Supplemental Material

Supplemental Methods:

MDCT

Acquisition of images was performed using a 128 slice (Siemens AS+, Siemens Medical Solutions) which has a spatial resolution of 0.30mm, 150ms of temporal resolution, 0.3 of rotation times for sequential scanning, 36mm of maximum z-axis x-ray beam collimation with sub-milimetre slices or 320-slice Aquillion One (Toshiba) CT scanning system with a 0.35mm spatial resolution, 175ms of temporal resolution, 0.33 of rotation times for sequential scanning and 160mm of maximum z-axis x-ray beam collimation with sub-milimetre slices.

For regional myocardial contractility analysis, previous studies[20], using electron beam computed tomography (EBCT), demonstrated that SEF can detect abnormalities and provide accurate identification of ischemic myocardium in patients with varying degrees of coronary artery occlusion. Similarly, by applying the principle of myocardial SEF to regenerative myocardial therapy, we have been able to analyze regional myocardial contractility and scarring following TESI in patients with chronic ischemic cardiomyopathy (Online-Figure II).

17-Segment Model Reconstruction: Biplane Left Ventriculography- Endocardial Tracings and Use of The 17-Segment Model for Recognition of Areas Injected

TESI can be performed with different devices[7], and some of them, such as the NOGA catheter[6], provide accurate segmental information from the apex and mid-ventricle but limited reconstruction of the cardiac basal segments[9]. For this purpose, even though not as precise as a cross sectional method as MDCT, we used biplane ventriculography endocardial tracings during TESI as an alternative of a complete reconstruction of the AHA 17-myocardial segment model and allocation of the sites of injection.

Online Figure I. Study flow diagram. MSCs indicates mesenchymal stem cells; MDCT, multidetector computer tomography; LV, left ventricle.

Online Figure II. Segmental Ejection Fraction (SEF) Calculation. The outer grey circle represents a short axis view of the left ventricle(LV) at the end diastolic phase and the red fan represents the volume of a micro-segment end diastolic volume. The inner black circle represents a short axis view of the LV at the end-systolic phase and the blue fan represents the same micro-segment end-systolic volume. The center of the end-systolic phase is used for both cardiac phases (so called “fixed axis”). The individual SEF value presented in the polar map for all 17 AHA myocardial segments represents the average SEF of all fan shaped micro-segments within the same particular myocardial segment ((Segmental LV End Diastolic Volume – Segmental LV End Systolic Volume) * 100) / Segmental LV End Diastolic Volume).

Online Figure III. Scar mass changes by cell type and dose. (Panel A) Scar size reduces in the ‘scar-injected’ myocardial segments treated by with autologous MSCs, 20 Million of autologous MSCs reduces scar size from 7.1±1.4g to 3.7±0.8g *p=0.02, between group comparison with all groups + p<0.01. A trend of reduction was observed with other autologous doses; 100M (from 11.3±3.9g to 5.9±1.6g **p=0.09, 200M from 12.1±3.4g to 6.5±1.5g ***p=0.05. (Panel B) Similar changes were observed in the ‘scar-injected’ segments treated with allogeneic MSCs, 20M from 9.0±2.5g to 3.5±1.0g ‡p=0.06, 100M 12.7±3.9g to 7.7±3.0g p=0.02. The ‘scar-non-injected’ myocardial segments showed a scar size reduction from 12.3±2.3g to 8.9±1.9g †p=0.01.

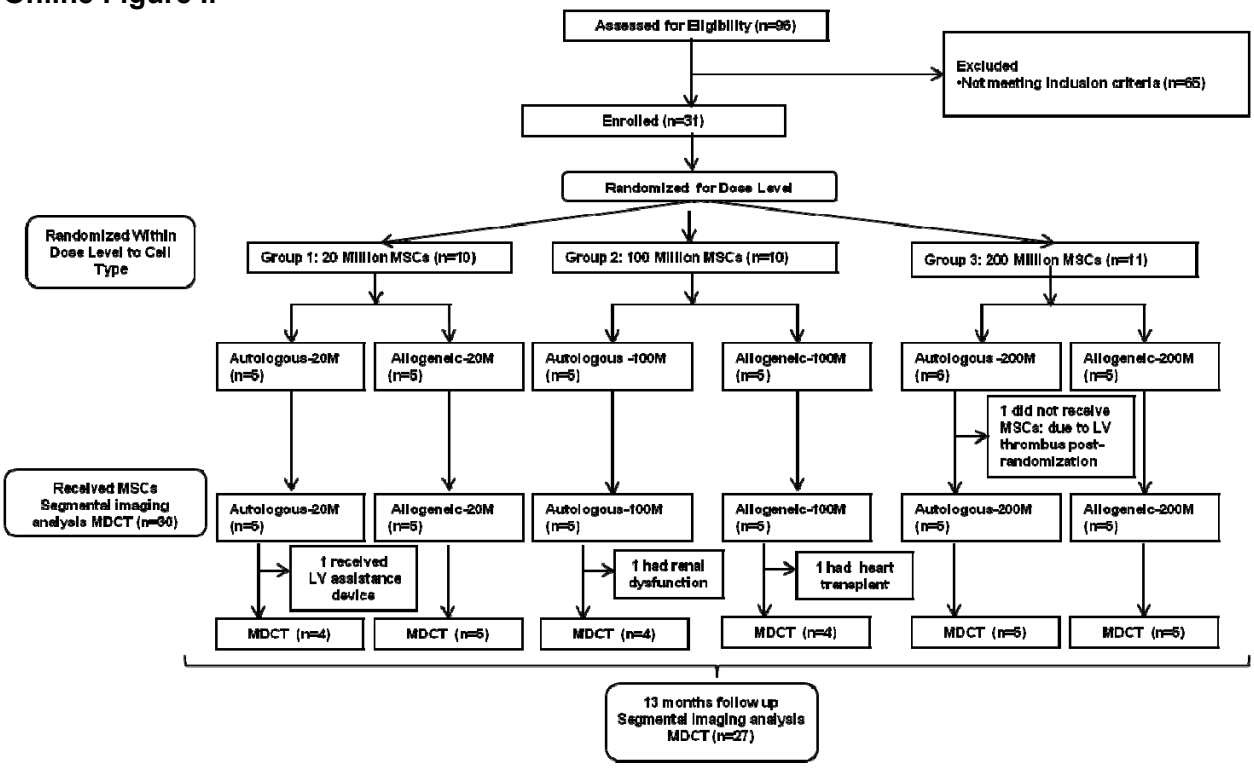
Online Table I. Patient baseline characteristics

Online Table II. Scar baseline characteristics

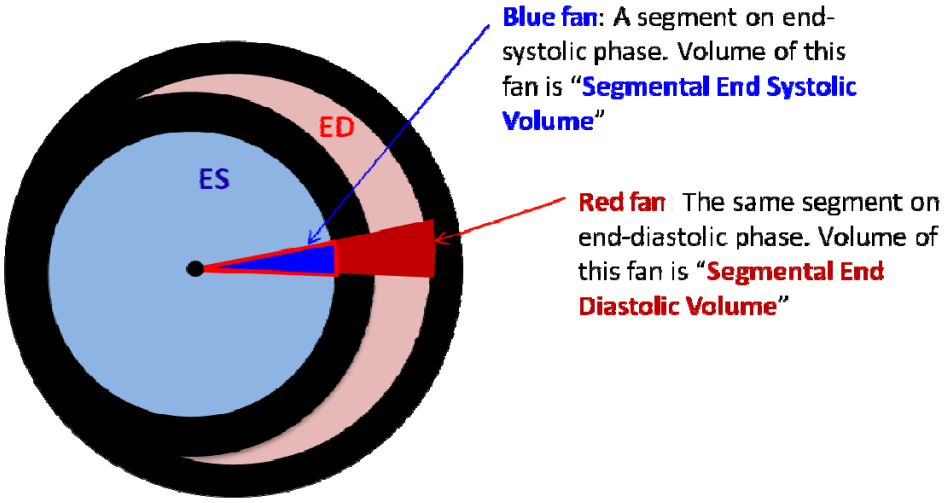
Online Video I. Volume rendered reformats of left ventricle with color encoding of scar tissue. 3D reconstructions of Multidetector computed tomography (MDCT) images depicting scar mass (green) of myocardial segments treated by transendocardial stem cell injection (TESI) with numbers representing sites of injection. Scar mass (orange) of myocardial segments not treated by TESI at baseline and at 13 months following TESI, respectively. Actual scar mass in grams is depicted below each panel. Baseline (left panel) and 13 months (right panel). 3D-recontructions in this figure correspond to SEED measurements of the same patient as in Figures 2 and 3.

Online Video II. Restoration in contractility only in scar injected myocardial segments. MDCT-CINE short axis videos of a patient with anterolateral and inferior chronic ischemic cardiomyopathy. (Left Panel) Baseline: Inferior myocardial segments. Segmental ejection fraction (SEF) 31% and segmental early enhancement defect (SEED) 5.9g, end diastolic volume (EDV) 173.0 mL, end systolic volume (ESV) 124.76 mL, sphericity index (SI) 0.419. (Right panel) 13 months after intramyocardial injections of allogeneic MSCs into inferior myocardial segments SEF 43.7% and SEED1.4g, EDV 131.9 mL, ESV 84.68 mL, SI 0.303.

Online Figure I.

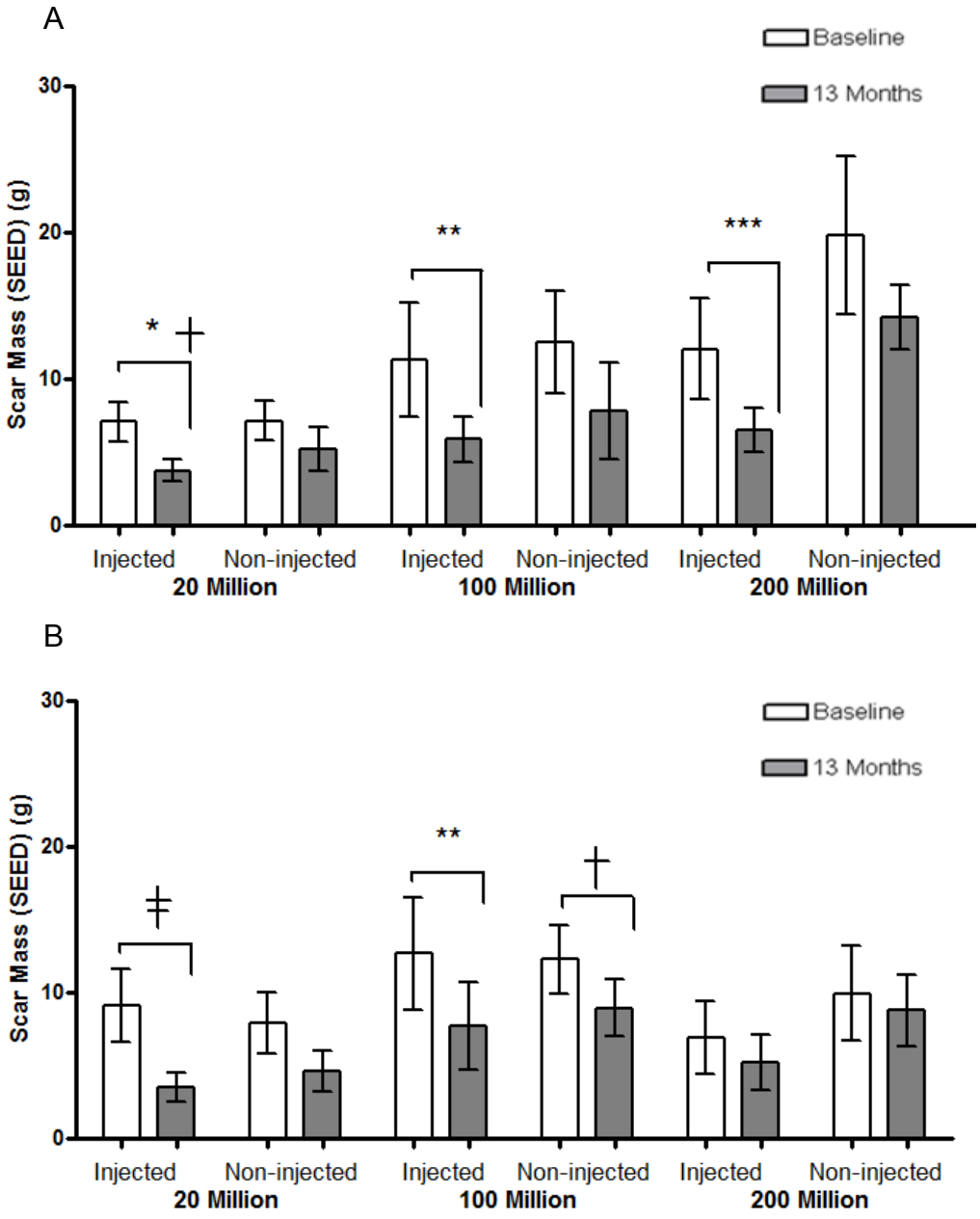


Online Figure II



$$\text{SEF Formula} = \frac{(\text{Segmental End Diastolic Volume} - \text{Segmental End Systolic Volume})}{\text{Segmental End Diastolic Volume}}$$

Online Figure III



Online Table I.

Baseline Characteristics	Cell Type	
	Allogeneic MSCs	Autologous MSCs
Treated	15	15
Age (years)	62.8 (10.5)	63.7 (9.3)
Gender: Male	13 (86.7%)	13 (86.7%)
Ethnicity: Hispanic or Latino	3 (20.0%)	3 (20.0%)
Race: White	13 (86.7%)	15 (100.0%)
Median Years since last MI (range)	9.0 (0.2-27.1)	12.8 (2.4-31.8)
History of Coronary Interventions	13 (86.7%)	13 (86.7%)
History of Atrial or Ventricular Arrhythmia	13 (86.7%)	11 (73.3%)
History of Hypertension	13 (86.7%)	13 (86.7%)
New York Heart Association Class		
Class I - No Limitation	2 (13.3%)	2 (13.3%)
Class II - Slight Limitation of Physical Activity	9 (60.0%)	9 (60.0%)
Class III - Marked Limitation of Physical Activity	4 (26.7%)	4 (26.7%)
History of Smoking	7 (46.7%)	12 (80.0%)
History of Diabetes	4 (26.7%)	4 (26.7%)
Treatment Pre-TESI		
ACE-I	9 (60.0%)	12 (80.0%)
Angiotensin 2 Blockers	3 (20.0%)	2 (13.3%)
Beta Blockers	15 (100.0%)	13 (86.7%)
Diuretic	10 (66.7%)	10 (66.7%)

Abbreviations: MSC, mesenchymal stem cells, TESI, transendocardial stem cell injection, ACE-I, angiotensin converting enzyme-Inhibitor. Data are presented as No. (%) unless otherwise specified.

Online Table II.

	Scar Injected		Scar Non-injected	
	Autologous n=15	**Allogeneic n=15**	**Autologous n=15**	**Allogeneic N=15**
Scar Mass-SEED in grams	10.2 (1.8)	9.6 (1.8)	13.3 (2.4)	10.1 (1.5)
Thickness of segment mm	7.7 (0.5)	7.7 (0.3)	7.5 (0.3)	7.4 (0.3)
Segmental EF %	19.0 (3.0)	20.6 (3.7)	20.0 (2.4)	22.2 (3.1)
	Autologous and Allogeneic combined n=30			
Scar Mass-SEED) in grams	9.8 (1.2)		11.7 (1.4)	
Thickness of segment mm	7.7 (0.3)		7.2 (0.3)	
Transmurality Extent (% of Wall Thickness)				
>50% Mean (SEM, N)	71.4 (2.8, 25)		65.4 (2.2,29)	
<50% Mean (SEM, N)	46.7 (0.8, 5)		43.6 (-, 1)	
Segmental EF %	19.6 (2.4)		21.5 (2.0)	

Abbreviations: SEED, segmental early enhancement defect, EF, ejection fraction. Data are presented as: Mean, SEM (standard error of mean) .