

Supplementary Table S1. Analysis of cell viability and biomechanical properties of each type of sample. Values are shown as means \pm standard deviations of each analysis group. F-0: fibrin hydrogels devoid of agarose; FA: all hydrogels containing fibrin and agarose, regardless the type and concentration of agarose. F-D1LE: fibrin-agarose biomaterials containing D1LE agarose; F-D2LE: fibrin-agarose biomaterials containing D21LE agarose; F-LM: fibrin-agarose biomaterials containing LM agarose; F-MS8: fibrin-agarose biomaterials containing MS8 agarose; F-D5: fibrin-agarose biomaterials containing D5 agarose.

Sample Type	Agarose Concentration	Cell Viability (%)	Young Modulus (MPa)	Stress At Fracture (MPa)	Strain At Fracture (%)	Break Load (N)
F-0	0%	100 \pm 3.14	0.1701 \pm 0.0117	0.4927 \pm 0.1775	221.9467 \pm 23.1921	0.2463 \pm 0.0888
FA	All concentrations	98.24 \pm 4.35	0.2987 \pm 0.1249	0.5012 \pm 0.2370	261.1046 \pm 76.4858	0.3038 \pm 0.1420
F-D1LE	All concentrations	99.13 \pm 2.36	0.3788 \pm 0.1681	0.4327 \pm 0.1745	210.7695 \pm 43.6563	0.2596 \pm 0.1047
F-D2LE	All concentrations	99.27 \pm 2.48	0.2763 \pm 0.0640	0.4741 \pm 0.1253	251.1447 \pm 41.4778	0.3036 \pm 0.0753
F-LM	All concentrations	97.87 \pm 3.41	0.2885 \pm 0.1188	0.6562 \pm 0.2764	325.8786 \pm 73.3308	0.3937 \pm 0.1658
F-MS8	All concentrations	97.53 \pm 6.71	0.2589 \pm 0.0878	0.4311 \pm 0.2709	236.2120 \pm 71.9679	0.2587 \pm 0.1625
F-D5	All concentrations	97.4 \pm 5.11	0.2852 \pm 0.1206	0.5181 \pm 0.2280	284.4259 \pm 83.7706	0.3109 \pm 0.1368
All types of agarose	0.05%	95.95 \pm 6.92	0.2862 \pm 0.1178	0.5912 \pm 0.2397	277.0291 \pm 62.5946	0.3547 \pm 0.1438
	0.10%	98.31 \pm 3.66	0.2914 \pm 0.0881	0.5986 \pm 0.2060	281.4055 \pm 72.2857	0.3592 \pm 0.1236
	0.20%	99.08 \pm 2.48	0.2757 \pm 0.0811	0.4653 \pm 0.2086	255.2131 \pm 85.5107	0.2906 \pm 0.1260
	0.30%	99.62 \pm 1.46	0.2816 \pm 0.2236	0.2161 \pm 0.1931	161.1427 \pm 116.9692	0.1297 \pm 0.1159
F-D1LE	0.05%	97.67 \pm 3.63	0.2800 \pm 0.1262	0.4536 \pm 0.1238	238.0654 \pm 61.8265	0.2722 \pm 0.0743
	0.10%	98.85 \pm 2.83	0.3822 \pm 0.1094	0.5105 \pm 0.2344	220.4391 \pm 29.9518	0.3063 \pm 0.1407
	0.20%	100 \pm 0	0.2921 \pm 0.0588	0.3462 \pm 0.1468	189.3716 \pm 38.8563	0.2077 \pm 0.0881
	0.30%	100 \pm 0	0.5611 \pm 0.1948	0.4204 \pm 0.1767	195.2020 \pm 26.2877	0.2522 \pm 0.1060
F-D2LE	0.05%	98.37 \pm 3.98	0.2641 \pm 0.0447	0.4575 \pm 0.0617	253.8015 \pm 18.1873	0.2745 \pm 0.0370
	0.10%	98.72 \pm 3.14	0.2454 \pm 0.0267	0.5044 \pm 0.1574	254.4134 \pm 71.0948	0.3027 \pm 0.0944
	0.20%	100 \pm 0	0.3194 \pm 0.0875	0.4605 \pm 0.1522	245.2191 \pm 20.0176	0.3336 \pm 0.0829
	0.30%	100 \pm 0	-	-	-	-
F-LM	0.05%	95.7 \pm 4.42	0.4186 \pm 0.1575	0.9074 \pm 0.0858	347.9151 \pm 43.4136	0.5444 \pm 0.0515
	0.10%	98.95 \pm 2.56	0.2713 \pm 0.0737	0.6589 \pm 0.2633	293.3282 \pm 88.6031	0.3953 \pm 0.1580
	0.20%	97.69 \pm 3.73	0.2208 \pm 0.0468	0.6307 \pm 0.2707	342.5928 \pm 74.5234	0.3784 \pm 0.1624
	0.30%	99.13 \pm 2.13	0.2433 \pm 0.0618	0.3137 \pm 0.0318	316.5785 \pm 91.6292	0.1882 \pm 0.0191
F-MS8	0.05%	93 \pm 11.97	0.2551 \pm 0.0798	0.5396 \pm 0.2649	246.8549 \pm 52.6898	0.3237 \pm 0.1589
	0.10%	97.1257 \pm 4.9441	0.2551 \pm 0.0669	0.6763 \pm 0.2162	299.0610 \pm 60.4168	0.4058 \pm 0.1297
	0.20%	100 \pm 0	0.2473 \pm 0.0828	0.3192 \pm 0.1892	178.3862 \pm 55.1791	0.1915 \pm 0.1135
	0.30%	100 \pm 0	0.2782 \pm 0.1309	0.1895 \pm 0.1163	220.5459 \pm 71.9095	0.1137 \pm 0.0698
F-D5	0.05%	95.0199 \pm 7.9788	0.2132 \pm 0.046	0.5981 \pm 0.2629	298.5086 \pm 61.3628	0.3588 \pm 0.1577
	0.10%	97.9186 \pm 5.0984	0.3033 \pm 0.0881	0.6429 \pm 0.1277	339.7860 \pm 53.7112	0.3857 \pm 0.0766
	0.20%	97.6918 \pm 3.7337	0.2990 \pm 0.1004	0.5699 \pm 0.0998	320.4957 \pm 72.2485	0.3420 \pm 0.0599
	0.30%	98.9548 \pm 2.5602	0.3253 \pm 0.1953	0.2616 \pm 0.1878	178.9132 \pm 39.6732	0.1569 \pm 0.1127

Supplementary Table S2. Statistical p values for the comparison of the cell viability and biomechanical properties among different groups of samples (global and specific groups). For the comparisons of global groups, analyses were carried out among types of biomaterials (regardless the concentration of agarose) and among concentrations (regardless the type of agarose). Statistically significant results are highlighted with asterisks (*). F-0: fibrin hydrogels devoid of agarose; FA: all hydrogels containing fibrin and agarose, regardless the type and concentration of agarose. F-D1LE: fibrin-agarose biomaterials containing D1LE agarose; F-D2LE: fibrin-agarose biomaterials containing D21LE agarose; F-LM: fibrin-agarose biomaterials containing LM agarose; F-MS8: fibrin-agarose biomaterials containing MS8 agarose; F-D5: fibrin-agarose biomaterials containing D5 agarose

		CELL VIABILITY (%)	YOUNG MODULUS (Mpa)	STRESS AT FRACTURE (MPa)	STRAIN AT FRACTURE (%)	BREAK LOAD (N)
All agarose concentrations within each type of fibrin- agarose biomaterial (global groups)	F-0 vs. F-D1LE	0.12860	0.00022*	0.40213	0.46221	0.97985
	F-0 vs. F-D2LE	0.15777	0.00001*	0.67292	0.05586	0.27959
	F-0 vs. F-LM	0.07311	0.00057*	0.09955	0.00158*	0.05166
	F-0 vs. F-MS8	0.11558	0.00753*	0.56053	0.82024	0.97985
	F-0 vs. F-D5	0.07311	0.00051*	0.74262	0.07312	0.25063
	F-D1LE vs. F-D2LE	0.84613	0.04809*	0.31904	0.00265*	0.13152
	F-D1LE vs. F-LM	0.26377	0.03742*	0.00539*	<0.00001*	0.00539*
	F-D1LE vs. F-MS8	0.76704	0.00676*	0.67527	0.26377	0.67527
	F-D1LE vs. F-D5	0.41884	0.04149*	0.13051	0.00149*	0.13051
	F-D2LE vs. F-LM	0.17185	0.79180	0.04482*	0.00055*	0.10041
	F-D2LE vs. F-MS8	0.60217	0.28339	0.28339	0.41286	0.13824
	F-D2LE vs. F-D5	0.32038	0.69669	0.34434	0.11282	0.62375
	F-LM vs. F-MS8	0.44288	0.56008	0.00825*	0.00021*	0.00825*
	F-LM vs. F-D5	0.84613	0.79845	0.08433	0.09271	0.08433
	F-MS8 vs. F-D5	0.67526	0.66038	0.17186	0.04828*	0.17186
All agarose types within each concentration of fibrin-agarose biomaterial (global groups)	0.05% vs. F-0	0.00022*	<0.00001*	0.24180	0.00002*	0.00918*
	0.1% vs. F-0	0.00234*	<0.00001*	0.01759*	0.00069*	0.00007*
	0.2% vs. F-0	0.0073*	<0.00001*	0.46707	0.07718	0.18718
	0.3% vs. F-0	0.01551*	0.07718	<0.00001*	0.00161*	0.00004*
	0.05% vs. 0.1%	0.24781	0.59200	0.65434	0.87755	0.65434
	0.05% vs. 0.2%	0.09349	0.91237	0.11585	0.15469	0.21876
	0.05% vs. 0.3%	0.03712*	0.66498	<0.00001*	0.00001*	<0.00001*
	0.1% vs. 0.2%	0.63326	0.54220	0.0073*	0.18718	0.01990*
	0.1% vs. 0.3%	0.35042	0.58188	<0.00001*	0.00002*	<0.00001*
	0.2% vs. 0.3%	0.65434	0.71915	0.00001*	0.00161*	<0.00001*
F-D1LE	0.05% vs. F-0	0.13203	0.06494	0.69913	0.81818	0.81818
	0.1% vs. F-0	0.24025	0.00866*	0.93723	0.81818	0.39394
	0.2% vs. F-0	0.39393	0.00216*	0.24026	0.17965	0.39394
	0.3% vs. F-0	0.39393	0.00216*	0.39394	0.13203	0.93723
	0.05% vs. 0.1%	0.69913	0.24026	0.81818	0.58874	0.81818
	0.05% vs. 0.2%	0.39393	0.48485	0.30952	0.09307	0.30952
	0.05% vs. 0.3%	0.39393	0.02597*	0.69913	0.24026	0.69913
	0.1% vs. 0.2%	0.69913	0.06494	0.17965	0.17965	0.17965
	0.1% vs. 0.3%	0.69913	0.09307	0.58874	0.17965	0.58874
	0.2% vs. 0.3%	0.93722	0.02597*	0.48485	0.93723	0.48485
F-D2LE	0.05% vs. F-0	0.24025	0.00216*	0.58874	0.00866*	0.69913
	0.1% vs. F-0	0.24025	0.00216*	0.81818	0.81818	0.39394
	0.2% vs. F-0	0.39393	0.00216*	0.48485	0.09307	0.24026
	0.3% vs. F-0	0.39393	-	-	-	-
	0.05% vs. 0.1%	0.93722	0.58874	0.93723	0.93723	0.93723
	0.05% vs. 0.2%	0.69913	0.24026	0.69913	0.93723	0.17965
	0.05% vs. 0.3%	0.69913	-	-	-	-
	0.1% vs. 0.2%	0.69913	0.24026	0.93723	0.93723	0.48485
	0.1% vs. 0.3%	0.69913	-	-	-	-
	0.2% vs. 0.3%	0.93722	-	-	-	-
F-LM	0.05% vs. F-0	0.09307	0.00216*	0.00216*	0.00216*	0.00216*
	0.1% vs. F-0	0.24025	0.00433*	0.13203	0.13203	0.06494
	0.2% vs. F-0	0.17965	0.02597*	0.30952	0.00216*	0.17965

	0.3% vs. F-0	0.30952	0.06494	0.09307	0.93723	0.13203
	0.05% vs. 0.1%	0.24025	0.09307	0.01515*	0.24026	0.01515*
	0.05% vs. 0.2%	0.39393	0.02597*	0.06494	0.93723	0.06494
	0.05% vs. 0.3%	0.13203	0.13203	0.00216*	0.24026	0.00216*
	0.1% vs. 0.2%	0.69913	0.17965	0.58874	0.30952	0.58874
	0.1% vs. 0.3%	0.93722	0.48485	0.02597*	0.58874	0.02597*
	0.2% vs. 0.3%	0.58874	0.39394	0.00433*	0.24026	0.00433*
F-MS8	0.05% vs. F-0	0.13203	0.02597*	0.93723	0.30952	0.58874
	0.1% vs. F-0	0.17965	0.00216*	0.09307	0.04113*	0.02597*
	0.2% vs. F-0	0.39393	0.06494	0.17965	0.09307	0.48485
	0.3% vs. F-0	0.39393	0.39394	0.02597*	0.58874	0.02597*
	0.05% vs. 0.1%	0.81818	0.93723	0.30952	0.13203	0.30952
	0.05% vs. 0.2%	0.39393	0.58874	0.17965	0.06494	0.17965
	0.05% vs. 0.3%	0.39393	0.93723	0.00866*	0.48485	0.00866*
	0.1% vs. 0.2%	0.39393	0.93723	0.01515*	0.00866*	0.01515*
	0.1% vs. 0.3%	0.39393	0.58874	0.00866*	0.13203	0.00866*
	0.2% vs. 0.3%	0.93722	0.69913	0.30952	0.17965	0.30952
F-D5	0.05% vs. F-0	0.13203	0.06494	0.48485	0.04113*	0.24026
	0.1% vs. F-0	0.24025	0.00216*	0.17965	0.00216*	0.02597*
	0.2% vs. F-0	0.17965	0.00866*	0.48485	0.01515*	0.06494
	0.3% vs. F-0	0.24025	0.39394	0.06494	0.09307	0.09307
	0.05% vs. 0.1%	0.69913	0.13203	0.69913	0.39394	0.69913
	0.05% vs. 0.2%	0.81818	0.24026	0.81818	0.69913	0.81818
	0.05% vs. 0.3%	0.58874	0.93723	0.04113*	0.00866*	0.04113*
	0.1% vs. 0.2%	0.81818	0.93723	0.39394	0.93723	0.39394
	0.1% vs. 0.3%	0.93722	0.93723	0.01515*	0.00216*	0.01515*
	0.2% vs. 0.3%	0.69913	0.93723	0.00866*	0.00433*	0.00866*
0.05% agarose concentration	F-D1LE vs. F-D2LE	0.81818	0.93723	0.69913	0.58874	0.69913
	F-D1LE vs. F-LM	0.58874	0.13203	0.00216*	0.01515*	0.00216*
	F-D1LE vs. F-MS8	0.81818	0.93723	0.93723	0.81818	0.93723
	F-D1LE vs. F-D5	0.81818	0.48485	0.39394	0.17965	0.39394
	F-D2LE vs. F-LM	0.24025	0.06494	0.00216*	0.00433*	0.00216*
	F-D2LE vs. F-MS8	0.58874	0.69913	0.93723	0.69913	0.93723
	F-D2LE vs. F-D5	0.58874	0.09307	0.48485	0.24026	0.48485
	F-LM vs. F-MS8	0.81818	0.06494	0.06494	0.00866*	0.06494
	F-LM vs. F-D5	0.69913	0.00866*	0.09307	0.17965	0.09307
0.1% agarose concentration	F-MS8 vs. F-D5	0.93722	0.30952	0.69913	0.30952	0.69913
	F-D1LE vs. F-D2LE	0.93722	0.06494	0.93723	0.81818	0.93723
	F-D1LE vs. F-LM	0.93722	0.06494	0.30952	0.13203	0.30952
	F-D1LE vs. F-MS8	0.69913	0.06494	0.17965	0.02597*	0.17965
	F-D1LE vs. F-D5	0.93722	0.17965	0.30952	0.00216*	0.30952
	F-D2LE vs. F-LM	0.93722	0.69913	0.17965	0.48485	0.17965
	F-D2LE vs. F-MS8	0.69913	0.81818	0.17965	0.30952	0.17965
	F-D2LE vs. F-D5	0.93722	0.30952	0.24026	0.09307	0.24026
	F-LM vs. F-MS8	0.69913	0.81818	0.93723	0.93723	0.93723
0.2% agarose concentration	F-LM vs. F-D5	0.93722	0.39394	0.58874	0.39394	0.58874
	F-MS8 vs. F-D5	0.81818	0.39394	0.58874	0.24026	0.58874
	F-D1LE vs. F-D2LE	0.93722	0.69913	0.17965	0.01515*	0.04113*
	F-D1LE vs. F-LM	0.39393	0.04113*	0.06494	0.00216*	0.06494
	F-D1LE vs. F-MS8	0.93722	0.39394	0.69913	0.39394	0.69913
	F-D1LE vs. F-D5	0.39393	0.93723	0.01515*	0.00433*	0.01515*
	F-D2LE vs. F-LM	0.39393	0.04113*	0.39394	0.01515*	0.93723
	F-D2LE vs. F-MS8	0.93722	0.13203	0.30952	0.06494	0.09307
	F-D2LE vs. F-D5	0.39393	0.93723	0.39394	0.04113*	0.93723
0.3% agarose concentration	F-LM vs. F-MS8	0.39393	0.48485	0.02597*	0.00433*	0.02597*
	F-LM vs. F-D5	0.93722	0.30952	0.81818	0.81818	0.81818
	F-MS8 vs. F-D5	0.39393	0.48485	0.02597*	0.00433*	0.02597*
	F-D1LE vs. F-D2LE	0.93722	-	-	-	-
	F-D1LE vs. F-LM	0.69913	0.01515*	0.35238	0.03810*	0.35238
	F-D1LE vs. F-MS8	0.93722	0.01515*	0.04113*	0.69913	0.04113*
	F-D1LE vs. F-D5	0.69913	0.09307	0.09307	0.24026	0.09307

F-D2LE vs. F-LM	0.69913	-	-	-	-
F-D2LE vs. F-MS8	0.93722	-	-	-	-
F-D2LE vs. F-D5	0.69913	-	-	-	-
F-LM vs. F-MS8	0.69913	0.69913	0.11429	0.17143	0.11429
F-LM vs. F-D5	0.93722	0.93723	0.47619	0.01905*	0.47619
F-MS8 vs. F-D5	0.69913	0.58874	0.58874	0.24026	0.58874

Supplementary Table S3. Statistical p values for the comparison of the histochemical and immunohistochemical staining among different samples versus control group and fibrin hydrogels. Statistically significant results are highlighted with asterisks (*). F-0: fibrin hydrogels devoid of agarose; FA: all hydrogels containing fibrin and agarose, regardless the type and concentration of agarose. F-D1LE: fibrin-agarose biomaterials containing D1LE agarose; F-D2LE: fibrin-agarose biomaterials containing D21LE agarose; F-LM: fibrin-agarose biomaterials containing LM agarose; F-MS8: fibrin-agarose biomaterials containing MS8 agarose; F-D5: fibrin-agarose biomaterials containing D5 agarose

		PICROSIRIUS RED	ALCIAN BLUE	MMP14	CD86	CD206
D1LE	0.05% vs. F-0	0.67627	0.66782	0.99283	0.25808	0.23204
	0.1% vs. F-0	0.720164	0.70861	0.99999	0.28503	0.07954
	0.2% vs. F-0	0.99618	0.99903	0.99924	0.70264	0.69030
	0.3% vs. F-0	0.00000*	0.87408	0.93992	0.98495	0.98698
	CTR vs. F-0	0.99992	0.94468	0.95323	0.97789	0.99977
	CTR vs. 0.05%	0.53278	0.17549	0.99966	0.66635	0.36085
	CTR vs. 0.1%	0.57902	0.99471	0.91651	0.70264	0.13971
	CTR vs. 0.2%	0.99980	0.99471	0.82652	0.97789	0.83930
	CTR vs. 0.3%	0.00000*	0.99994	0.48455	1.00000	0.99906
D2LE	0.05% vs. F-0	0.999838	0.325850	0.191671	0.067429	0.389224
	0.1% vs. F-0	0.221595	0.996204	0.233849	0.309696	0.092955
	0.2% vs. F-0	0.962280	1.000000	0.999568	0.282619	0.133617
	0.3% vs. F-0	0.008459*	0.999999	0.999431	0.988063	1.000000
	CTR vs. F-0	0.999986	0.989836	0.891524	0.982386	0.999796
	CTR vs. 0.05%	0.999998	0.099257	0.792508	0.257129	0.548315
	CTR vs. 0.1%	0.292956	0.877611	0.845076	0.711859	0.158832
	CTR vs. 0.2%	0.985042	0.993355	0.973792	0.677663	0.220260
	CTR vs. 0.3%	0.01331*	0.995511	0.976446	1.000000	0.999796
LM	0.05% vs. F-0	0.999954	0.805083	0.370240	0.091787	0.499527
	0.1% vs. F-0	0.802965	0.999288	0.047878*	0.780640	0.875117
	0.2% vs. F-0	0.042474*	0.628928	0.145490	0.529283	0.262275
	0.3% vs. F-0	0.000001*	0.997397	0.198126	0.626977	0.903306
	CTR vs. F-0	0.999990	0.992953	0.814252	0.988174	0.999919
	CTR vs. 0.05%	0.999316	0.459844	0.025360*	0.295808	0.637185
	CTR vs. 0.1%	0.871984	0.941855	0.001289*	0.983078	0.947290
	CTR vs. 0.2%	0.061116	0.291890	0.005826*	0.879428	0.371047
	CTR vs. 0.3%	0.000001*	0.909415	0.009196*	0.933068	0.963254
MS8	0.05% vs. F-0	0.723208	0.956470	0.998967	0.058828	0.468489

	0.1% vs. F-0	0.753252	0.804197	0.971761	0.205186	0.788273
	0.2% vs. F-0	0.004884*	0.999933	0.973739	0.999979	0.982551
	0.3% vs. F-0	0.000108*	0.992417	0.901035	0.999741	0.989716
	CTR vs. F-0	0.999991	0.989984	0.948428	0.983699	0.999907
	CTR vs. 0.05%	0.803312	0.691591	0.804303	0.226620	0.609290
	CTR vs. 0.1%	0.829251	0.431392	0.567924	0.554359	0.892383
	CTR vs. 0.2%	0.007498*	0.961968	0.576134	0.995626	0.997301
	CTR vs. 0.3%	0.000177*	0.843920	0.396486	0.998674	0.998871
D5	0.05% vs. F-0	0.930422	0.990045	0.999494	0.101285	0.850421
	0.1% vs. F-0	0.144177	0.999964	0.996269	0.895543	0.999404
	0.2% vs. F-0	0.011574*	0.998778	0.943754	0.338749	0.984506
	0.3% vs. F-0	0.000000*	0.999633	0.999908	0.823788	0.999404
	CTR vs. F-0	0.999936	0.986889	0.912450	0.984433	0.999854
	CTR vs. 0.05%	0.975880	0.808533	0.764363	0.338749	0.939866
	CTR vs. 0.1%	0.219739	0.997401	0.664237	0.998738	0.999999
	CTR vs. 0.2%	0.021031*	0.904063	0.404573	0.734685	0.998252
	CTR vs. 0.3%	0.000000*	0.931546	0.815401	0.993197	0.991528