1). Assuming a linear model of correlation, the correlation equation was $y = 1.024x + 1.185$. Therefore, stroke volume was lightly overestimated by CT method when compared with the gold standard. The 97.5% confidence intervals are indicated in Figure 3. Approximation to linearity was good ($r = 0.94$). The mean difference of the respective stroke volumes was 1.75 mL, distributing uniformly along the measured range of mean volumes with one exception (see Fig 3).

To determine intraobserver variability, the SD of the calculated LVEDV-CT was 0.49 mL (mean 46.49 mL), the SD of LVESV-CT was 0.31 mL (mean 22.45 mL). For observer 2, the SD of the calculated LVEDV-CT was 0.23 mL (mean 47.49 mL), the SD of LVESV-CT was 0.11 mL (mean 22.63 mL). The differences between the two observers in determining LVEDV-CT ($p = 0.21$) and LVESV-CT ($p = 0.06$) were not significant when assuming significance at a p less than 0.05 level. Therefore the five observations were merged, resulting in LVEDV-CT of 46.89 ± 0.78 mL and LVESV-CT of 22.52 ± 0.26 mL (mean ± SD). The resulting LVSV-CT was 24.37 mL. Again, the values differed nonsignificantly from LVSV-FM ($p = 0.24$).

Comment

In vivo validation of cardiac functional imaging using spiral CT and retrospective gating was performed in the present study. The accuracy and variability of the new method were shown to be clinically acceptable. The image data are useful for qualitative functional assessment owing to the achieved high temporal resolution. However, several limitations of the study must be pointed out.

The examined ranges of systolic stroke volume do not

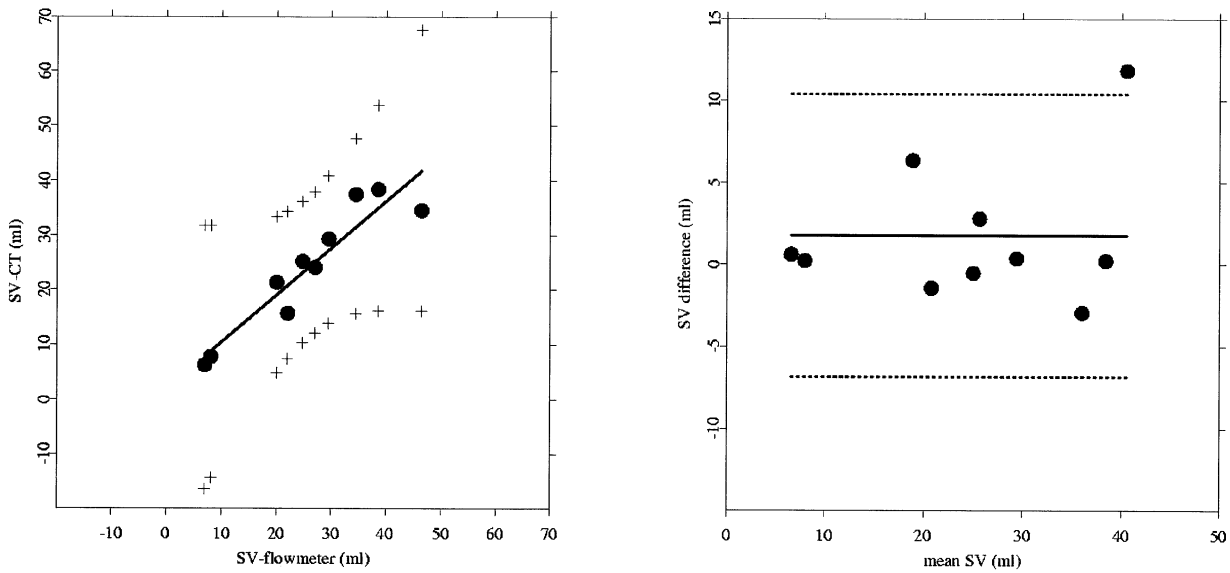

Fig 3. Accuracy and clinical value of computed tomography (CT) *method. (Left) Values of stroke volume* (SV) *calculated from CT method* (SV-CT, ordinate) *showed good correlation with SV taken from the gold standard* (SV-flowmeter, abscissa). r = *0.9387;* y = 1.024x + 1.185. *Linear approximation is indicated by the* solid line; 97.5% confidence intervals are delineated with +. *(Right) Bland-Altman plot of SV derived by the two methods. Mean difference = −1.75 mL; SD = 4.312 mL.* Dotted lines *represent the two times standard deviation distance from the mean difference.*

represent values of adult humans, rather they are comparable to pediatric values. Stroke volumes were additionally reduced by administration of a β-blocker. Measurements of higher volumes were not carried out. Therefore the data may lead to false interpolations when regarding adult human hemodynamics. Volumetric errors may be caused by partial volume effects. Systematic errors of the used validation setup may contribute to accuracy values. The mean difference in stroke volume shown in the present study was 1.75 mL, representing a value within the gold standard error. The detection of roentgenogram-on signal period was performed electronically. This may be more accurate compared with optical detection used in the literature [3]. The thermodilution method using pulmonary artery-catheterization serves as gold standard in the clinical setting for assessing cardiac output [4]. In the experimental setting however, we chose the Doppler flowmeter method for validation purposes [5].

A time resolution of 170 ms at a constant cardiac cycle time of 667 ms may not be high enough for exact functional assessment [6]. However, the validation data of the present study showed acceptable accuracy of stroke volume determination indicating the clinical usefulness not an ideal approximation. Motion artifacts were clearly reduced compared with conventional CT images. However, artifacts arising from epicardium were visible. These may have been caused in part by the boundaries between soft tissue and thoracic air due to the open-chest condition. The CT methodology was shown to reduce motion artifacts in cardiac imaging [7]. At present, algorithms were transferred to multidetector systems [8].

Exposure to radiation may limit the beneficial advances of the new method for cardiac functional imaging. In the literature, the maximum dosage used 1 Gy per level of radiation exposure [9]. In conjunction with subsecond CT scanners [8] these disadvantages should be surpassed. Improvements in reducing scanning time will further decrease radiation dose while keeping constant image quality [10]. In comparison with other volumetric imaging modalities, the effective doses for thoracic examinations are reported to be 11 mSv using electron beam CT, 4 mSv using sequential mode CT, and 2 mSv using spiral mode CT [11].

Based on these first experimental validation data the following clinical use may be suitable: All patients with regular normal-frequent heart rate may be examined. Beta blockade is not the prerequisite for CT examination. However, heart frequency of more than 90 beats per minute or tachyarrhythmia currently prohibits patients from examinations using retrospective gating even when using multidetector systems [12]. Look-up tables for the combination of the patient's heart rate, scanner rotation time, and number of rotations [13] may facilitate clinical suitability. Termination of the scan job within 30 minutes should be feasible when gating algorithms are implemented at the scanner console. Thus time-consuming data transfer may be avoided. It has to be stressed that any CT method cannot replace imaging during heart catheterization and echocardiography, in particular for the characterization of flow [14], owing to its worse resolution in plane and in the third dimension. With the need for true three-dimensional information, however, the new CT method provides volumetric data of clinically

relevant morphologic and temporal resolution. Cost effectiveness plays an increasing role in health care systems. A potential contribution to cost reduction may be provided by this new spiral CT method: the technology uses software portable to nearly all CT scanners available and may be easily extended to multidetector systems. Moreover, with one CT examination it is feasible to perform both classic morphologic imaging and functional cardiac imaging. No additional radiation exposure or expensive acquisition time is needed. The only additional effort consists of computer calculation time.

General usefulness of four-dimensional CT volumetry has been validated in the present study. For human use, experiences in the literature are reported in a qualitative study assessing wall motion abnormalities in 3 patients suffering from myocardial infarction [15]. From the same group, case-report evidence is demonstrated for the usefulness of contrast-enhanced CT for the diagnosis of myocardial infarction [16]. However, no quantitative analysis is provided.

Regarding failure rates using the new CT technology, there may be cases of tachycardia as mentioned above. However, in the present validation study heart beat frequency was kept constant artificially. In clinical practice no major failure rates are reported in the literature when examining patients with heart rates of less than 80 beats per minute. When using appropriate determinants [13] the failure rate should be in negligible range.

In summary, a new spiral CT methodology using retrospective gating was validated in vivo in the present study. Clinically acceptable temporal resolution and accuracy in determining cardiac stroke volume were found. As a true volumetric imaging modality the new CT method may now be ready to play a potential role in operation planning and simulation. These important interdisciplinary fields contain three-dimensional quantification of wall motion abnormalities, three-dimensional imaging of coronary arteries including calcifications, three-dimensional-valve imaging, interventional approaches including minimally invasive procedures, and three-dimensional navigation as the prerequisite for modern cardiac robotics.

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References

1. Greene DG, Carlisle R, Grant C, et al. Estimation of left ventricular volume by one-plane cineangiography. Circulation 1967;35:61–70.
2. Becker CR, Schatzl M, Schoepf UJ, et al. Technical basis and acquisition conditions of electron-beam computed tomography. Radiologe 1998;38:987–92.
3. Achenbach S, Giesler T, Ropers D, et al. Detection of coronary artery stenoses by contrast-enhanced, retrospectively electrocardiographically-gated, multislice spiral computed tomography. Circulation 2001;103:2535–8.
4. Swan HJ, Ganz W, Forrester J, et al. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 1970;283:447–51.
5. Wong DH, Watson T, Gordon IL, et al. Comparison of changes in transit time ultrasound, esophageal Doppler and thermodilution cardiac output after changes in preload, afterload, and contractility in pigs. Anesthesiol Anal 1991;72:584–8.
6. Ritchie CJ, Godwin JD, Crawford CR, et al. Minimum scan speeds for suppression of motion artifacts in CT. Radiology 1992;185:37–42.
7. Woodhouse CE, Janowitz WR, Viamonte M. Coronary arteries: retrospective gating technique to reduce cardiac motion artifact at spiral CT. Radiology 1997;204:566–9.
8. Kachelriess M, Kalender WA. Electrogram-correlated image reconstruction from subsecond spiral computed tomography scans of the heart. Med Phys 1998;25:2417–31.
9. Johnson GA, Godwin JD, Fram EK. Gated multiplanar cardiac computed tomography. Radiology 1982;145:195–7.
10. Hu H, He HD, Foley WD, et al. Four multidetector-row helical CT: image quality and volume coverage speed. Radiology 2000;215:55–62.
11. Becker CR, Schätzl M, Feist H, et al. Radiation dose for investigation of the chest and abdomen. Comparison of sequential, spiral and electron beam computed tomography. Radiologe 1998;38:726–9.
12. Kopp AF, Ohnesorge B, Flohr T, et al. Cardiac multidetector-row CT: first clinical results of retrospectively ECG-gated spiral with optimized temporal and spatial resolution. Röfo Fortschr Geb Röntgenstr Neuen Bildgeb Verfahr 2000;172:429–35.
13. Boese JM, Bahner ML, Albers J, et al. Optimization of temporal resolution in CT using retrospective ECG-gating. Radiologe 2000;40:123–9.
14. De Simone R, Glombitza G, Vahl CF, Albers J, Meinzer HP, Hagl S. Assessment of mitral regurgitant jets by three-dimensional color Doppler. Ann Thorac Surg 1999;67:494–9.
15. Koyama Y, Matsuoka H, Higasino H, et al. Four-dimensional cardiac image by helical computed tomography. Circulation 1999;100:e61–2.
16. Mochizuki T, Murase K, Higashino H, et al. Demonstration of acute myocardial infarction by subsecond spiral computed tomography. Early defect and delayed enhancement. Circulation 1999;99:2058–9.