

# Determination of left ventricular wall thickness and muscle mass by intravenous digital subtraction angiocardiology: validation of the method

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*Left ventricular (LV) wall thickness and muscle mass are important measures of LV hypertrophy. In 24 patients LV end-diastolic wall thickness and muscle mass were determined (two observers) by digital subtraction angiocardiology (DSA) and conventional LV angiocardiology (LVA). Wall thickness was determined over the anterolateral wall of the left ventricle according to the technique of Rackley (method 1) or by planimetry (method 2). Seventeen patients were studied at rest and seven during dynamic exercise. Wall thickness correlated well between LVA and DSA; the best correlations were obtained by a combined subtraction mode using either method 1 or 2 (method 1,  $r \geq 0.80$ ; method 2,  $r \geq 0.75$ ). The standard error of estimate of the mean (SEE) was slightly lower for method 2 ( $\leq 10\%$ ) than for method 1 ( $\leq 13\%$ ). DSA significantly overestimated wall thickness by 5–7% with method 1 and underestimated by 12–14% with method 2. Muscle mass correlated well between LVA and DSA; the SEE was  $\leq 15\%$  for method 1 and  $\leq 12\%$  for method 2. Overestimation of muscle mass by DSA was 7–11% with method 1 and underestimation was 13–15% with method 2.*

*It is concluded that LV wall thickness can be determined accurately by DSA with an SEE ranging between 10 and 13%. Determination of LV muscle mass is slightly less accurate and the SEE is slightly larger ranging between 13 to 17%. With method 1, wall thickness and muscle mass were over estimated and with method 2 underestimated.*

## Introduction

Left ventricular LV wall thickness and muscle mass are important measures of LV hypertrophy. Determination of LV wall thickness can be performed by several non-invasive techniques such as echocardiography, computer tomography or magnetic resonance<sup>[1–5]</sup>. As most of these techniques do not allow accurate wall thickness measurements at rest and during exercise, angiocardiological methods<sup>[6]</sup> are often used for assessment of LV wall thickness and muscle mass<sup>[7,8]</sup>. The purpose of the present study was to evaluate the accuracy of digital subtraction angiocardiology for determination of LV end-diastolic wall thickness and muscle mass at rest and during bicycle exercise. Three different

subtraction modes<sup>[9]</sup> and two different methods for LV wall thickness determination were tested and the results were compared to wall thickness and muscle mass data obtained from conventional LV angiocardiology. Conventional cinefilm was used as a data carrier for digital subtraction angiocardiology to guarantee high temporal and spatial resolution which is especially important during bicycle exercise.

## Patients and methods

Twenty-five patients (22 male, 3 female; 27–64 years of age, mean 51 years) who underwent cardiac catheterization for routine diagnostic purposes were included in the present study. These patients were selected from a previous study on the comparison of digital subtraction angiocardiology with conventional contrast ventriculography<sup>[9]</sup>. Coronary artery disease was diagnosed in 24 patients. One patient had normal coronary arteries. One of the 25 patients had to be excluded for technical reasons.

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Seventeen of the 24 patients with coronary artery disease had a history of myocardial infarction (one posterior, six inferior, seven anterior and three infarctions which could not be localized in the ECG).

The patients at rest had first conventional left ventricular cineangiography in the right anterior oblique projection (RAO) with injection of 45 ml Urographin 76% ( $12 \text{ ml s}^{-1}$ ) into the left ventricle with a 8F-pigtail catheter. The angiogram was recorded on cinefilm by means of a Siemens Angioscope system at a frame rate of 50 frames  $\text{s}^{-1}$ . Simultaneously, a standard lead of the ECG and a numerical code which also appeared on the cinefilm were recorded on an oscillograph (Electronics for Medicine VR12) at a paper speed of  $250 \text{ mm s}^{-1}$ . After the first angiogram, an interval of 15 min was allowed for dissipation of the hemodynamic effects of the contrast agent. Then, a second injection of 45 ml Urographin ( $15 \text{ ml s}^{-1}$ ) was performed into the superior vena cava. The entire sequence starting one or two heart cycles before the injection and ending after the contrast agent had passed through the left ventricle was recorded on cinefilm at the same frame rate of 50 frames  $\text{s}^{-1}$ . During the passage of the contrast agent from the vena cava to the left ventricle, the patients were asked to stop breathing to avoid misregistration from patient motion.

Seven patients were studied during bicycle exercise at a mean workload of 55 W (range 50–75 W) for 2 min. The exercise test was carried out at a low or a moderate workload because it had to be performed twice and the patients had to stop breathing. At the end of the exercise period, conventional RAO LV cineangiography was carried out first by injection of 60 ml Urographin 76% into the left ventricle with a flow rate of  $16\text{--}18 \text{ ml s}^{-1}$ . After the first angiogram, an interval of 15 min was allowed for dissipation of the hemodynamic effects of the contrast agent. Then, the bicycle exercise test was repeated at the same workload and duration as before and 60 ml Urographin 76% (flow rate  $16\text{--}18 \text{ ml s}^{-1}$ ) were injected into the superior vena cava. No patient experienced angina pectoris during the exercise test.

At the end of the procedure, a metal sphere of known diameter (6 cm) was filmed to correct for radiographic magnification and pincushion distortion.

#### DIGITAL IMAGE PROCESSING

The cinefilm was scanned on a computer-assisted

(VAX 750) image processing system with a modified Vanguard XR-35 film-projector and a high resolution photodiode camera (Eikonix 78/99). The observer entered the numbers of the desired frames for digitization at the computer terminal. The cinefilm was transported automatically under computer control. Individual image points were digitized with 12-bit resolution and stored on disk, averaged and subtracted on an image processor with  $512 \times 512$  pixels resolution. Two to four frames were usually digitized and averaged to reduce image noise. From the averaged image the mask was subtracted to increase image contrast. After subtraction, the image was linearly amplified to extend the brightness over the whole dynamic range of the image processing system<sup>[9]</sup>.

Three different subtraction modes were tested to determine the most accurate technique for left ventricular mass determination with conventional angiograms as the reference method<sup>[9]</sup>.

#### MASK MODE SUBTRACTION (MMS)

The subtraction mask was usually taken before the agent was injected into the patient at the beginning of the film sequence<sup>[9-11]</sup>. In certain patients the mask was taken at the end of the film sequence when the contrast agent had passed the left ventricle because of movement between the initial lung passage and the contrast sequence (Fig. 1).

#### TIME INTERVAL DIFFERENCE (TID)

Time interval difference imaging was based on the same algorithm as the mask mode subtraction except that the time between the mask and the opacified image was very short<sup>[9,12]</sup>, in the range of 60–100 ms (Fig. 1). As a result, rapidly moving objects are visualized accurately in the TID mode whereas stationary and slowly moving parts are subtracted and hence not seen. TID images were usually less noisy than MMS images because averaging of multiple frames did not have to be performed.

#### MMS AND TID MODE (COMBINED METHOD)

A combined method which allowed sequential superimposition of MMS and TID images was used<sup>[9]</sup> to take advantage of the relative imaging strengths of each method (e.g. the TID mode was used to determine the rapidly moving sections of the LV wall and MMS was used to detect the slowly moving parts of the wall) (Fig. 1).

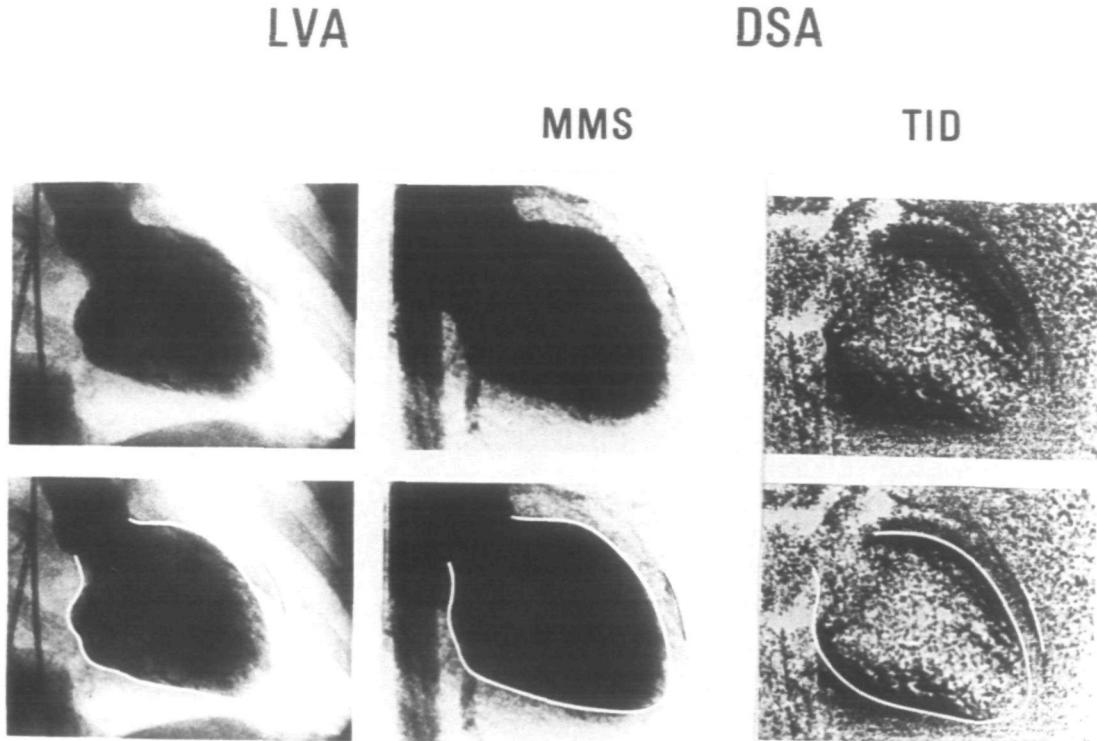


Figure 1 Conventional (LVA; left), mask mode (MMS; middle) and time interval difference (TID; right) subtracted angiograms. The upper panels show the end-diastolic silhouettes as they are displayed on the video monitor and the lower panels show the silhouettes after completion of the contour detection. The left ventricular wall thickness can be identified in all three images at the anterolateral region of the left ventricle.

#### CONTOUR DETECTION AND VOLUME CALCULATION

Contour detection and LV volume determination have been described previously<sup>[9]</sup>. In the meantime, the system has been adapted for LV wall thickness and muscle mass determination. The silhouette was traced by a semi-automatic contour detection algorithm on the high-resolution monitor. As noise and motion artifacts often lead to poor image quality, a fully automatic contour detection of the ventricle was not used. Boundary detection was performed on the monitor using a 'mouse' controlled cursor. Two observers selected a variable number of boundary points which were connected by a cubic spline function<sup>[9]</sup>. Usually, a set of 10–15 points resulted in an acceptable definition of the LV contour. This method was used for MMS, TID and, in an extended implementation, also for the combined MMS and TID method. In the combined subtraction mode, the LV contour was determined by the

MMS image alternating with the TID image which was exactly superimposed over the MMS image with retention of previously selected boundary points. According to Rackley and coworkers<sup>[16]</sup> LV wall contour was delineated at the lateral edge of the RAO cardiac silhouette and its average thickness was determined using two different methods (Fig. 1):

- method 1: LV end-diastolic wall thickness was determined according to the technique of Rackley using the average wall thickness of multiple wall diameters which were inscribed orthogonally to the epicardial border;
- method 2: LV end-diastolic wall thickness was determined by planimetry of the wall segment dividing the wall area by its midwall length.

Wall thickness can be delineated due to the fact

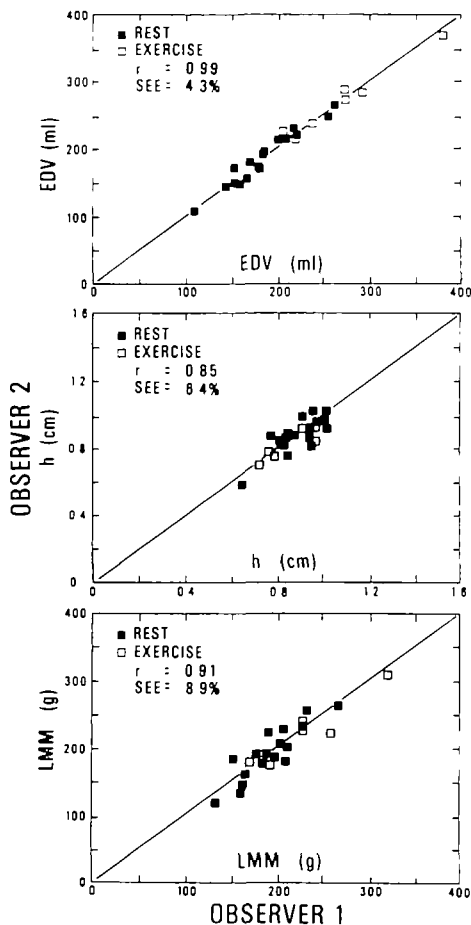


Figure 2 Interobserver comparison for end-diastolic volume (EDV, upper panel), LV end-diastolic wall thickness (h, middle panel) and LV muscle mass (LMM, lower panel) using conventional angiography. All three parameters show an excellent correlation between the two observers with a standard error of estimate of the mean (SEE) smaller than 10%.

that the myocardium is already opacified at the time of digitisation, otherwise it would have been subtracted.

LV volume was calculated using the 'area-length' method for monoplane angiograms<sup>[13]</sup> and left ventricular muscle mass (LMM) was calculated according to Rackley and coworkers<sup>[6]</sup> as follows:

$$\text{LMM} = 1.05 \left\{ \left[ \frac{4\pi}{3} \right] \left( \frac{L}{2} + h \right) \left( \frac{D}{2} + h \right)^2 \right\} - \text{LVEDV}$$

where L is the LV end-diastolic long axis in the RAO view, D is the LV end-diastolic short axis in

the RAO view calculated according to the 'area-length' method<sup>[13]</sup>, h is the LV end-diastolic wall thickness. LVEDV is the LV end-diastolic volume, and  $1.05 \text{ g ml}^{-1}$  the specific gravity of heart muscle. All parameters were determined by two independent observers from conventional angiograms as well as from digital angiograms using the MMS, TID and MMS+TID techniques. The correlations for LV end-diastolic volume, LV end-diastolic wall thickness and LV muscle mass (Fig. 2) were excellent between the two observers using conventional angiography.

#### STATISTICAL METHODS

Data obtained by digital subtraction angiography and LV angiography were compared by a paired Student's *t*-test; rest and exercise data were compared by an unpaired Student's *t*-test.

A linear regression analysis was used to compare data obtained by digital subtraction and conventional LV angiography. The line of identity is indicated in all the Figures and the correlation coefficient (*r*) and the standard error of estimate (SEE) were calculated for both observers and all comparisons. The mean difference (*d*) and the standard deviation of the mean difference were calculated according to the technique of Bland and Altman<sup>[14]</sup>. It was found that the standard deviation of the mean difference and the standard error of estimate of the regression analysis are very similar with only small variations. The correlation between these two measures was very good with a correlation coefficient of 0.92 for LV volume, 0.91 for wall thickness, and 0.96 for muscle mass determination. This observation can be explained by the fact that the mean difference between two measurements (*d*) and the residuals between the observed data and the calculated regression line (standard error of estimate) are almost identical when the slope of the regression line between two variables (digital subtraction angiography vs. LV angiography) is close to 1. Thus, only standard errors of estimate are reported in the present paper.

In all the Figures and Tables, mean  $\pm 1$  standard deviation are given.

#### Results

Conventional and digitally subtracted angiograms for wall thickness determination are shown in Fig. 1. The MMS and TID subtraction were used in the digital subtraction angiogram for delineation

Table 1 Standard hemodynamic data

	LVA			DSA		
	HR	LVEDP	LVSP	HR	LVEDP	LVSP
<i>Rest</i>						
Mean	66	17	132	66	19	142
±SD	15	7	22	18	7	27
<i>Exercise</i>						
Mean	95	31	148	97	31	142
±SD	8	7	10	12	9	20
<i>P</i> (rest vs. ex.)	<0.001	<0.001	NS	<0.001	<0.005	NS

LVA, left ventricular angiocardiography; DSA, digital subtraction angiocardiography; HR, heart rate (bpm); LVEDP, left ventricular end-diastolic pressure (mmHg); LVSP, left ventricular peak systolic pressure (mmHg); SD, standard deviation; ex, exercise; *P*, probability; NS, not significant.

Table 2 Left ventricular angiocardiography versus digital subtraction angiocardiography (method 1)

	LVA			DSA						
	EDV	h	LMM	MMS			TID		MMS+TID	
				EDV	h	LMM	h	LMM	h	LMM
<i>Rest</i>										
<b>OB 1</b>										
Mean	185	0.87	189	198	0.97	220	0.93	228	0.94	218
±SD	39	0.12	40	35	0.17	49	0.15	59	0.18	56
<b>OB 2</b>										
Mean	189	0.89	194	196	0.91	201	0.90	203	0.93	211
±SD	40	0.11	39	35	0.13	37	0.17	55	0.14	49
<i>Exercise</i>										
<b>OB 1</b>										
Mean	268	0.84	226	255	0.98	248	0.88	244	0.89	231
±SD	58	0.13	60	63	0.14	49	0.15	59	0.12	59
<b>OB 2</b>										
Mean	272	0.82	219	256	0.95	253	0.88	233	0.87	228
±SD	52	0.09	47	48	0.10	54	0.12	57	0.13	53
<i>P</i> (rest vs. ex.)										
OB 1	<0.001	NS	NS	<0.01	NS	NS	NS	NS	NS	NS
OB 2	<0.001	NS	NS	<0.01	NS	NS	NS	NS	NS	NS
<i>P</i> (OB 1 vs. OB 2; n=24)										
	NS	NS	NS	NS	<0.05	NS	NS	NS	NS	NS
<i>P</i> (LVA vs. DSA; n=24)										
OB 1				NS	<0.005	<0.001	NS	<0.05	<0.005	<0.005
OB 2				NS	NS	<0.050	NS	NS	<0.020	<0.010

MMS, mask mode subtraction; TID, time interval difference subtraction; EDV, end-diastolic volume (ml); h, end-diastolic wall thickness (cm); LMM, left ventricular muscle mass (g); OB, observer; other abbreviations are as in Table 1.

Table 3 Left ventricular angiocardiography and digital subtraction angiocardiography (method 2)

	LVA		DSA					
			MMS		TID		MMS+TID	
	h	LMM	h	LMM	h	LMM	h	LMM
<i>Rest</i>								
OB 1								
Mean	0.89	190	0.81	174	0.76	164	0.78	170
±SD	0.10	33	0.14	38	0.11	37	0.13	41
OB 2								
Mean	0.89	193	0.75	191	0.72	158	0.76	164
±SD	0.11	39	0.12	35	0.13	40	0.12	37
<i>Exercise</i>								
OB 1								
Mean	0.84	226	0.83	189	0.73	197	0.73	184
±SD	0.10	51	0.10	35	0.12	50	0.08	45
OB 2								
Mean	0.82	219	0.79	203	0.77	185	0.72	182
±SD	0.08	47	0.08	42	0.11	47	0.10	43
<i>P (rest vs. ex.)</i>								
OB 1	NS	NS	NS	NS	NS	NS	NS	NS
OB 2	NS	NS	NS	NS	NS	NS	NS	NS
<i>P (OB 1 vs. OB 2; n=24)</i>								
	NS	NS	<0.020	NS	NS	NS	NS	NS
<i>P (LVA vs. DSA; n=24)</i>								
OB 1			<0.050	<0.010	<0.001	<0.005	<0.001	<0.001
OB 2			<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Abbreviations as in Table 1 and 2.

of LV wall thickness. The TID image allows a better delineation of the endo- and epicardial border of LV wall thickness than the MMS image due to its better resolution.

#### HEMODYNAMIC MEASUREMENTS

Heart rate, LV end-diastolic and peak systolic pressure were similar during conventional and digital subtraction angiocardiography at rest and during exercise (Table 1). Heart rate and LV end-diastolic pressure were significantly higher during exercise than at rest.

#### COMPARISON OF LV ANGIOCARDIOGRAPHIC DATA.

##### LVA VERSUS DSA

Data for method 1 are given in Table 2 and for method 2 in Table 3.

##### Method 1

*LV volume.* LV end-diastolic volume was not significantly different at rest and during exercise

Table 4 Correlation coefficients ( $\tau$ ) and standard error of the mean (SEE) for LV volume determination

	$r$	$P$	SEE (%)
<i>(a) LVA vs. DSA (n=24)</i>			
EDV <sub>LVA</sub> vs EDV <sub>DSA</sub> (MMS+TID)			
OB 1			
Rest	0.93	<0.001	7
Exercise	0.99	<0.001	4
All	0.96	<0.001	7
OB 2			
Rest	0.92	<0.001	8
Exercise	0.98	<0.001	4
All	0.96	<0.001	6
<i>(b) OB 1 vs. OB 2 (n=24)</i>			
EDV <sub>LVA</sub>			
Rest	0.98	<0.001	5
Exercise	0.99	<0.001	4
All	0.99	<0.001	4
EDV <sub>DSA</sub> (MMS+TID)			
Rest	0.98	<0.001	4
Exercise	0.99	<0.001	3
All	0.98	<0.001	5

Abbreviations are as in Tables 1 and 2.

between conventional and digital subtraction angiocardiology. LV end-diastolic volume was overestimated by 4–7% ( $P < 0.02$ ) at rest but underestimated by 5–6% ( $P < 0.001$ ) during exercise using digital subtraction angiocardiology.

thickness and muscle mass were systematically overestimated at rest and during exercise by digital subtraction angiocardiology with MMS, TID and MMS+TID subtraction when compared to conventional angiocardiology. In two patients, neither observer was able to trace LV wall thickness

*LV wall thickness and muscle mass.* LV wall

Table 5 Correlation coefficients ( $r$ ) and standard error of estimate of the mean (SEE) for LV wall thickness and muscle mass determination (LVA vs DSA): methods 1 and 2

	Method 1			Method 2			
	$r$	$P$	SEE (%)	$r$	$P$	SEE (%)	
$h_{LVA}$ vs. $h_{MMS}$ ( $n = 22$ )							
OB 1	Rest	0.72	<0.005	14	0.69	<0.005	12
	Ex.	0.05	NS	19	0.25	NS	13
	All	0.49	<0.025	12	0.44	<0.050	14
OB 2	Rest	0.66	<0.010	11	0.52	<0.050	12
	Ex	0.14	NS	13	0.05	NS	11
	All	0.84	<0.025	12	0.34	NS	12
$h_{LVA}$ vs. $h_{TID}$ ( $n = 24$ )							
OB 1	Rest	0.64	<0.010	13	0.59	<0.020	11
	Ex.	0.42	NS	18	0.44	NS	14
	All	0.59	<0.050	14	0.55	<0.005	11
OB 2	Rest	0.60	<0.020	16	0.47	NS	14
	Ex.	0.63	NS	12	0.61	<0.005	5
	All	0.59	<0.050	15	0.55	<0.010	12
$h_{LVA}$ vs. $h_{MMS+TID}$ ( $n = 24$ )							
OB 1	Rest	0.79	<0.001	13	0.80	<0.001	9
	Ex.	0.86	<0.020	8	0.85	<0.020	6
	All	0.84	<0.001	10	0.81	<0.001	8
OB 2	Rest	0.83	<0.001	9	0.76	<0.001	9
	Ex.	0.66	NS	13	0.68	NS	10
	All	0.80	<0.001	10	0.75	<0.001	9
$LMM_{LVA}$ vs. $LMM_{MMS}$ ( $n = 22$ )							
OB 1	Rest	0.76	<0.005	18	0.75	<0.005	14
	Ex.	0.60	NS	19	0.69	NS	12
	All	0.69	<0.001	19	0.72	<0.001	13
OB 2	Rest	0.71	<0.005	14	0.62	<0.020	14
	Ex.	0.65	NS	20	0.60	NS	17
	All	0.72	<0.001	17	0.66	<0.001	16
$LMM_{LVA}$ vs. $LMM_{TID}$ ( $n = 24$ )							
OB 1	Rest	0.56	<0.020	25	0.70	<0.005	14
	Ex.	0.84	<0.020	15	0.28	NS	23
	All	0.63	<0.005	22	0.58	<0.005	18
OB 2	Rest	0.72	<0.005	20	0.66	<0.005	16
	Ex.	0.82	<0.050	17	0.88	<0.010	11
	All	0.77	<0.001	18	0.76	<0.001	14
$LMM_{LVA}$ vs. $LMM_{MMS+TID}$ ( $n = 24$ )							
OB 1	Rest	0.85	<0.001	16	0.83	<0.001	12
	Ex.	0.93	<0.005	11	0.93	<0.005	7
	All.	0.85	<0.001	15	0.83	<0.001	12
OB 1	Rest	0.91	<0.001	11	0.84	<0.001	11
	Ex.	0.77	<0.050	17	0.80	<0.050	13
	All	0.86	<0.001	13	0.83	<0.001	11

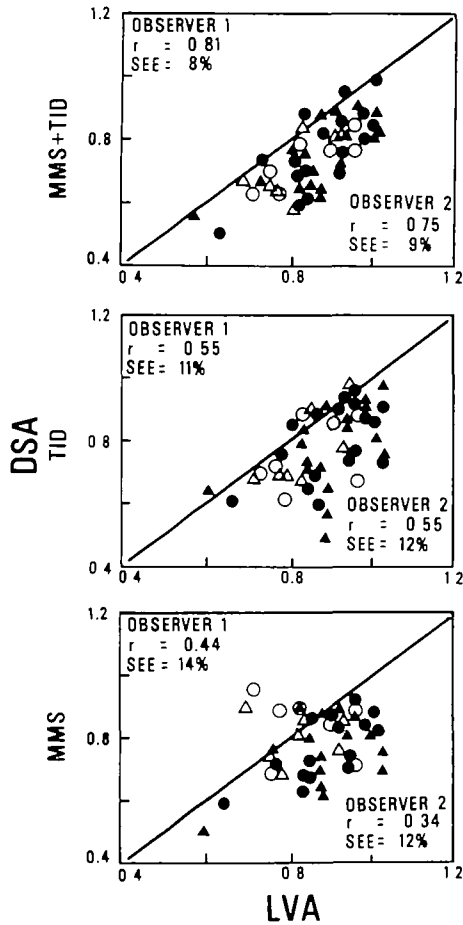


Figure 3 Intraobserver comparisons for LV end-diastolic wall thickness (cm) between digital subtraction (DSA; ordinate) and conventional LV angiography (LVA; abscissa). Correlation coefficient ( $r$ ) and standard error of estimate of the mean (SEE) are given separately for observer 1 (●, rest; ○, exercise) and 2 (▲, rest; △, exercise) with mask mode (MMS; lower panel), time-interval difference (TID; middle panel) and combined subtraction (MMS+TID; upper panel) using method 2. The best correlations were observed for the combined subtraction mode with standard errors of 8 and 9% (of LVA wall thickness), respectively.

using MMS subtraction due to low-contrast images. LV wall thickness was overestimated by 5–7% ( $P < 0.02$ ) and LV muscle mass by 7–11% ( $P < 0.01$ ) using digital subtraction angiography (MMS+TID subtraction).

#### Method 2

*LV wall thickness and muscle mass.* LV wall

thickness and muscle mass were systematically underestimated at rest and during exercise by digital subtraction angiography with MMS, TID and MMS+TID subtraction when compared to conventional angiography. Underestimation was 12–14% ( $P < 0.001$ ) for LV wall thickness (MMS+TID subtraction) and 13–15% ( $P < 0.001$ ) for LV muscle mass (MMS+TID subtraction).

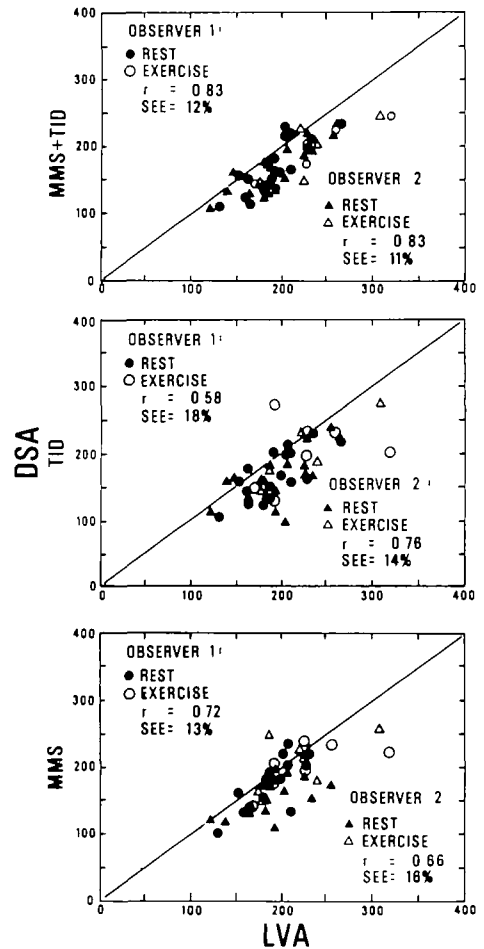


Figure 4 Intraobserver comparisons for LV muscle mass (g) between digital subtraction (DSA; ordinate) and conventional LV angiography (LVA; abscissa). Correlation coefficient ( $r$ ) and standard error of estimate of the mean (SEE) are given for observers 1 and 2 with mask mode (MMS; lower panel), time-interval difference (TID; middle panel) and combined subtraction (MMS+TID; upper panel) using method 2. The best correlations were observed for the combined subtraction mode with standard errors of 12 and 11% (of LVA muscle mass), respectively.



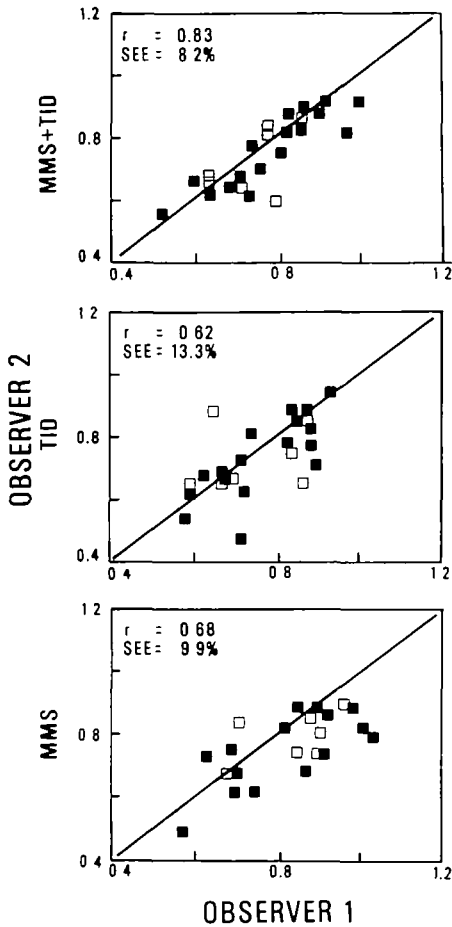


Figure 5 Interobserver comparison for LV end-diastolic wall thickness (cm) using digital subtraction angiography (DSA). Correlation coefficient ( $r$ ) and standard error of estimate of the mean (SEE) are given for mask mode (MMS; lower panel), time interval difference (TID; middle panel) and combined subtraction (MMS+TID; upper panel) using method 2. The best correlation is observed with the combined subtraction mode; the SEE amounting to 8%. ■, Rest; □, Exercise.

#### INTRA- AND INTEROBSERVER COMPARISON OF LV END-DIASTOLIC VOLUME; LVA VERSUS DSA

High correlation coefficients ( $\geq 0.92$ ) with a small standard error of estimate of the mean ( $\leq 8\%$ ) were found for both observers between conventional and digital angiography (Table 4). Interobserver data also showed high correlation coefficients ( $\geq 0.98$ ) with a small standard error of estimate of the mean ( $\leq 5\%$ ) for both conventional and digital subtraction angiography (Table 4).

#### INTRAOBSERVER COMPARISON FOR LV WALL THICKNESS AND MUSCLE MASS; LVA VERSUS DSA

Both methods showed similar results for LV wall thickness and muscle mass determination by LV angiography and digital subtraction angiography (Table 5, Figs 3 and 4). Method 2 showed similar correlations but smaller standard errors of estimate of the mean than method 1. The correlations between conventional and digital subtraction angiography were similar for rest and exercise data but the best correlations were observed with the combined subtraction technique (MMS+TID) for both wall thickness (Fig. 3) and muscle mass (Fig. 4). The lowest correlations were shown with the mask mode subtraction (MMS) followed by the time interval difference subtraction (TID). The smallest standard error of estimate of the mean was observed with method 2 using the combined subtraction mode: the error was  $\leq 10\%$  for wall thickness and  $\leq 13\%$  for muscle mass determination (Figs 3 and 4).

#### INTEROBSERVER COMPARISONS FOR LV VOLUME, WALL THICKNESS AND MUSCLE MASS; Table 4b and 6, Figs 2 and 5

Correlation coefficients and standard errors of estimate of the mean were excellent for interobserver comparison of LV volume, wall thickness and muscle mass (Fig. 2) using conventional angiography. Interobserver comparison of LV wall thickness using digital subtraction angiography (Fig. 5) showed good correlations for mask mode subtraction (MMS) and combined subtraction (MMS+TID) with a standard error of estimate of the mean of less than 10%. The correlation between the two observers was slightly less good for time-interval difference (TID) subtraction. Similar data were observed for LV muscle mass (Table 6) although the standard error of estimate of the mean was generally higher than for LV wall thickness. There was no differences in correlation coefficients for method 1 or 2 and for data at rest and during exercise, although the agreement of the data during exercise tended to be less good than that of the data recorded at rest.

#### Discussion

LV wall thickness and muscle mass have been used for the assessment of LV hypertrophy in different forms of cardiac disease<sup>[7,8,15]</sup>. Severe myocardial hypertrophy has been shown to be associated with a poor postoperative outcome in patients with

chronic pressure and volume overload due to aortic valve disease<sup>[15-18]</sup>. Thus, LV wall thickness and muscle mass are important determinants for post-operative outcome and prognosis in patients with valvular heart disease<sup>[16]</sup>. Several methods have been used for the assessment of LV wall thickness and muscle mass including several non-invasive (echocardiography, computer tomography and magnetic resonance<sup>[1-4,15,19-23]</sup>) and invasive techniques (angiocardiology and digital subtraction angiocardiology<sup>[6,9,24]</sup>). Angiocardiology has been, and is still, the reference method for assessing myocardial muscle mass in man<sup>[6]</sup>. It has been shown that angiocardiology provides excellent correlation with post-mortem determinations of muscle mass<sup>[6,25]</sup>. Similar correlation can be

obtained with magnetic resonance<sup>[4]</sup> due to its high resolution and good structural recognition capabilities<sup>[19]</sup>. One limiting factor is, however, the long sampling time which renders the method especially sensitive to motion artifacts.

In the present study, we evaluated the accuracy of digital subtraction angiocardiology for the assessment of LV end-diastolic wall thickness and muscle mass not only at rest but also during supine bicycle exercise. Determination of LV wall thickness is important for calculation of LV wall stress and stress-shortening relations to identify patients with resting or exercise-induced myocardial dysfunction. Furthermore, estimation of LV muscle mass from rest to exercise represents an easy and simple test for assessing the accuracy of muscle-mass

Table 6 Interobserver variability of LV volume, wall thickness and muscle mass determination (OB 1 vs. OB 2): methods 1 and 2

	Method 1			Method 2		
	<i>r</i>	<i>P</i>	SEE (%)	<i>r</i>	<i>P</i>	SEE (%)
<i>h</i> <sub>LVA</sub> ( <i>n</i> = 24)						
Rest	0.88	<0.001	6.4	0.85	<0.001	6.7
Ex.	0.87	<0.020	6.1	0.87	<0.010	5.3
All	0.87	<0.001	6.4	0.85	<0.001	6.4
<i>h</i> <sub>MMS</sub> ( <i>n</i> = 22)						
Rest	0.79	<0.001	8.6	0.72	<0.005	10.4
Ex.	0.48	NS	9.5	0.50	NS	8.9
All	0.72	<0.001	8.8	0.68	<0.001	9.9
<i>h</i> <sub>TID</sub> ( <i>n</i> = 24)						
Rest	0.76	<0.001	12.5	0.75	<0.001	12.2
Ex.	0.25	NS	14.2	0.21	NS	15.1
All	0.65	<0.001	13.3	0.62	<0.005	13.3
<i>h</i> <sub>MMS+TID</sub> ( <i>n</i> = 24)						
Rest	0.95	<0.001	4.8	0.89	<0.001	6.8
Ex.	0.62	NS	11.4	0.55	NS	13.0
All	0.88	<0.001	7.0	0.83	<0.001	8.2
LMM <sub>LVA</sub> ( <i>n</i> = 24)						
Rest	0.91	<0.001	8.8	0.90	<0.001	9.5
Ex.	0.92	<0.005	9.7	0.94	<0.005	7.7
All	0.92	<0.001	8.9	0.91	<0.001	8.9
LMM <sub>MMS</sub> ( <i>n</i> = 22)						
Rest	0.80	<0.001	10.5	0.69	<0.005	13.7
Ex.	0.57	NS	19.5	0.51	NS	19.8
All	0.72	<0.001	15.2	0.66	<0.001	17.0
LMM <sub>TID</sub> ( <i>n</i> = 24)						
Rest	0.84	<0.001	14.5	0.83	<0.001	14.0
Ex.	0.47	NS	22.5	0.36	NS	24.6
All	0.73	<0.001	17.7	0.69	<0.001	18.4
LMM <sub>MMS+TID</sub> ( <i>n</i> = 24)						
Rest	0.95	<0.001	7.3	0.92	<0.001	8.9
Ex.	0.80	<0.050	14.9	0.80	<0.050	15.2
All	0.91	<0.001	9.6	0.88	<0.001	10.6

Table 7 Data from the literature for comparison of LV wall thickness and muscle mass determination with echocardiography and digital subtraction angiography

Echocardiography	<i>n</i>	<i>r</i>	SEE (mm)	SEE (%)	Mean <sub>echo</sub> (mm)	Mean <sub>angio</sub> (mm)	<i>P</i>
LV wall thickness							
Troy <i>et al.</i> <sup>(1)</sup>	24	0.89	1.3	14	8.5	9.2	<0.025
Hahn <i>et al.</i> <sup>(20)</sup>	18	0.29	—	—	—	—	—
Sjoegren <i>et al.</i> <sup>(21)*</sup>	20	0.77	4.0	26	15.4	15.3	NS
Murray <i>et al.</i> <sup>(22)</sup>	21	0.77	1.9	21	8.8	9.8	<0.020
LV muscle mass							
Troy <i>et al.</i> <sup>(1)</sup>	24	0.88	(g)	(%)	(g)	(g)	<0.020
Hahn <i>et al.</i> <sup>(20)</sup>	18	0.73	49	20	214	246	—
Sjoegren <i>et al.</i> <sup>(21)*</sup>	—	—	—	—	—	—	—
Murray <i>et al.</i> <sup>(22)</sup>	21	0.83	55	46	120	249	<0.001
Digital subtraction angiography	<i>n</i>	<i>r</i>	SEE (mm)	SEE (%)	Mean <sub>DSA</sub> (mm)	Mean <sub>angio</sub> (mm)	<i>P</i>
LV wall thickness							
Lauber <i>et al.</i> <sup>(24)</sup>	20	0.74	1.6	16	10.2	11.0	NS
Own data (method 2)†	24	0.81	0.7	9	7.7	8.9	<0.001
LV muscle mass							
Lauber <i>et al.</i> <sup>(24)</sup>	20	0.85	(g)	(%)	(g)	(g)	NS
Own data (method 2)†	24	0.83	50	19	260	285	<0.001

\*Systolic and diastolic data.

†Represent the mean of both observers for resting data

Abbreviations as in Tables 1 and 2. Conventional LV angiography was used as the reference method for both echocardiography and digital subtraction angiography.

determination under varying loading conditions with a change in heart size and wall thickness. Conventional LV angiography was used as the reference method for wall-thickness and muscle-mass determination. The advantage of digital subtraction angiography is related to the semi-invasive nature of the technique which allows evaluation of patients on an ambulatory basis and also during exercise. The high resolution of angiography and the determination of the maximal outer border (not a tomographic section as with echocardiography, computer tomography or magnetic resonance) by angiographic techniques allow a more accurate determination of LV muscle mass due to the fact that LV geometry is obtained more exactly than with most other techniques. It is obvious that digital subtraction angiography produces images which are similar to conventional angiography. Thus, a comparison between these two techniques seems to be appropriate to test the validity of digital subtraction angiography for LV wall-thickness and muscle-mass determination.

The present analysis shows that LV wall thickness and muscle mass can be determined accurately by digital subtraction angiography (Tables 5 and 6) but there was a significant over- (method 1) or underestimation (method 2) when compared to conventional angiography. This over- or underestimation of LV wall thickness and muscle mass is explained by the fact that the Rackley technique (method 1) is a better approximation of true wall thickness because it is based on the measurements of multiple wall diameters, whereas method 2 (planimetry) is based on an 'area-length' method which tends to underestimate true wall thickness<sup>(13)</sup>. Method 1 slightly overestimated true angiographic wall thickness by 5–7% ( $P < 0.02$ ), whereas method 2 underestimated true angiographic wall thickness by 12–14% ( $P < 0.001$ ). Similar data were obtained at rest and during exercise.

The specific subtraction mode is especially important in digital subtraction angiography for obtaining meaningful results of LV wall thickness and muscle mass. In a previous study<sup>(9)</sup> it was demonstrated that a combined subtraction mode

with mask mode (MMS) and time-interval difference (TID) subtraction for the determination of LV volumes and ejection fraction showed the best correlations between conventional and digital subtraction angiocardiology. A similar trend was observed in the present analysis, because correlations for LV wall thickness and muscle mass were best for the combined subtraction mode (Table 5) and worst for mask mode subtraction alone. Time-interval difference subtraction was somewhat better due to its high spatial resolution and good contour recognition capabilities for fast-moving LV regions (Table 5). Thus, the combined subtraction mode (MMS+TID) is recommended for the assessment of LV wall thickness and muscle mass by digital subtraction angiocardiology.

The standard error of estimate of the mean was larger for determination of LV muscle mass than wall thickness because the errors of measuring wall thickness and volume are added for calculation of LV muscle mass (Figs 3 and 4). Wall-thickness determination by method 1 (Rackley method) was somewhat less good with a larger standard error of estimate of the mean than method 2 (planimetry) probably due to the fact that method 2 reduces the measuring error by using wall thickness area rather than wall thickness diameter.

The interobserver comparison (Table 6) showed excellent results for LV wall thickness and muscle mass when conventional angiocardiology was used. The results for digital subtraction angiocardiology were less good than for conventional angiocardiology especially for data during exercise. The combined subtraction technique showed the best results with regard to interobserver variability; the standard error of estimate was smaller than 10% for data at rest, but larger than 10% for data during exercise.

When the present data are compared to results reported in the literature (Table 7) similar correlations are observed between conventional angiocardiology and digital subtraction angiocardiology. Most other authors, however, used either mask mode<sup>[5]</sup> or time-interval difference<sup>[24]</sup> subtraction but not a combined subtraction mode for LV wall-thickness determination. This probably explains the slightly smaller standard error of estimate of the mean in our study than those reported by others, although the correlation coefficients were similar. It is generally accepted that a reliable technique for assessment of cardiac dimensions should be associated with a standard error of estimate of the mean smaller or equal to 10% of the mean of the

reference technique; for example, when wall thickness is 10 mm and muscle mass 150 g, the technique with a standard error of estimate of the mean of 10% measures wall thickness to be between 9 and 11 mm and muscle mass between 135 and 165 g. In the present study a standard error of 10% or less was achieved for LV wall thickness, but a slightly larger standard error, namely 13% or less for LV muscle mass. However, most data reported in the literature (Table 7) do not fulfil this requirement, i.e. a standard error of more than 10% is reported. When these data from the literature and ours are compared with data obtained by other imaging techniques, such as echocardiography, a considerably larger standard error is observed (14–26% for wall thickness and 20–46% for muscle mass) than for digital subtraction angiocardiology.

Limitations of DSA for assessing LV wall thickness are related to misregistration of the subtraction mask and the iodinated frame which becomes especially important for mask-mode subtraction. Time-interval difference subtraction is almost insensitive to motion artifacts and produces a good contrast for the fast-moving ventricular wall but fails to detect local hypokinetic regions. Thus, a combination of both subtraction modes was used in the present study to optimize contour detection for the assessment of LV wall thickness. Another limiting factor of digital subtraction angiocardiology is related to the semi-invasive nature of the technique because a central venous catheter has to be placed for large volume injection with flow rates in the range of 12–18 ml s<sup>-1</sup>. Cineangiocardiology was used in the present study to guarantee high temporal (50 frames s<sup>-1</sup>) and spatial resolution. Most other authors<sup>[5,10–12]</sup> have used videoangiocardiology, but temporal (25 frames s<sup>-1</sup>) and spatial (256 × 256 pixel) resolution of the video system might be a limiting factor especially under exercise conditions with high heart rates. Further developments in the near future might, however, provide a cineangiographic system which allows triggered radiation at end-diastole and end-systole to limit radiation exposure but guarantee high-quality images.

Repeated contrast medium injections might be associated with alterations in basic hemodynamics and, therefore, affect the functional parameters of the left ventricle. This is not of great importance for assessing LV muscle mass, because this variable is not dependent on the actual loading conditions. The 'area-length' method was used for calculation of the LV short axis diameter according to the

technique of Rackley *et al.*<sup>[6]</sup>. This technique reduces the measuring error by calculating the short-axis diameter from the area and the long axis of the left ventricle<sup>[13]</sup>. Furthermore, the Rackley technique assumes uniform wall thickness around the left ventricle which in a strict sense is not true. However, validation of the Rackley technique by autopsy<sup>[6,25]</sup> showed excellent correlation between angiocardiology and direct measurements of LV mass. It is clear that this technique is not appropriate for calculation of LV muscle mass in the presence of myocardial infarction because of the thinning of LV wall thickness in the infarcted area. However, the purpose of the present study was to compare digital subtraction and conventional angiocardiology for assessing LV wall thickness and muscle mass. It was not the purpose of this study to test the validity of the Rackley technique for estimating LV muscle mass in patients with coronary artery disease.

In summary, subtraction angiocardiology is a reliable tool for assessing LV wall thickness at rest and during supine bicycle exercise. Determination of LV muscle mass is less accurate than that of LV wall thickness due to the fact that the measuring error of LV wall thickness and volume are added. Possible drawbacks of digital subtraction angiocardiology are motion artifacts at high workloads and the hemodynamic alterations induced by contrast dye injections. Other imaging techniques provide reasonably good estimates of LV wall thickness and muscle mass with a slightly larger standard error of estimate than for digital subtraction angiocardiology, but most of these techniques do not allow assessment of LV wall thickness and muscle mass under exercise conditions. A combined subtraction mode using method 2 was shown to be the most reliable technique for assessing LV wall thickness by digital subtraction angiocardiology.

## References

- [1] Troy BL, Pombo J, Rackley CE. Measurement of left ventricular wall thickness and mass by echocardiography. *Circulation* 1972; 45: 602-11.
- [2] Devereux RB, Casale PN, Eisenberg RR, Miller DH, Klingfield P. Electrocardiographic detection of left ventricular hypertrophy using echocardiographic determination of left ventricular mass as the reference standard. *J Am Coll Cardiol* 1984; 3: 82-7.
- [3] Miller SW, Dinsmore RE, Wittenberg J, Maturi RA, Powell WJ JR. Right and left ventricular volumes and wall measurements: determination by computed tomography in arrested canine hearts. *Am J Roentgenol* 1977; 129: 257-61.
- [4] Florentine MS, Grosskreutz CL, Chang W, *et al.* Measurement of left ventricular mass in vivo using gated nuclear magnetic resonance imaging. *J Am Coll Cardiol* 1986; 8: 107-12.
- [5] Radtke W, Buersch JH, Brennecke R, Hahne HJ, Heintzen PH. Assessment of left ventricular muscle volume by digital angiocardiology. *Invest Radiol* 1983; 18: 149-54.
- [6] Rackley CE, Dodge HT, Coble YD, Hay RE. A method for determining left ventricular mass in man. *Circulation* 1964; 29: 666-71.
- [7] Krayenbuehl HP, Hess OM, Schneider J, Turina M. Rückbildung der Herzhypertrophie bei Patienten mit operierten Aortenklappenfehlern. *Z Kardiol* 1985; 74 (Suppl 7): 145-52.
- [8] Kennedy JW, Twiss RD, Blackmon JR, Merendino KA. Hemodynamic studies one year after homograft aortic valve replacement. *Circulation* 1968; 37 (Suppl II): 110-8.
- [9] Birchler B, Hess OM, Murakami T, Niederer P, Anliker M, Krayenbuehl HP. Comparison of intravenous digital subtraction cineangiocardiology with conventional contrast ventriculography for the determination of the left ventricular volume at rest and during exercise. *Eur Heart J* 1985; 6: 497-509.
- [10] Brennecke R, Brown TK, Buersch J, Heintzen PH. Digital processing of videoangiocardiology image series using a mini computer. In: *Computers in cardiology*. St Louis, 1976: 255-60.
- [11] Vas R, Diamond GA, Forrester JS, Whiting JS, Swan HJC. Computer enhancement of direct and venous-injected left ventricular contrast angiography. *Am Heart J* 1981; 102: 719-28.
- [12] Lauber A, Fischbach T, Poelitz B, Schmiel FK, Spiller P, Loogen F. Digitale Subtraktionsangiographie. Genauigkeit der linksventrikulären Volumenbestimmung bei intravenöser Kontrastmittelinjektion. *Z Kardiol* 1983; 71: 262-7.
- [13] Sandler H, Dodge HT. Angiographic methods for determination of left ventricular geometry and volume. In: Mirsky I, Ghista DN, Sandler H, eds. *Cardiac mechanics*. New York: Wiley, 1974: 141-70.
- [14] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; I: 307-10.
- [15] Devereux RB, Reichek N. Left ventricular hypertrophy. *Cardiovasc Rev Rep* 1980; 1: 55-68.
- [16] Krayenbuehl HP, Hess OM, Schneider J, Turina M. Physiologic or pathologic hypertrophy. *Eur Heart J* 1983; 4 (Suppl A): 29-34.
- [17] Clark DG, McNulty JH, Rahimtoola SH. Valve replacement in aortic insufficiency with left ventricular dysfunction. *Circulation* 1980; 61: 411-21.
- [18] Herremans F, Ameur A, de Vernejoul F, *et al.* Pre- and postoperative haemodynamic and cineangiographic assessment of left ventricular function in patients with aortic regurgitation. *Am Heart J* 1979; 98: 63-72.
- [19] Fisher MR, von Schulthess GK, Higgins CB. Multiphasic cardiac magnetic resonance imaging: normal regional ventricular wall thickening. *Am J Roentgenol* 1985; 145: 27-30.
- [20] Hahn B, Bohn I, Strauer BE. Funktionsbeurteilung des Herzens mittels zweidimensionaler Echokardiographie: vergleichende Untersuchungen zur Cineangiographie

- und Erstellung von Normalwerten für Erwachsene. *Z Kardiol* 1982; 71: 445–51.
- [21] Sjoegren AL, Hytoenen I, Frick MH. Ultrasonic measurements of left ventricular wall thickness. *Chest* 1970; 57: 37–40.
- [22] Murray JA, Johnston FW, Reid JM. Echocardiographic determination of left ventricular dimension, volumes and performance. *Am J Cardiol* 1972; 30: 252–7.
- [23] Sasayama S, Franklin D, Ross Jr J, Kemper WS, McKown D. Dynamic changes in left ventricular wall thickness and their use in analyzing cardiac function in the conscious dog: A study based on a modified ultrasonic technique. *Am J Cardiol* 1976; 38: 870–9.
- [24] Lauber A, Deetjen W, Jehle J, Poelitz B, Schmiel FK, Spiller P. Digitale Subtraktionsangiographie: Genauigkeit der Messung von linksventrikulären Wanddicken und Wandvolumina bei intravenöser Kontrastmittelinjektion. *Z Kardiol* 1984; 73: 257–63.
- [25] Kennedy JW, Reichenbach DD, Baxley WA, Dodge HT. Left ventricular mass: a comparison of angiographic measurements with autopsy weight. *Am J Cardiol* 1967; 19: 221–3.