

Imaging 4D morphology and dynamics of mitral annulus in humans using cardiac cine MR feature tracking

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Supplementary Table S1. Dynamics of mitral annulus with quantitative parameters obtained by feature tracking (n = 30, 16 controls and 14 patients).

Dynamic Parameters		18 Slices (reference)	9 Slices (every 2)	6 Slice (every 3)	3 Slices* (2-, 3-, 4-C)
Sm	Mean (cm/s)	6.9	6.9	7.0	6.8
	SD (cm/s)	1.7	1.7	1.8	1.7
	Correlation coefficient (<i>r</i>)	-	0.992	0.986	0.987
	Mean difference (cm/s)	-	-0.021	0.054	-0.114
	SD of difference, <i>s_d</i> (cm/s)	-	0.21	0.30	0.28
	Limits of agreement (cm/s)	-	(-0.44, 0.40)	(-0.54, 0.65)	(-0.66, 0.43)
	ICC (<i>r_I</i>)	-	0.996	0.993	0.993
	Regression equation	-	y = 1.01x-0.03	y = 0.96x+0.22	y = 1.00x+0.08
Em	Mean (cm/s)	7.4	7.4	7.5	7.5
	SD (cm/s)	3.5	3.5	3.6	3.5
	Correlation coefficient (<i>r</i>)	-	0.999	0.998	0.994
	Mean difference (cm/s)	-	-0.017	0.011	0.050
	SD of difference, <i>s_d</i> (cm/s)	-	0.17	0.20	0.40
	Limits of agreement (cm/s)	-	(-0.36, 0.32)	(-0.39, 0.41)	(-0.73, 0.83)
	ICC (<i>r_I</i>)	-	0.999	0.999	0.997
	Regression equation	-	y = 0.99x+0.08	y = 0.98x+0.12	y = 1.00x-0.05
Am	Mean (cm/s)	7.0	7.0	7.0	6.9
	SD (cm/s)	2.3	2.3	2.4	2.3
	Correlation coefficient (<i>r</i>)	-	0.997	0.995	0.991
	Mean difference (cm/s)	-	-0.001	-0.011	-0.051
	SD of difference, <i>s_d</i> (cm/s)	-	0.18	0.25	0.32
	Limits of agreement (cm/s)	-	(-0.35, 0.35)	(-0.50, 0.47)	(-0.67, 0.57)
	ICC (<i>r_I</i>)	-	0.999	0.997	0.995
	Regression equation	-	y = 1.00x+0.01	y = 0.98x+0.15	y = 1.01x-0.04
MAPSE	Mean (mm)	13.1	13.1	13.1	13.0
	SD (mm)	2.7	2.6	2.7	2.6
	Correlation coefficient (<i>r</i>)	-	0.999	0.997	0.994
	Mean difference (mm)	-	-0.005	0.030	-0.105

	SD of difference, s_d (mm)	-	0.13	0.20	0.30
	Limits of agreement (mm)	-	(-0.27, 0.26)	(-0.37, 0.43)	(-0.69, 0.48)
	ICC (r_1)	-	0.999	0.999	0.997
	Regression equation	-	$y = 1.01x - 0.15$	$y = 0.99x + 0.06$	$y = 1.01x - 0.07$

*Clinically routinely acquired 2-, 3-, and 4-chamber long-axis views. Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion; SD: standard deviation; ICC: intra-class correlation coefficient. Regression equation, y: 18-slices-derived results, x: 9-, 6-, and 3-slices-derived results.

Supplementary Table S2. Morphology of mitral annulus with quantitative parameters obtained by feature tracking and geometry reconstruction (n = 30, 16 controls and 14 patients).

Morphological Parameters		18 Slices (reference)	9 Slices (every 2)	6 Slice (every 3)	3 Slices* (2-, 3-, 4-C)
3D Area	Mean (cm ²)	10.8	10.8	10.7	10.1
	SD (cm ²)	2.2	2.3	2.0	2.2
	Correlation coefficient (<i>r</i>)	-	0.993	0.985	0.957
	Mean difference (cm ²)	-	0.07	-0.11	-0.71
	SD of difference, <i>s_d</i> (cm ²)	-	0.27	0.41	0.64
	Limits of agreement (cm ²)	-	(-0.46, 0.61)	(-0.91, 0.69)	(-1.96, 0.54)
	ICC (<i>r_I</i>)	-	0.996	0.990	0.953
	Regression equation	-	y = 0.95x+0.47	y = 1.08x-0.78	y = 0.97x+0.99
Perimeter	Mean (mm)	120.9	122.0	120.3	115.1
	SD (mm)	11.2	12.1	10.4	12.0
	Correlation coefficient (<i>r</i>)	-	0.982	0.958	0.919
	Mean difference (mm)	-	1.15	-0.64	-5.75
	SD of difference, <i>s_d</i> (mm)	-	2.40	3.22	4.74
	Limits of agreement (mm)	-	(-3.56, 5.85)	(-6.96, 5.67)	(-15.03, 3.54)
	ICC (<i>r_I</i>)	-	0.987	0.977	0.900
	Regression equation	-	y = 0.91x+10.2	y = 1.03x-3.41	y = 0.85x+22.6
AP Diameter	Mean (mm)	29.9	30.1	29.8	30.3
	SD (mm)	3.6	3.7	3.9	3.4
	Correlation coefficient (<i>r</i>)	-	0.985	0.955	0.966
	Mean difference (mm)	-	0.21	-0.09	0.35
	SD of difference, <i>s_d</i> (mm)	-	0.63	1.17	0.95
	Limits of agreement (mm)	-	(-1.02, 1.44)	(-2.39, 2.20)	(-1.50, 2.21)
	ICC (<i>r_I</i>)	-	0.992	0.976	0.980
	Regression equation	-	y = 0.98x+0.50	y = 0.89x+3.44	y = 1.03x-1.37
IC Diameter	Mean (mm)	35.1	35.1	35.1	33.9
	SD (mm)	3.7	3.6	3.7	3.9
	Correlation coefficient (<i>r</i>)	-	0.985	0.968	0.871
	Mean difference (mm)	-	-0.04	-0.07	-1.24

	SD of difference, s_d (mm)	-	0.63	0.94	1.95
	Limits of agreement (mm)	-	(-1.28, 1.20)	(-1.91, 1.77)	(-5.06, 2.59)
	ICC (r_I)	-	0.993	0.984	0.906
	Regression equation	-	$y = 1.01x - 0.23$	$y = 0.96x + 1.41$	$y = 0.81x + 7.58$
AP/IC Ratio	Mean	0.86	0.86	0.86	0.90
	SD	0.10	0.10	0.11	0.10
	Correlation coefficient (r)	-	0.976	0.933	0.784
	Mean difference	-	0.01	< 0.001	0.04
	SD of difference, s_d	-	0.02	0.04	0.07
	Limits of agreement	-	(-0.04, 0.05)	(-0.08, 0.08)	(-0.09, 0.18)
	ICC (r_I)	-	0.987	0.964	0.842
	Regression equation	-	$y = 1.01x - 0.02$	$y = 0.85x + 0.13$	$y = 0.79x + 0.15$
Height	Mean (mm)	7.7	7.8	7.9	6.8
	SD (mm)	1.7	1.7	1.6	2.3
	Correlation coefficient (r)	-	0.922	0.814	0.788
	Mean difference (mm)	-	0.12	0.16	-0.96
	SD of difference, s_d (mm)	-	0.67	1.00	1.44
	Limits of agreement (mm)	-	(-1.19, 1.43)	(-1.80, 2.11)	(-3.78, 1.87)
	ICC (r_I)	-	0.959	0.898	0.805
	Regression equation	-	$y = 0.89x + 0.78$	$y = 0.83x + 1.18$	$y = 0.56x + 3.93$

*Clinically routinely acquired 2-, 3-, and 4-chamber long-axis views. AP: antero-posterior; IC: inter-commissural; SD: standard deviation; ICC: intra-class correlation coefficient. Regression equation, y: 18-slices-derived results, x: 9-, 6-, and 3-slices-derived results.

Supplementary Table S3. Pearson correlation coefficients and mean differences for mitral annular dynamics (18 slices vs. 3 routine slices) in normal and patient groups.

	Correlation coefficient <i>r</i> , 18 slices vs. 3 slices (2-, 3-, 4-chamber)				Mean difference, 18 slices vs. 3 slices (2-, 3-, 4-chamber)			
	All (<i>n</i> = 30)	Controls (<i>n</i> = 16)	Patients (<i>n</i> = 14)	<i>P</i> value*	All (<i>n</i> = 30)	Controls (<i>n</i> = 16)	Patients (<i>n</i> = 14)	<i>P</i> value [#]
Sm	0.987	0.978	0.988	0.294	-0.114	-0.082	-0.151	0.504
Em	0.994	0.992	0.989	0.373	0.050	0.005	0.102	0.512
Am	0.991	0.981	0.990	0.274	-0.051	-0.060	-0.041	0.872
MAPSE	0.994	0.989	0.992	0.378	-0.105	-0.110	-0.101	0.942

*Pearson correlation coefficients computed for Normal and Patient groups and compared using Fisher z-statistic test. [#]Mean differences computed for Normal and Patient groups and compared using two-sample t-test. Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion.

Supplementary Table S4. Pearson correlation coefficients and mean differences for mitral annular morphology (18 slices vs. 6 slices) in normal and patient groups.

	Correlation coefficient r, 18 slices vs. 6 slices				Mean difference, 18 slices vs. 6 slices			
	All (n = 30)	Controls (n = 16)	Patients (n = 14)	<i>P</i> value*	All (n = 30)	Controls (n = 16)	Patients (n = 14)	<i>P</i> value [#]
3D Area	0.985	0.960	0.988	0.126	-0.11	-0.10	-0.11	0.940
Perimeter	0.958	0.938	0.952	0.378	-0.64	-0.65	-0.63	0.991
AP Diameter	0.955	0.941	0.959	0.360	-0.09	0.02	-0.23	0.583
IC Diameter	0.968	0.959	0.977	0.305	-0.07	-0.12	-0.03	0.793
AP/IC Ratio	0.933	0.926	0.936	0.391	< 0.001	0.005	-0.007	0.458
Height	0.814	0.797	0.824	0.391	0.16	0.20	0.12	0.827

*Pearson correlation coefficients computed for Normal and Patient groups and compared using Fisher z-statistic test. [#]Mean differences computed for Normal and Patient groups and compared using two-sample t-test. AP: antero-posterior; IC: inter-commissural.

Supplementary Table S5. Mitral annular dynamics derived with different mask sizes (n = 4 subjects, 2 controls and 2 patients).

	Mask size 8 × 8 pixels	Mask size 12 × 12 pixels	Mask size 16 × 16 pixels	<i>P</i> value*
Sm	7.8 ± 2.1	7.7 ± 2.3	7.7 ± 2.3	0.875
Em	10.7 ± 4.2	10.4 ± 4.0	10.3 ± 3.8	0.676
Am	7.9 ± 2.2	7.9 ± 2.3	8.0 ± 2.4	0.945
MAPSE	14.7 ± 2.7	14.8 ± 2.9	14.7 ± 2.7	0.940

Data were presented as mean ± SD. Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion; **P* value obtained by one-way ANOVA test.

Supplementary Table S6. Comparisons between semi-automatic and manual tracking results (n = 4, 2 controls and 2 patients).

Variables	Technique	Mean	Bias (limits of agreement)	<i>P</i> value*
Sm	Manual	8.2 ± 2.2		
	Semi-automatic	7.8 ± 2.1	-0.4 (-1.5, 0.8)	0.144
Em	Manual	11.0 ± 4.2		
	Semi-automatic	10.7 ± 4.2	-0.3 (-1.5, 1.0)	0.609
Am	Manual	8.1 ± 2.3		
	Semi-automatic	7.9 ± 2.2	-0.2 (-1.6, 1.1)	0.409
MAPSE	Manual	14.9 ± 2.8		
	Semi-automatic	14.7 ± 2.7	-0.2 (-1.1, 0.7)	0.579
3D Area	Manual	9.12 ± 1.40		
	Semi-automatic	9.08 ± 1.37	-0.04 (-0.09, 0.01)	0.814
Perimeter	Manual	110.48 ± 8.56		
	Semi-automatic	110.41 ± 8.51	-0.07 (-0.44, 0.30)	0.943
AP Diameter	Manual	28.11 ± 2.91		
	Semi-automatic	28.06 ± 2.87	-0.05 (-0.22, 0.12)	0.901
IC Diameter	Manual	33.71 ± 1.44		
	Semi-automatic	33.65 ± 1.42	-0.06 (-0.25, 0.13)	0.742
Height	Manual	7.05 ± 1.12		
	Semi-automatic	6.94 ± 1.05	-0.11 (-0.26, 0.04)	0.349

Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion; AP: antero-posterior; IC: inter-commissural. **P* value obtained by two-sample t-test.

Supplementary Table S7. Mitral annular dynamics derived using multiple sub-datasets (n = 4, 2 controls and 2 patients).

	Sm, cm/s	Em, cm/s	Am, cm/s	MAPSE, mm
18 slices	7.8 ± 2.1	10.7 ± 4.2	7.9 ± 2.2	14.7 ± 2.7
9 slices (slice no.: 1, 3,...,17)	7.8 ± 2.1	10.6 ± 4.1	7.8 ± 2.2	14.7 ± 2.7
9 slices (slice no.: 2, 4,...,18)	7.8 ± 2.0	10.8 ± 4.4	8.0 ± 2.1	14.7 ± 2.8
6 slices (slice no.: 1, 4,...,16)	7.7 ± 2.1	10.7 ± 4.2	7.9 ± 2.2	14.8 ± 2.8
6 slices (slice no.: 2, 5,...,17)	7.8 ± 2.0	10.9 ± 4.3	8.0 ± 2.1	14.7 ± 2.7
6 slices (slice no.: 3, 6,...,18)	8.0 ± 2.1	10.5 ± 4.2	7.8 ± 2.2	14.7 ± 2.8
3 slices (2-, 3-, 4-chamber)	7.6 ± 2.0	10.7 ± 4.0	8.1 ± 2.1	14.6 ± 2.6
<i>P</i> value*	0.988	0.999	0.954	0.998

Data were presented as mean ± SD. Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion. **P* value obtained by one-way ANOVA test.

Supplementary Table S8. Mitral annular morphology derived using multiple sub-datasets (n = 4, 2 controls and 2 patients).

	3D Area, cm²	Perimeter, mm	AP Diameter, mm	IC Diameter, mm	Height, mm
18 slices	9.1 ± 1.4	110.4 ± 8.5	28.1 ± 2.9	33.7 ± 1.4	6.9 ± 1.0
9 slices (slice no.: 1, 3,...,17)	9.2 ± 1.6	111.7 ± 11.1	28.4 ± 3.1	33.4 ± 1.6	6.9 ± 1.0
9 slices (slice no.: 2, 4,...,18)	9.2 ± 1.3	110.9 ± 8.3	28.8 ± 2.6	33.5 ± 1.5	7.3 ± 1.2
6 slices (slice no.: 1, 4,...,16)	9.0 ± 1.3	109.3 ± 7.5	28.4 ± 2.8	33.7 ± 1.6	7.0 ± 0.8
6 slices (slice no.: 2, 5,...,17)	9.0 ± 1.3	108.6 ± 8.3	29.7 ± 2.9	33.1 ± 1.6	6.7 ± 1.3
6 slices (slice no.: 3, 6,...,18)	9.4 ± 1.4	111.3 ± 9.4	30.1 ± 2.5	33.6 ± 1.4	7.4 ± 1.0
<i>P</i> value*	0.944	0.959	0.685	0.951	0.668

Data were presented as mean ± SD. AP: antero-posterior; IC: inter-commissural. **P* value obtained by one-way ANOVA test.

Supplementary Table S9. Mitral annular dynamics derived using conventional two-, three-, and four-chamber views.

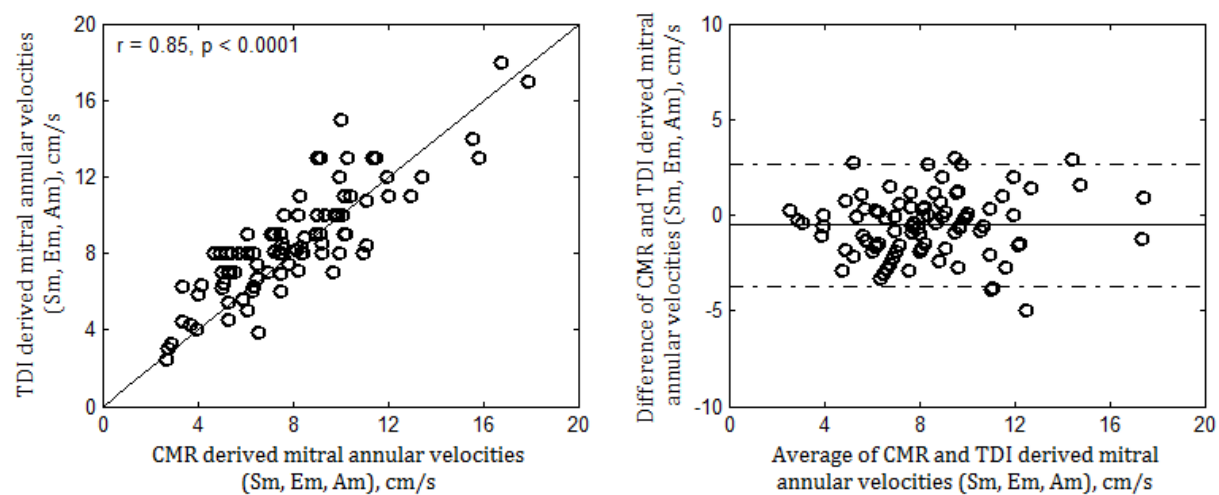
	Variables	<i>r</i>	Bias (limits of agreement)	<i>P</i> value*
Conventional vs. Radially rotational 2-, 3-, and 4-chamber views	Sm	0.975	0.05 (-0.57, 0.68)	0.916
	Em	0.980	-0.37 (-1.60, 0.86)	0.723
	Am	0.982	0.22 (-0.53, 0.98)	0.730
	MAPSE	0.959	-0.12 (-1.22, 0.97)	0.855
Conventional 2-, 3-, and 4-chamber views vs. 18 reference views	Sm	0.953	-0.32 (-1.19, 0.55)	0.537
	Em	0.954	0.32 (-1.46, 2.10)	0.760
	Am	0.952	-0.35 (-1.49, 0.79)	0.590
	MAPSE	0.925	0.01 (-1.45, 1.47)	0.986

Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion; *r*: Pearson correlation coefficient; **P* value obtained by one-way ANOVA test.

Supplementary Table S10. Mitral annular dynamics derived using all radial slices with different numbers of cardiac phases.

	Variables	<i>r</i>	Bias (limits of agreement)	<i>P</i> value*
20 vs. 40 cardiac phases	Sm	0.980	-0.61 (-1.48, 0.26)	0.043
	Em	0.965	-1.44 (-3.92, 1.04)	0.011
	Am	0.917	-1.48 (-3.18, 0.22)	< 0.001
	MAPSE	0.993	-0.21 (-0.85, 0.44)	0.587

Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity; MAPSE: mitral annular plane systolic excursion; r: Pearson correlation coefficient; **P* value obtained by two-sample t-test.



Supplementary Figure S1. Comparison of CMR and TDI derived mitral annular velocities.

Supplementary Video S1. Feature tracking of 4D MA dynamics in a normal control subject in all 18 cine CMR slices, each with two annular points over the entire cardiac cycle. Details see text.

Supplementary Video S2. Feature tracking of 4D MA dynamics in a patient with mitral regurgitation in all 18 cine CMR slices, each with two annular points over the entire cardiac cycle. Details see text.

Supplementary Video S3. Feature tracking of 4D MA morphology in a normal control in cine CMR with different numbers of equidistant radially rotational long-axis slices. These include all 18 slices, 9 slices (every other slices), 6 slices (every three slices), and 3 slices (routine 2-, 3-, 4-chamber views), respectively. Dots indicate intersection points along the mitral valve orifice, which is represented by the interpolated curve. Details see text.

Supplementary Appendix S1 – Robustness evaluation of the tracking method

To evaluate the robustness of the tracking method, analysis has been performed in a subset of patients and normal controls with two subjects in each category to test the correspondence of feature tracking via slight variations on the initial position around the feature of interest.

The robustness testing for each point around the mitral annulus was conducted as follows:

- 1) The position of original mask in the initial frame is denoted as (x_o, y_o) . The size of the mask is $w \times h$.
- 2) The new mask position (x_n, y_n) was obtained by slightly varying the original as $(x_n = x_o + \Delta w, y_n = y_o + \Delta h)$, where Δw and Δh were randomly generated between $-0.15\Delta w$ and $+0.15\Delta w$, and between $-0.15\Delta h$ and $+0.15\Delta h$, respectively.
- 3) Semi-automatic tracking was executed with the new mask without manual intervention.
- 4) Mitral annular dynamic and morphological measurements were then derived and compared with the original results.

The comparison results are given in the table below. Good agreements were observed for all mitral annular measurements between the two sets of results, indicating good robustness of the tracking method.

Supplementary Table S11. Robustness test results by comparing measurements from slight variation of mask position with original measurements.

	Variables	r	Bias (limits of agreement)	ICC
Original results vs. Results by slight variation of mask position	Sm	0.990	0.01 (-0.58, 0.60)	0.995
	Em	0.989	0.02 (-1.23, 1.26)	0.994
	Am	0.961	-0.10 (-1.30, 1.09)	0.980
	MAPSE	0.984	-0.08 (-1.05, 0.88)	0.991
	3D Area	0.997	0.13 (-0.09, 0.35)	0.996
	Perimeter	0.980	1.47 (-2.30, 5.24)	0.977
	AP Diameter	0.991	-0.22 (-0.99, 0.55)	0.994
	IC Diameter	0.943	0.63 (-0.30, 1.55)	0.923
	AP/IC Ratio	0.947	0.08 (-0.81, 0.97)	0.961

Sm: peak systolic velocity; Em: peak early diastolic velocity; Am: peak late diastolic velocity;
MAPSE: mitral annular plane systolic excursion; AP: antero-posterior; IC: inter-commissural;
r: Pearson correlation coefficient; ICC: intra-class correlation coefficient.