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New Technique for Evaluating Regional Myocardial Function Using SPAMM Tagging in Patients with Myocardial Infarction.

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ABSTRACT We utilized SPAMM tagging for estimating the myocardial regional strain during early diastole (ε) in patients with myocardial infarction. Normal volunteers (C; n=10), myocardial infarction patients with successful early reperfusion(R(+);n=10) and patients without reperfusion (R(−); n=10) were imaged one month after myocardial infarction. The circumferential distances between each tag in subendocardium and subepicardium were measured. In R(−), both ε epi and ε endo were remarkably reduced compared to C. Compared to R(−), R(+) showed significantly ameliorated εepi and εendo (both $p<0.01$). Thus, SPAMM tagging provides a useful tool for detecting subendocardial and subepicardial regional diastolic function in clinical setting and proved that early reperfusion therapy improved both subendocardial and subepicardial diastolic function.

Key words : Magnetic resonance imaging, Myocardial infarction, Regional wall motion

Introduction

Regional myocardial wall motion can be assessed by several methods, including echocardiography, radionuclide angiography, conventional ventriculography during cardiac catheterization and cine MRI (magnetic resonance imaging). Endocardial surface motion has been estimated by conventional ventriculography and cardiac radionuclide ventriculography. Transmural wall motion can be estimated by echocardiography and cine-MRI. However, intramural motion can not be estimated by any of these methods. Intramural motion has been observed by implanting metal markers or ultrasonic crystals within the wall of the left ventricle in animal studies(1, 2), but these methods are limited in clinical applications.

The use of magnetic tagging with MRI has made it possible to evaluate regional wall motion noninvasively (3, 4). Spatial modulation of magnetization (SPAMM) tagging creates many landmarks which can be tracked throughout the heart wall within milliseconds by using a sequence of nonselective radio-frequency pulses separated by magnetic field gradients(5, 6). We utilized SPAMM tagging to estimate both the early diastolic subendocardial and subepicardial strain and estimate the effects of reperfusion therapy 1 month after myocardial infarction.

Methods

Patient Population

Normal volunteers (C; n=10, six men, four women; mean age, 61years; range, 51- 71 years), myocardial infarction patients with successful early reperfusion (R(+); n=10, six men, four women; mean age, 60years; range, 44- 74 years) and patients without reperfusion (R(-); n=10, six men, four women; mean age, 61years; range, 44- 71 years) were imaged 1 month after myocardial infarction (Table1, 2). Patients with valvular heart disease or previous coronary revascularization were excluded. The reperfusion therapy was performed by PTCR (percutaneous transluminal coronary recanalization) or PTCA (percutaneous transluminal coronary angioplasty) and the TIMI (thrombolysis in myocardial infarction) grade 3 was considered successful reperfusion. Patients with unsuccessful reperfusion therapy or too late for reperfusion were included in non-reperfused group and was treated with conventional therapy.

Table 1. Data of normal volunteers

Subject	AGE	SEX	BSA	LVMI	EDV	ESV	EF	HR	BP
1	55	F	1.61	80	86	24	72	74	112/78
2	59	F	1.31	66	82	24	70	72	132/74
3	63	F	1.54	76	85	27	68	86	126/68
4	71	F	1.46	77	62	15	75	73	134/78
5	51	M	1.77	63	92	30	67	77	136/88
6	57	M	1.72	67	87	29	67	70	138/78
7	60	M	1.51	67	92	30	67	62	130/78
8	61	M	1.65	67	149	60	60	64	136/80
9	67	M	1.66	75	81	27	67	62	138/80
10	68	M	1.47	79	86	33	62	63	132/70
Mean	61		1.57	72	90	30	68	70	
SD	6		0.14	6	22	12	4	8	

BSA indicated body surface area (m^2); LVMI, left ventricle mass index (g/m^2); EDV, end-diastolic volume (ml); ESV, end-systolic volume (ml); EF, ejection fraction (%); HR, heart rate (beats/minute); and BP, blood pressure (mm Hg).

Table 2. Data of myocardial infaretion patients with and without early reperfusion

A:

Patient	AGE	SEX	RISK AREA	LVESP	LVEDP	PCWP	CI	EF	HR
1	55	M	A-S	118	11	7	2.7	53	60
2	71	F	A-S	160	22	9	2.6	45	72
3	61	M	A-S	138	22	6	2.2	43	65
4	53	M	A-S	114	12	6	2.4	36	62
5	63	F	A-S	129	10	4	2.4	33	60
6	67	F	A-S	142	14	6	2.5	46	72
7	64	M	Inf-Post	164	12	6	2.9	38	74
8	63	M	Inf-Post	148	14	5	2.7	52	80
9	44	M	Inf-Post	146	14	4	2.3	31	80
10	63	M	Inf-Post	140	12	6	2.5	45	71
Mean	61			140	14	6	2.5	42	70
SD	8			16	4	1	0.2	8	7

B:

Patient	AGE	SEX	RISK AREA	LVESP	LVEDP	PCWP	CI	EF	HR
1	56	M	A-S	132	11	5	2.8	57	63
2	71	M	A-S	140	5	4	2.6	53	67
3	44	F	A-S	128	2	13	3.7	49	94
4	45	F	A-S	146	3	9	2.6	63	83
5	65	F	A-S	132	8	4	3:1	59	85
6	56	M	A-S	132	5	11	3.9	57	69
7	69	M	Inf-Post	145	16	5	3.6	59	70
8	55	M	Inf-Post	124	27	12	2.5	41	65
9	62	F	Inf-Post	136	18	12	2.9	58	58
10	74	M	Inf-Post	141	22	8	2.9	52	60
Mean	60			136	12	8	3.1	55	71
SD	10			7	9	4	0.5	6	12

A: without reperfusion B: with early reperfusion
LVESP indicated left ventricular end-systolic pressure (mm Hg); LVEDP, left ventricular end-diastolic pressure (mm Hg);PCWP, pulmonary capillary wedge pressure (mm Hg); CI, cardiac index ($l/min/m^2$); EF, ejection fraction (%); HR, heart rate (beats/minute),A-S; antero-septum, Inf-Post; infero-posterior.

This protocol was approved by the ethical committee of this institute and the written informed consent was obtained from each patient.

1) Cine MRI imaging

MRI images were obtained using a 1.5 T superconducting magnet (Siemens, Magnetom H15). After the scout images were obtained, cine MRI of the long axis image of the left ventricle was obtained using double oblique technique as previously reported(5). Myocardial tagging was performed in the short-axis planes at two equidistant anatomic levels between heart base and apex. Short axis images of the mid ventricle were obtained. Slices thickness was 8 mm, flip angle was 30°, echo time 12 milliseconds, and three times signal averaging were used. Field of view was 33-cm and a 128×256 matrix was used.

2) SPAMM tagging imaging

The SPAMM tagging pulse sequence was performed at the timing of end-systole. End-systole was defined as the instant of minimum cavity area confirmed from the cine MRI of the mid-ventricle. A tagging grid with 7 mm stripe spacing and approximately 2 mm stripe width was generated. The orientation of tagging was in the short axis of the left ventricular and identical to the cine MRI images. Figure 1 shows time-area curve of left ventricle short axis from a normal volunteer using cine MRI. The SPAMM grid is generated at end systole, at 350 ms from R wave. SPAMM images were obtained at 390, 450, 510 and 570 ms after R wave.

3) Image analysis

Circumferential distances between each tag in subendocardial and subepicardial regions were measured by caliper method from the tracing of the magnified images and early diastolic circumferential strain (ε) was calculated as follows, $\varepsilon = (L510 - L390)/L390$ (L390 ; Tag distance at 390 ms from R wave, L510; Tag distance at 510 ms from R wave).

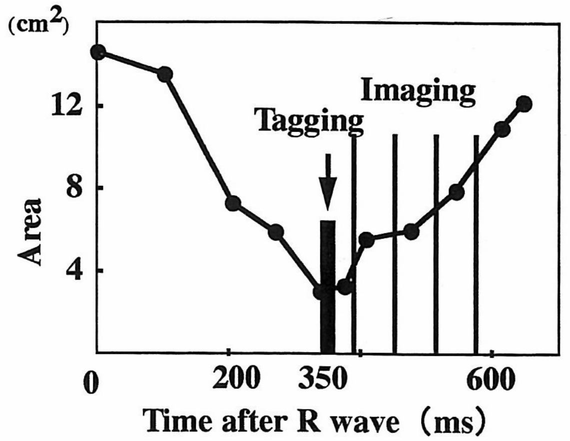

Fig.1 Time-area curve of left ventricle short axis from a normal volunteer using cine MRI. The SPAMM grid was generated at end systole, at 350 ms from R wave. SPAMM images were obtained at 390, 450, 510 and 570 ms after R wave.

Subendocardial early diastolic strain (εendo) and subepicardial early diastolic strain (ε epi) were calculated. Circumferential regions in a short-axis view were divided into anterior, lateral, inferior and septal regions. Radial regions were also divided into endocardial and epicardial halves. Data from the papillary muscles were excluded from the analysis. Reproducibility of strain analysis was studied by calculating the same data in 20 patients and 10 normal volunteers by a same examiner 3 month later (r=0.95).

Statistical Analysis

Data are expressed as mean ±SD. Statistical analysis was performed using the Stat View software package. Comparisons between normal volunteers and myocardial infarction patients were performed with ANOVA and when overall significance was detected, Scheffe test was performed for multiple comparisons. A value of $p<0.05$ was considered significant.

Results

Figure 2 and 3 show the tagging image of

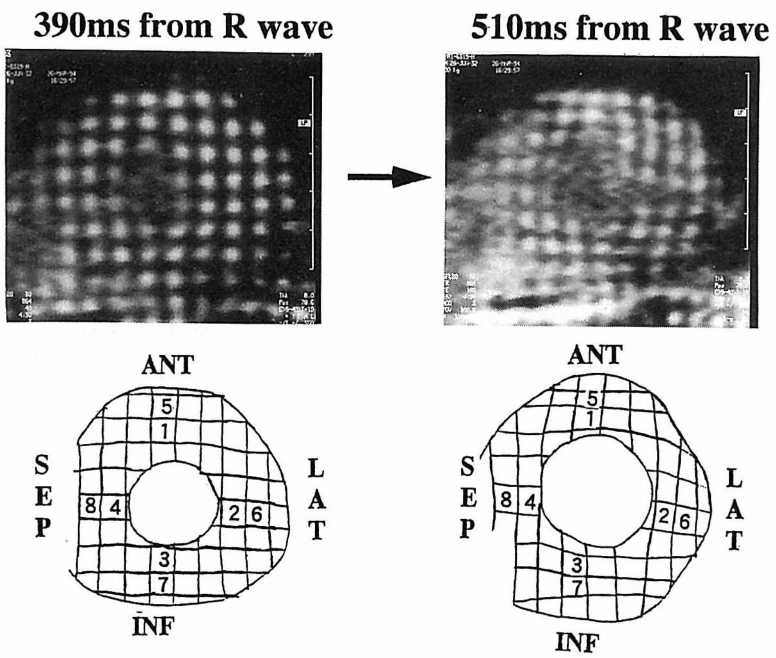

Fig 2. Early diastolic left ventricular short-axis image tagged with SPAMM from a normal volunteer. Every tagged myocardium was elongated circumferentially. The numbers in the figure shows the grids used for the strain measurement.
ANT: anterior wall LAT: lateral wall INF: inferior wall SEP: septum

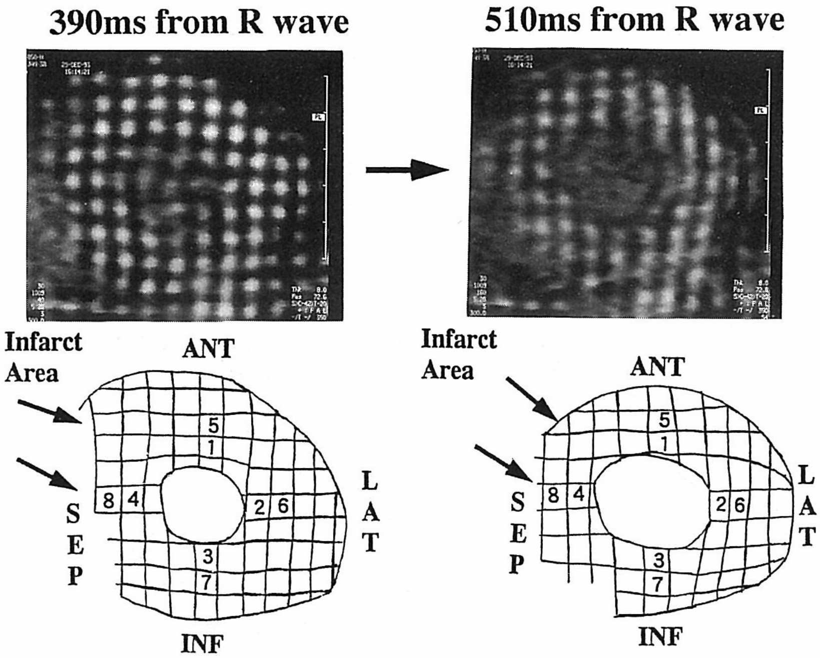

Fig 3. Early diastolic left ventricular short axis image tagged with SPAMM from a 55-year-old myocardial infarction patient without reperfusion. The mid of the left anterior descending artery was occluded. Neither tagged subendocardium nor subepicardium in infarct area (SEP) was elongated circumferentially. The numbers in the figure shows the grids used for the strain measurement.
ANT: anterior wall LAT: lateral wall INF: inferior wall SEP: septum

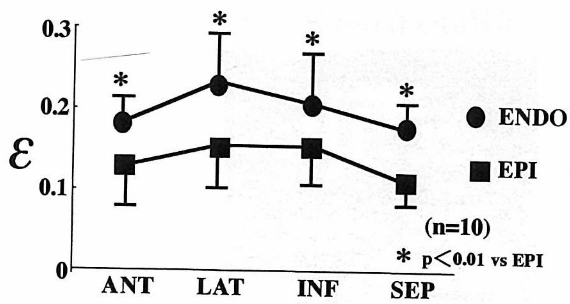

Fig 4. Early diastolic strains obtained from 10 normal volunteers. The subendocardial strain was significantly greater than subepicardial strain in every region.
ANT: anterior wall LAT: lateral wall INF: inferior wall SEP: septum
(*: $p<0.01$ vs EPI)

a normal volunteer and that of infarcted patient without reperfusion respectively.

Left Ventricular early Subendocardial and Subepicardial Diastolic Strain of normal Volunteers

Figure 4 shows the regional strains of normal volunteers. ε endo was significantly greater than ε epi in all areas (0.20±0.07 vs 0.14 ±0.06, $p<0.01$). ε endo of the lateral wall was greater than that of the other areas (Lat 0.24 ±0.08, Ant 0.19 ±0.05, Inf 0.21 ± 0.07, Sep 0.18 ±0.05). ε epi of the lateral and inferior wall were greater than those of other areas (Lat 0.16 ±0.05, Inf 0.16 ±0.05, Ant 0.13 ±0.07, Sep 0.11 ±0.02).

The effect of reperfusion in ε endo and ε epi

Figure 5 shows early diastolic strain in a myocardial infarction patient without reperfusion. In septum of infarct area, early diastolic strains at both subendocardium and subepicardium were remarkably lower than those of normal areas. Figure 6 shows early diastolic strain in a representative myocardial infarction patient with early reperfusion.

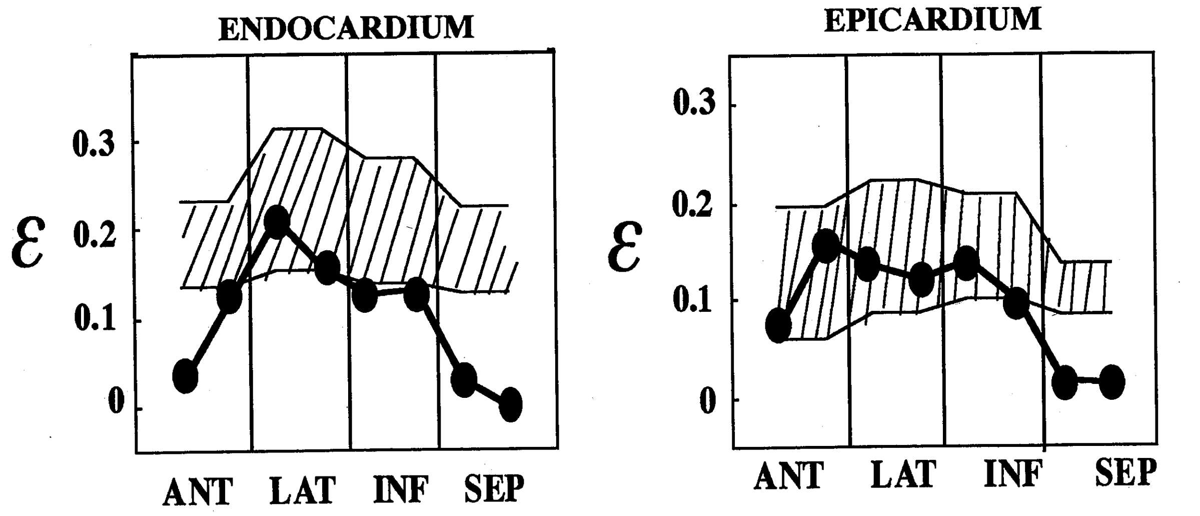

Fig 5. Early diastolic strains in a myocardial infarction patient without reperfusion. In infarct area (SEP),early diastolic strains at both subendocardium and subepicardium were remarkably lower than those of normal areas. The shaded area shows mean± SD obtained from 10 normal volunteers.
ANT: anterior wall LAT: lateral wall INF: inferior wall SEP: septum

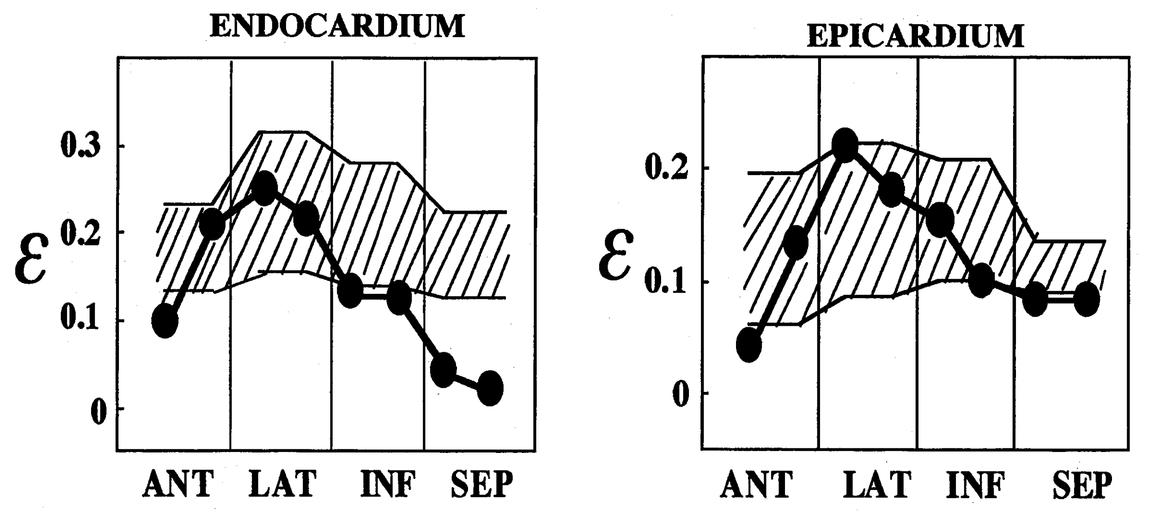

Fig 6. Early diastolic strains in a 71-year-old myocardial infarction patient with early reperfusion. In infarct area (SEP), early diastolic strain at subendocardium was remarkably decreased, however, the strain of subepicardium was improved to normal range. The shaded area shows normal range obtained from 10 normal volunteers.
ANT: anterior wall LAT: lateral wall INF: inferior wall SEP: septum

In septum of infarct area, early diastolic strain at subendocardium was remarkably decreased, however, the strain of subepicardium showed normal values.

Compared to normal volunteers, both ε endo and ε epi were remarkably reduced in the non-reperfused post MI patients (ε endo; 0.02±0.03, ε epi; 0.03±0.04, $p<0.01$). When reperfused group was compared with non-reperfused group, both ε endo and ε epi

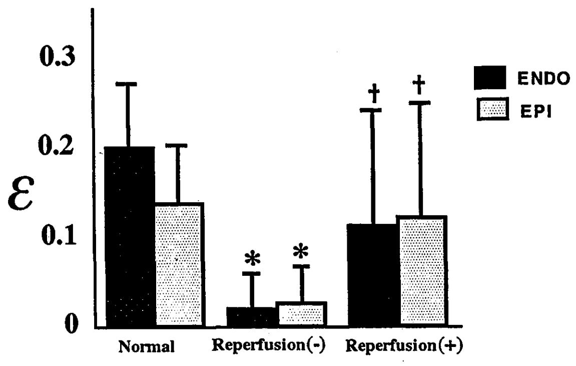

Fig 7. Early diastolic strains of subepicardium (ε epi) and subendocardium (ε endo) in normal group, reperfusion(−) group, reperfusion(+) group. In reperfusion(−) group, both ε epi and ε endo were remarkably reduced compared to normal group(*: $p<0.01$ vs Normal). Both ε epi and ε endo showed significantly higher values in reperfusion(+) group compared to reperfusion (−) group (†: $p<0.01$ vs Reperfusion (−)).

were significantly improved in the early reperfused group and εepi in early reperfused group showed almost equivalent value of normal group (ε endo; 0.11±0.11, ε epi; 0.12±0.11 $p<0.01$) (Figure 7).

Discussion

A major finding of the present study is that early reperfusion therapy within 6 hours after the onset of acute myocardial infarction improves both subendocardial and subepicardial early diastolic function as assessed by subendocardial and subepicardial early diastolic strain with SPAMM tagging. Particularly, early subepicardial diastolic function showed almost normal values after 1 month when successful early reperfusion was obtained despite only a modest improvement in subendocardial function. Theroux et al (11-13) demonstrated that during coronary occlusion, endocardial ischemia is usually more severe than epicardial ischemia. It has been reported that in the dog model, reperfusion after 3 hours of coronary occlusion can salvage subepicardial tissue despite subendocardial infarction (14). However, the present study is the first report in human myocardial infarction that demonstrates a difference in the recovery of subendocardial and subepicardial function after reperfusion therapy.

This study utilized a new method of creating tags at end-systole. This method has two major advantages compared to the conventional tagging at end diastole. First, wall thickness at end-systole is thicker than at end-diastole and more tags could be placed on the myocardium when compared to the conventional method. Secondly, the change in strains at early diastole is greater than at early systole. This produces more rapid changes in strains in early diastole than in early systole. The left ventricular wall thickness at the mid level of ventricle in all patients in the present study was more than 7 mm at end-systole and at least two cross points of tag lines existed in the wall.

A wringing motion of the heart which has been reported by Maier et al influences on the wall motion analysis by ventriculography or echocardiography (5). This motion consists of the clockwise rotation of the base and counterclockwise rotation of the apex. However, the wringing motion did not affect the strain analysis in SPAMM tagging method which is a potent advantage of utilizing regional wall motion. Maier et al have demonstrated that in the normal heart the strain of the septum was minimum and the endocardial torsion was twice that of the epicardial region (5). The normal volunteers in our study showed the similar result as that of Maier et al. They also showed the radial displacement in hypertrophic cardiomyopathy patients. In the present study, however, the left ventricular wall thickness in the infarcted area was thin, and thus it is not reliable to calculate the radial displacement with a 7 mm tag distance because of the unclear boundary between the ventricle and the surrounding tissues. Clark et al (15,16) assessed regional circumferential shortening by measuring the end-systolic interstripe distance in tagged MR images. In their study, the average subendocardial circumferential shortening in healthy volunteers was 44%

and subepicardial shortening was 22%. In the present study the early diastolic circumferential strain was 20% for subendocardium and 14% for subepicardium with a ratio between endo/epi of 1.4. The difference between our data and that of Clark et al may be caused by the difference of the method. Only early diastolic strain, not full cardiac cycle strain was obtained in this study. This may suggest that the subepicardial and subendocardial strain distribution varies depending on the phase of the cardiac cycle.

The tag contrast became weak after 300 ms and it is impossible to analyze the period beyond 300 ms. Maier et al assessed the subendocardial and subepicardial strain only during systole. The changes during early diastole have not seen previously assessed using a SPAMM tagging method because of the above limitation. We selected the appropriate delay for putting the tag at end -systole and this enabled the evaluation of the early diastolic changes.

Previous studies showed greater systolic shortening and thickening in the inner layer compared to the outer layer in the normal dog and human heart and a transmural strain gradient exists between the endocardial and epicardial layer (7-10). Ono et al showed in a canine experimental study that coronary reperfusion after 2 to 4 hours of ischemia results in improvement in epicardial and the impairment of subendocardial strain after 3 and 12 weeks (17). These results further support our conclusions.

Limitations

Translational motion along the long axis may cause artifact in the calculation of strain, but translational motion vertical to the long axis, or rotation around the long axis did not cause such artifact for the measurement of tag distance. Roger et al (4) have showed that the long axis translational movement of the base portion is 12.8 mm. Ingel et al (1) showed with the implantation of a radiopaque marker in the human ventricle during cardiac surgery have demonstrated that the heart contracts toward a point of 68% between the base and apex in the long axis. Thus, through-plane motion is a source of inaccuracy in the MR tagging method. We selected the mid-wall plane which has been shown in prior studies to have minimal through plane motion and wringing motion when compared to other regions(5). Thus the result of the present study has been little affected by above mentioned artifacts.

Tags persist for about 250 millisecond, but images acquired 120 millisecond after placing the tag are most desirable for the image analysis. We manually traced and measured the circumferential distances between each tag. Although the reproducibility is quite acceptable(r=0.95), automated computer applications for an objective quantification of the circumferential distances between each tag may provide even greater accuracy in estimating the myocardial regional strain .

Conclusion

SPAMM tagging has been shown to be useful in estimating the early diastolic subendocardial and subepicardial functions separately. Using SPAMM tagging, it was demonstrated that early reperfusion therapy led to a marked improvement in subepicardial function and a smaller improvement in subendocardial function.

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