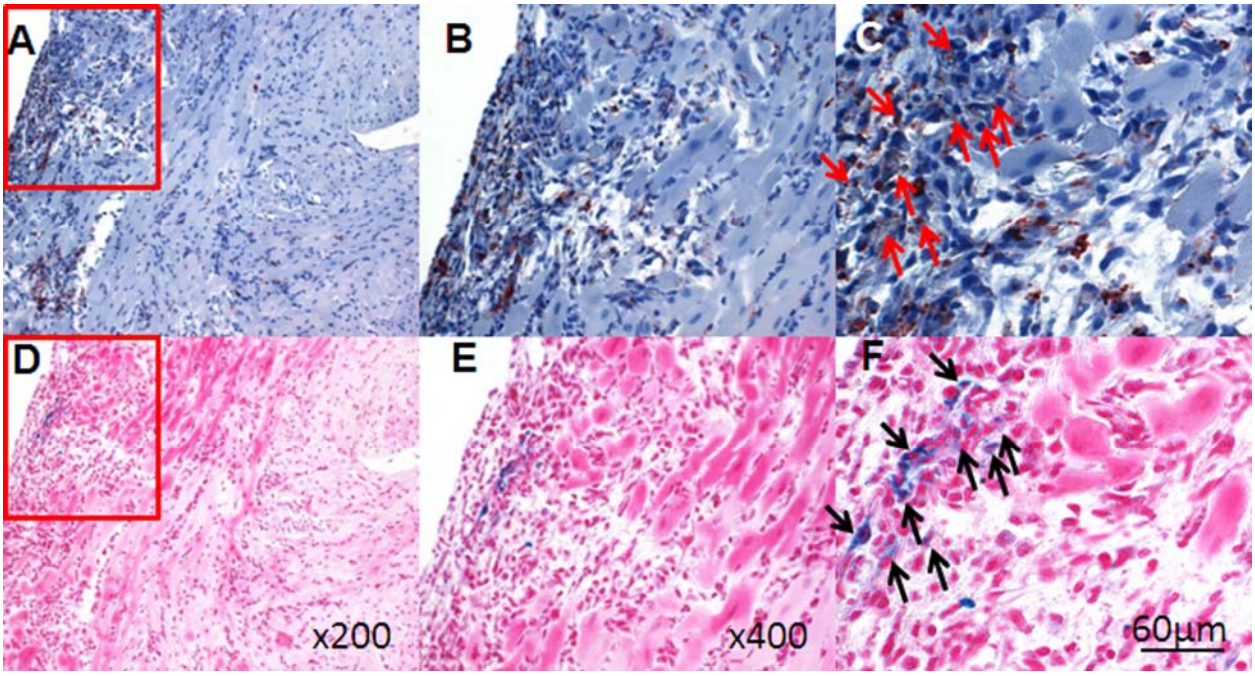
SUPPLEMENTAL MATERIAL

Supplemental Figure 1

Videos: corresponding movies of 3D volume rendering with rotating 360^0 viewing angles of 3D MRM image stacks from Figure 3: (A) no-treatment allograft heart; (B) native heart from the same no-treatment animal as A; (C) clodronate-liposome-treated allograft heart; (D) native heart from the same clodronate-liposome-treated animal as C; (E) PBS-liposome-treated allograft heart; and (F) native heart from the same PBS-liposome-treated animal as E.

Supplemental Figure 2

Representative optical micrographs of a clodronate-liposome treated allograft harvested on POD 9. A and D are two neighboring 5-μm sections with immunohistochemical staining with anti-rat ED1 antibody for macrophages and Perl's Prussian blue staining for iron, respectively. B and E are the expansion of the boxed region in A and D. C and F are enlarged regions from B and E to illustrating that the iron-positive cells (blue color, black arrows) are all ED1+ macrophages (Brown color, red arrows), though not all the ED1+ cells contain iron particles.



Supplemental Table 1. Results from linear mixed-effects model analysis for circumferential strains (Ecc) for 3 treatment groups: PBS-liposome (PBS), Clodronate-liposome (Clodronate), No Treatment (No Treatment); and 5 time points: POD 5, POD 6, POD 7, POD 8, POD 9; where POD = post operational day.

Parameter estimates from the linear mixed-effects model

Effect	F value $F(df_n, df_d)$	p
Time	F(4,70)=7.65	<0.0001
Group	F(2,47)=2.96	0.0617
Group*Time	F(5,70)=3.49	0.0071

*df_n = numerator degrees of freedom; df_d = denominator degrees of freedom

Estimated circumferential strains (Ecc) values for each group at each time point are expected means from the linear mixed-effects model.

	Estimate	SE	t value t(df)	p
PBS POD 5	-8.9491	0.9728	t(85)=-9.20	<0.0001
PBS POD 6	-8.1961	0.7739	t(77)=-10.59	<0.0001
PBS POD 7	-6.7415	0.7739	t(77)=-8.71	<0.0001
PBS POD 8	-4.0853	1.1707	t(87)=-3.49	0.0008
PBS POD 9	-0.9676	1.2273	t(81)=-0.79	0.4328
Clodronate POD 5	-6.0730	0.6998	t(81)=-8.68	<0.0001
Clodronate POD 6	-6.9274	0.6488	t(80)=-10.68	<0.0001
Clodronate POD 7	-6.7087	0.6329	t(78)=-10.60	<0.0001
Clodronate POD 9	-4.8390	1.2274	t(81)=-3.94	0.0002
No Treatment POD 5	-7.2245	0.8640	t(78)=-8.36	<0.0001
No Treatment POD 6	-5.7824	0.9154	t(81)=-6.32	<0.0001
No Treatment POD 7	-3.0449	1.0753	t(84)=-2.83	0.0058

*SE = standard error; df = degrees of freedom

Estimated treatment differences at each time point adjusted using Sidak approach to correct for multiple comparisons.

Time	Group Comparison	Estimate	SE	t value t(df)	Adjusted p
POD 9	PBS vs Clodronate	-3.8714	1.7358	t(81)=-2.23	0.0289
POD 7	Clodronate vs No Treatment	3.6638	1.2477	t(82)=2.94	0.0134
POD 7	PBS vs No treatment	3.6967	1.3249	t(82)=2.79	0.0202
POD 7	PBS vs Clodronate	0.03286	0.9997	t(77)=0.03	1.0000
POD 6	Clodronate vs No Treatment	1.1450	1.1220	t(80)=1.02	0.6729
POD 6	PBS vs No treatment	2.4138	1.1987	t(79)=2.01	0.1369
POD 6	PBS vs Clodronate	1.2688	1.0099	t(78)=1.26	0.5128
POD 5	Clodronate vs No Treatment	-1.1515	1.1118	t(79)=-1.04	0.6627
POD 5	PBS vs No treatment	1.7247	1.3011	t(82)=1.33	0.4671
POD 5	PBS vs Clodronate	2.8762	1.1984	t(84)=2.40	0.0560

*SE = standard error; df = degrees of freedom

Estimated time differences for each treatment group adjusted using Sidak approach for multiple comparisons.

Group	Time Comparison	Estimate	SE	t value t(df)	Adjusted p
No treatment	POD 7 vs POD 6	2.7375	1.1287	t(60)=2.43	0.0527
No treatment	POD 7 vs POD 5	4.1796	1.2944	t(83)=3.23	0.0057
No treatment	POD 6 vs POD 5	1.4421	1.0129	t(64)=1.42	0.4050
Clodronate	POD 9 vs POD 7	1.8696	1.3429	t(86)=1.39	0.6689
Clodronate	POD 9 vs POD 6	2.0883	1.3750	t(85)=1.52	0.5761
Clodronate	POD 9 vs POD 5	1.2339	1.4089	t(83)=0.88	0.9454
Clodronate	POD 7 vs POD 6	0.2187	0.7089	t(59)=0.31	0.9998
Clodronate	POD 7 vs POD 5	-0.6357	0.8781	t(83)=-0.72	0.9782
Clodronate	POD 6 vs POD 5	-0.8544	0.7586	t(61)=-1.13	0.8409
PBS	POD 9 vs POD 8	3.1177	1.2970	t(52)=2.40	0.1734
PBS	POD 9 vs POD 7	5.7739	1.3775	t(87)=4.19	0.0008
PBS	POD 9 vs POD 6	7.2285	1.4259	t(86)=5.07	<0.0001
PBS	POD 9 vs POD 5	7.9815	1.5584	t(86)=5.12	<0.0001
PBS	POD 8 vs POD 7	2.6561	1.2069	t(69)=2.20	0.2704
PBS	POD 8 vs POD 6	4.1107	1.3340	t(81)=3.08	0.0290
PBS	POD 8 vs POD 5	4.8638	1.4987	t(86)=3.25	0.0178
PBS	POD 7 vs POD 6	1.4546	0.8545	t(59)=1.70	0.6237
PBS	POD 7 vs POD 5	2.2076	1.1650	t(81)=1.89	0.4740
PBS	POD 6 vs POD 5	0.7530	1.0161	t(64)=0.74	0.9979

*SE = standard error; df = degrees of freedom

Supplemental Table 2. Mixed model analysis for radial strains (Err) for 3 treatment groups: PBS-liposome, Clodronate-liposome, No Treatment; and 5 time points: POD 5, POD 6, POD 7, POD 8, POD 9; where POD = post operational day.

Parameter estimates from the linear mixed-effects model

Effect	F value $F(df_n, df_d)$	p
Time	F(4,67)=9.58	<0.0001
Group	F(2,40)=3.20	0.0514
Group*Time	F(5,66)=5.81	0.0002

*df_n = numerator degrees of freedom; df_d = denominator degrees of freedom

Estimated radial strains (Err) values for each group at each time point are expected means from the linear mixed-effects model.

	Estimate	SE	t value t(df)	p
PBS POD 5	7.7810	0.9714	t(83)=8.01	<0.0001
PBS POD 6	9.0806	0.7511	t(82)=12.09	<0.0001
PBS POD 7	6.2863	0.7512	t(82)=8.37	<0.0001
PBS POD 8	3.1508	1.1915	t(83)=2.64	0.0098
PBS POD 9	1.3327	1.1915	t(83)=1.12	0.2666
Clodronate POD 5	7.4544	0.6867	t(83)=10.86	<0.0001
Clodronate POD 6	6.2690	0.6353	t(82)=9.87	<0.0001
Clodronate POD 7	5.7289	0.6136	t(82)=9.34	<0.0001
Clodronate POD 9	7.1819	1.1916	t(83)=6.03	<0.0001
No Treatment POD 5	8.4125	1.0635	t(83)=7.91	<0.0001
No Treatment POD 6	5.6100	0.9700	t(82)=5.78	<0.0001
No Treatment POD 7	2.2055	1.0636	t(82)=2.07	0.0412

*SE = standard error; df = degrees of freedom

Estimated treatment differences at each time point adjusted using Sidak approach to correct for multiple comparisons.

Time	Group Comparison	Estimate	SE	t value t(df)	Adjusted p
POD 9	PBS vs Clodronate	5.8492	1.6851	t(83)=3.47	0.0009
POD 7	Clodronate vs No Treatment	-3.5234	1.2279	t(82)=-2.87	0.0164
POD 7	PBS vs No treatment	-4.0808	1.3021	t(82)=-3.13	0.0077
POD 7	PBS vs Clodronate	-0.5575	0.9699	t(82)=-0.57	0.9190
POD 6	Clodronate vs No Treatment	-0.6591	1.1595	t(82)=-0.57	0.9214
POD 6	PBS vs No treatment	-3.4707	1.2268	t(82)=-2.83	0.0184
POD 6	PBS vs Clodronate	-2.8116	0.9838	t(82)=-2.86	0.0170
POD 5	Clodronate vs No Treatment	0.9581	1.2659	t(83)=0.76	0.8353
POD 5	PBS vs No treatment	0.6315	1.4404	t(83)=0.44	0.9616
POD 5	PBS vs Clodronate	-0.3266	1.1896	t(83)=-0.27	0.9900

*SE = standard error; df = degrees of freedom

Estimated time differences for each treatment group adjusted using Sidak approach for multiple comparisons.

Group	Time Comparison	Estimate	SE	t value t(df)	Adjusted p
No treatment	POD 7 vs POD 6	-3.4045	1.3629	t(61)=-2.50	0.0443
No treatment	POD 7 vs POD 5	-6.2070	1.4343	t(65)=-4.33	0.0002
No treatment	POD 6 vs POD 5	-2.8025	1.3799	t(67)=-2.03	0.1325
Clodronate	POD 9 vs POD 7	1.4530	1.3166	t(77)=1.10	0.8533
Clodronate	POD 9 vs POD 6	0.9128	1.3251	t(77)=0.69	0.9831
Clodronate	POD 9 vs POD 5	-0.2725	1.3566	t(79)=-0.20	1.0000
Clodronate	POD 7 vs POD 6	-0.5402	0.8372	t(61)=-0.65	0.9879
Clodronate	POD 7 vs POD 5	-1.7255	0.8818	t(66)=-1.96	0.2860
Clodronate	POD 6 vs POD 5	-1.1854	0.8893	t(62)=-1.33	0.7115
PBS	POD 9 vs POD 8	-1.8181	1.5815	t(57)=-1.15	0.9469
PBS	POD 9 vs POD 7	-4.9537	1.3622	t(69)=-3.64	0.0054
PBS	POD 9 vs POD 6	-7.7480	1.3623	t(69)=-5.69	<.0001
PBS	POD 9 vs POD 5	-6.4483	1.5032	t(73)=-4.29	0.0006
PBS	POD 8 vs POD 7	-3.1355	1.3622	t(69)=-2.30	0.2197
PBS	POD 8 vs POD 6	-5.9298	1.3623	t(69)=-4.35	0.0005
PBS	POD 8 vs POD 5	-4.6302	1.5032	t(73)=-3.08	0.0297
PBS	POD 7 vs POD 6	-2.7943	1.0072	t(61)=-2.77	0.0696
PBS	POD 7 vs POD 5	-1.4946	1.1847	t(68)=-1.26	0.9071
PBS	POD 6 vs POD 5	1.2996	1.1747	t(64)=1.11	0.9585

*SE = standard error; df = degrees of freedom