

Supplementary file 1. PCoA distances between naïve, infected and treatment groups.

We performed detailed distance analysis between infected and uninfected samples (Tables A and B, Figure A), and between treatment groups (all experimental samples included, Table C-E, Figure B, Figure C). To control for any possible confounding effects from the one outlier with high parasite burden post-BNZ treatment, we also performed the same analysis, excluding that mouse (Tables F-H, Figure D, Figure E).

Table A. Distance analysis between naïve and infected at 50, 75, and 142 days post infection (DPI).

	DPI	pseudo-F	p-value	q-value
LA	50	3.029144	0.014	0.014
	70	2.330901	0.023	0.023
	142	1.09537	0.321	0.321
RA	50	1.578709	0.12	0.12
	70	2.910362	0.013	0.013
	142	2.511789	0.039	0.039
LV-top	50	3.652951	0.005	0.005
	70	1.460853	0.143	0.143
	142	1.187019	0.282	0.282
LV-bottom	50	5.163818	0.003	0.003
	70	3.503573	0.002	0.002
	142	4.459738	0.001	0.001
RV-top	50	2.060866	0.009	0.009
	70	4.613933	0.001	0.001
	142	3.914494	0.001	0.001
RV-bottom	50	1.45523	0.139	0.139
	70	4.282155	0.001	0.001
	142	5.425939	0.001	0.001

Table B. Kruskal-Wallis with FDR-corrected post-hoc Dunn's test between naïve and infected at 50, 75, and 142 days post infection (DPI).

Heart section	Pair 1	Pair 2	FDR-corrected P value
LA	naive_VS_infected_50DPI	naive_VS_infected_75DPI	3.327069e-01
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	2.678613e-18
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	6.183185e-22
RA	naive_VS_infected_50DPI	naive_VS_infected_75DPI	0.7474485
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	0.7727821
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	0.6268322
LVT	naive_VS_infected_50DPI	naive_VS_infected_75DPI	0.007282892
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	0.092750387
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	0.244127579
LVB	naive_VS_infected_50DPI	naive_VS_infected_75DPI	2.233079e-09
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	9.915717e-17
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	1.686405e-02
RVT	naive_VS_infected_50DPI	naive_VS_infected_75DPI	0.05464850
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	0.40073528
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	0.01009132
RVB	naive_VS_infected_50DPI	naive_VS_infected_75DPI	0.2803490
	naive_VS_infected_50DPI	naive_VS_infected_142DPI	0.1506789
	naive_VS_infected_75DPI	naive_VS_infected_142DPI	0.9722301

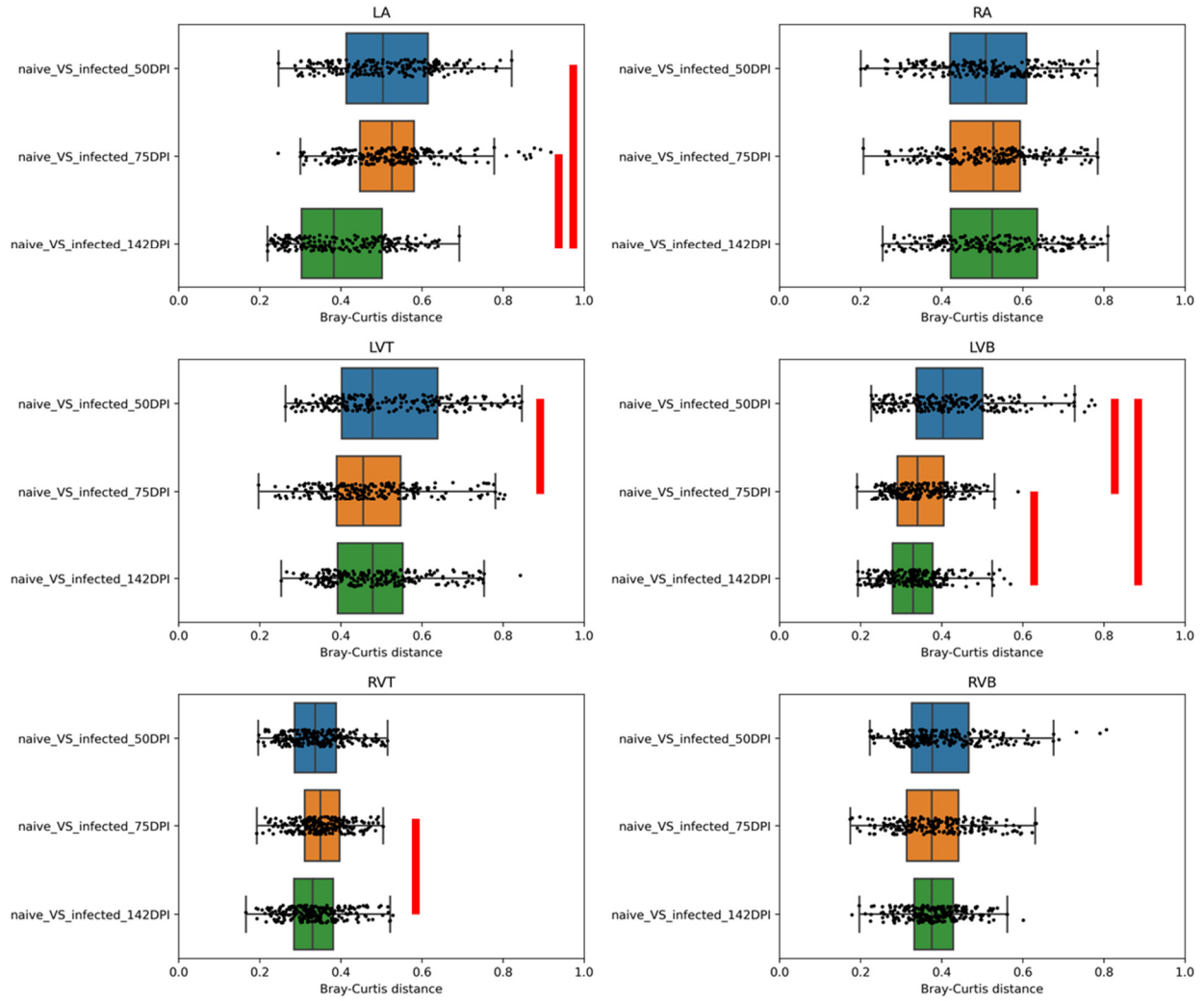


Figure A. Distance analysis boxplot between naïve and infected at 50, 75, and 142 days post infection (DPI). Red line, p-value <0.05 by Mann-Whitney U Test, FDR-corrected.

Table C. Distance analysis between different treatment groups at 142 DPI.

Heart section	Group 1	Group 2	pseudo-F	p-value
LA	naive	BNZ	1.356518	0.219
	naive	infected	1.095370	0.292
	naive	combo	1.359726	0.228
	infected	BNZ	0.975107	0.379
	infected	combo	0.831580	0.459
	combo	BNZ	0.654794	0.647
RA	naive	BNZ	1.247886	0.238
	naive	infected	2.511789	0.041
	naive	combo	1.288730	0.235
	infected	BNZ	0.929379	0.407
	infected	combo	1.144374	0.293
	combo	BNZ	0.346012	0.943
LVT	naive	BNZ	1.484447	0.159
	naive	infected	1.187019	0.292
	naive	combo	1.461685	0.166
	infected	BNZ	1.051550	0.362
	infected	combo	1.214317	0.245
	combo	BNZ	2.061494	0.043
LVB	naive	BNZ	2.715189	0.004
	naive	infected	4.459738	0.002
	naive	combo	3.321633	0.001
	infected	BNZ	1.295228	0.273
	infected	combo	1.753522	0.083
	combo	BNZ	1.869084	0.046
RVT	naive	BNZ	3.087695	0.001
	naive	infected	3.914494	0.001
	naive	combo	2.366988	0.012
	infected	BNZ	2.117736	0.035
	infected	combo	2.610696	0.002
	combo	BNZ	1.013534	0.419
RVB	naive	BNZ	4.910679	0.001
	naive	infected	5.425939	0.001
	naive	combo	3.276360	0.001
	infected	BNZ	2.552585	0.010
	infected	combo	4.760043	0.001
	combo	BNZ	2.368141	0.008

Table D. Kruskal-Wallis with FDR-corrected post-hoc Dunn's test between different treatment groups at 142 DPI.

	Pair 1	Pair 2	FDR-corrected p value
LA	naive_VS_BNZ	naive_VS_naive	0.139782138
	naive_VS_BNZ	naive_VS_infected	0.160693030
	naive_VS_naive	naive_VS_infected	0.776120010
	naive_VS_BNZ	naive_VS_combo	0.179862414
	naive_VS_naive	naive_VS_combo	0.010418740
	naive_VS_infected	naive_VS_combo	0.005658156
RA	naive_VS_BNZ	naive_VS_naive	0.1908288
	naive_VS_BNZ	naive_VS_infected	0.1936673
	naive_VS_naive	naive_VS_infected	0.0262561
	naive_VS_BNZ	naive_VS_combo	0.4614456
	naive_VS_naive	naive_VS_combo	0.1038900
	naive_VS_infected	naive_VS_combo	0.4266253
LVT	naive_VS_BNZ	naive_VS_naive	0.88251583
	naive_VS_BNZ	naive_VS_infected	0.03130183
	naive_VS_naive	naive_VS_infected	0.05686250
	naive_VS_BNZ	naive_VS_combo	0.01622882
	naive_VS_naive	naive_VS_combo	0.03320798
	naive_VS_infected	naive_VS_combo	0.67229235
LVB	naive_VS_BNZ	naive_VS_naive	9.456508e-10
	naive_VS_BNZ	naive_VS_infected	9.802618e-03
	naive_VS_naive	naive_VS_infected	5.412709e-05
	naive_VS_BNZ	naive_VS_combo	8.212829e-03
	naive_VS_naive	naive_VS_combo	5.778669e-05
	naive_VS_infected	naive_VS_combo	8.944717e-01
RVT	naive_VS_BNZ	naive_VS_naive	1.523759e-04
	naive_VS_BNZ	naive_VS_infected	1.761728e-01
	naive_VS_naive	naive_VS_infected	1.729419e-06
	naive_VS_BNZ	naive_VS_combo	1.527634e-01
	naive_VS_naive	naive_VS_combo	6.861743e-03
	naive_VS_infected	naive_VS_combo	8.017866e-03
RVB	naive_VS_BNZ	naive_VS_naive	8.521031e-01
	naive_VS_BNZ	naive_VS_infected	1.436145e-07
	naive_VS_naive	naive_VS_infected	2.818214e-06
	naive_VS_BNZ	naive_VS_combo	7.745506e-01
	naive_VS_naive	naive_VS_combo	8.225285e-01
	naive_VS_infected	naive_VS_combo	3.581962e-07

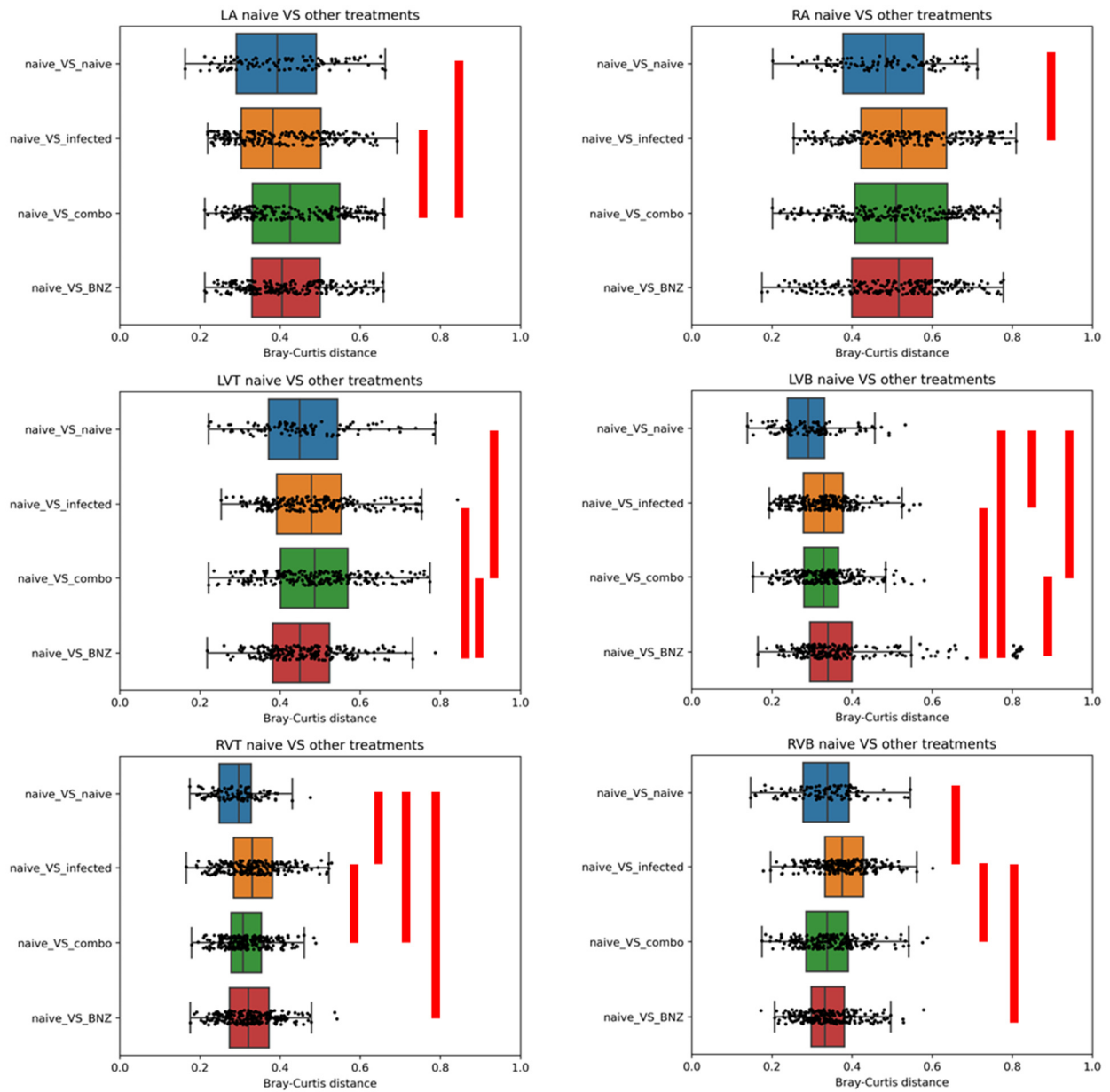


Figure B. Distance analysis boxplot between naïve groups and other experimental groups at 142DPI.
 Red line, p-value < 0.05 by Mann-Whitney U Test, FDR-corrected.

Table E. Kruskal-Wallis with FDR-corrected post-hoc Dunn's test between infected no treatment group and other treatment groups at 142 DPI.

Heart section	Pair 1	Pair 2	FDR-corrected p value
LA	infected_VS_BNZ	infected_VS_infected	0.4411514
	infected_VS_BNZ	infected_VS_combo	0.1796762
	infected_VS_infected	infected_VS_combo	0.1328960
RA	infected_VS_BNZ	infected_VS_infected	0.7325454
	infected_VS_BNZ	infected_VS_combo	0.8818900
	infected_VS_infected	infected_VS_combo	0.9304309
LVT	infected_VS_BNZ	infected_VS_infected	0.11787664
	infected_VS_BNZ	infected_VS_combo	0.01237103
	infected_VS_infected	infected_VS_combo	0.59656541
LVB	infected_VS_BNZ	infected_VS_infected	0.01219156
	infected_VS_BNZ	infected_VS_combo	0.62243881
	infected_VS_infected	infected_VS_combo	0.01968717
RVT	infected_VS_BNZ	infected_VS_infected	0.3474791
	infected_VS_BNZ	infected_VS_combo	0.8204677
	infected_VS_infected	infected_VS_combo	0.5053970
RVB	infected_VS_BNZ	infected_VS_infected	1.123535e-01
	infected_VS_BNZ	infected_VS_combo	7.433810e-08
	infected_VS_infected	infected_VS_combo	6.365436e-03

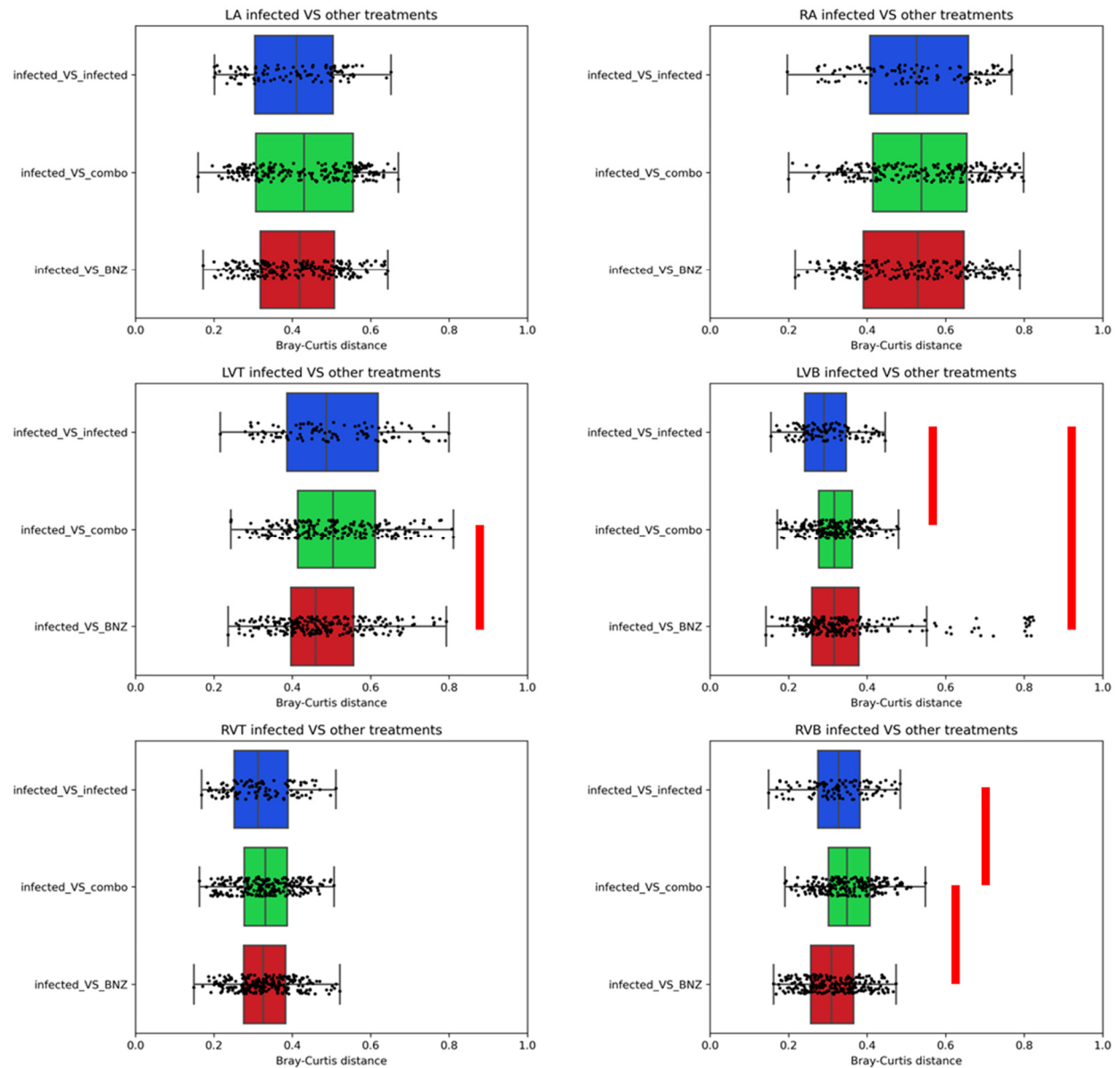


Figure C. Distance analysis boxplots between infected no treatment group and other treatment groups at 142 DPI. Red line, p-value <0.05 by Mann-Whitney U Test, FDR-corrected.

Table F. Distance analysis between different treatment groups at 142 DPI without high parasite burden post-BNZ treatment outlier mouse.

Heart section	Group 1	Group 2	pseudo-F	p-value
LA	naive	BNZ	1.325617	0.232
	naive	infected	1.09537	0.31
	naive	combo	1.359726	0.222
	infected	BNZ	0.894473	0.443
	infected	combo	0.83158	0.484
	combo	BNZ	0.769384	0.543
RA	naive	BNZ	1.406805	0.186
	naive	infected	2.511789	0.044
	naive	combo	1.28873	0.214
	infected	BNZ	0.7668	0.522
	infected	combo	1.144374	0.279
	combo	BNZ	0.457876	0.852
LVT	naive	BNZ	1.949067	0.054
	naive	infected	1.187019	0.277
	naive	combo	1.461685	0.173
	infected	BNZ	1.384779	0.182
	infected	combo	1.214317	0.265
	combo	BNZ	2.323148	0.026
LVB	naive	BNZ	2.845178	0.001
	naive	infected	4.459738	0.001
	naive	combo	3.321633	0.001
	infected	BNZ	1.295049	0.279
	infected	combo	1.753522	0.078
	combo	BNZ	2.067337	0.031
RVT	naive	BNZ	3.638358	0.002
	naive	infected	3.914494	0.001
	naive	combo	2.366988	0.008
	infected	BNZ	2.032209	0.046
	infected	combo	2.610696	0.002
	combo	BNZ	1.295884	0.224
RVB	naive	BNZ	5.356061	0.001
	naive	infected	5.425939	0.001
	naive	combo	3.27636	0.004
	infected	BNZ	2.336337	0.018
	infected	combo	4.760043	0.001
	combo	BNZ	2.566525	0.004

Table G. Kruskal-Wallis with FDR-corrected post-hoc Dunn's test between different treatment groups at 142 DPI without high parasite burden post-BNZ treatment outlier mouse.

	Pair1	Pair2	FDR-corrected p value
LA	naive_VS_BNZ	naive_VS_naive	0.295489565
	naive_VS_BNZ	naive_VS_infected	0.251628525
	naive_VS_naive	naive_VS_infected	0.774607473
	naive_VS_BNZ	naive_VS_combo	0.095755447
	naive_VS_naive	naive_VS_combo	0.010810319
	naive_VS_infected	naive_VS_combo	0.006009265
RA	naive_VS_BNZ	naive_VS_naive	0.20069214
	naive_VS_BNZ	naive_VS_infected	0.20583003
	naive_VS_naive	naive_VS_infected	0.02704533
	naive_VS_BNZ	naive_VS_combo	0.47119782
	naive_VS_naive	naive_VS_combo	0.10686888
	naive_VS_infected	naive_VS_combo	0.42504515
LVT	naive_VS_BNZ	naive_VS_naive	0.788488612
	naive_VS_BNZ	naive_VS_infected	0.011706694
	naive_VS_naive	naive_VS_infected	0.057448034
	naive_VS_BNZ	naive_VS_combo	0.003267821
	naive_VS_naive	naive_VS_combo	0.022433229
	naive_VS_infected	naive_VS_combo	0.672722645
LVB	naive_VS_BNZ	naive_VS_naive	2.406726e-09
	naive_VS_BNZ	naive_VS_infected	1.397022e-02
	naive_VS_naive	naive_VS_infected	5.705367e-05
	naive_VS_BNZ	naive_VS_combo	1.221490e-02
	naive_VS_naive	naive_VS_combo	5.932090e-05
	naive_VS_infected	naive_VS_combo	9.001797e-01
RVT	naive_VS_BNZ	naive_VS_naive	2.671548e-04
	naive_VS_BNZ	naive_VS_infected	1.818625e-01
	naive_VS_naive	naive_VS_infected	1.764897e-06
	naive_VS_BNZ	naive_VS_combo	1.660460e-01
	naive_VS_naive	naive_VS_combo	6.799045e-03
	naive_VS_infected	naive_VS_combo	8.235658e-03
RVB	naive_VS_BNZ	naive_VS_naive	6.714309e-01
	naive_VS_BNZ	naive_VS_infected	1.777988e-06
	naive_VS_naive	naive_VS_infected	2.842693e-06
	naive_VS_BNZ	naive_VS_combo	8.226742e-01
	naive_VS_naive	naive_VS_combo	6.694273e-01
	naive_VS_infected	naive_VS_combo	6.575513e-07

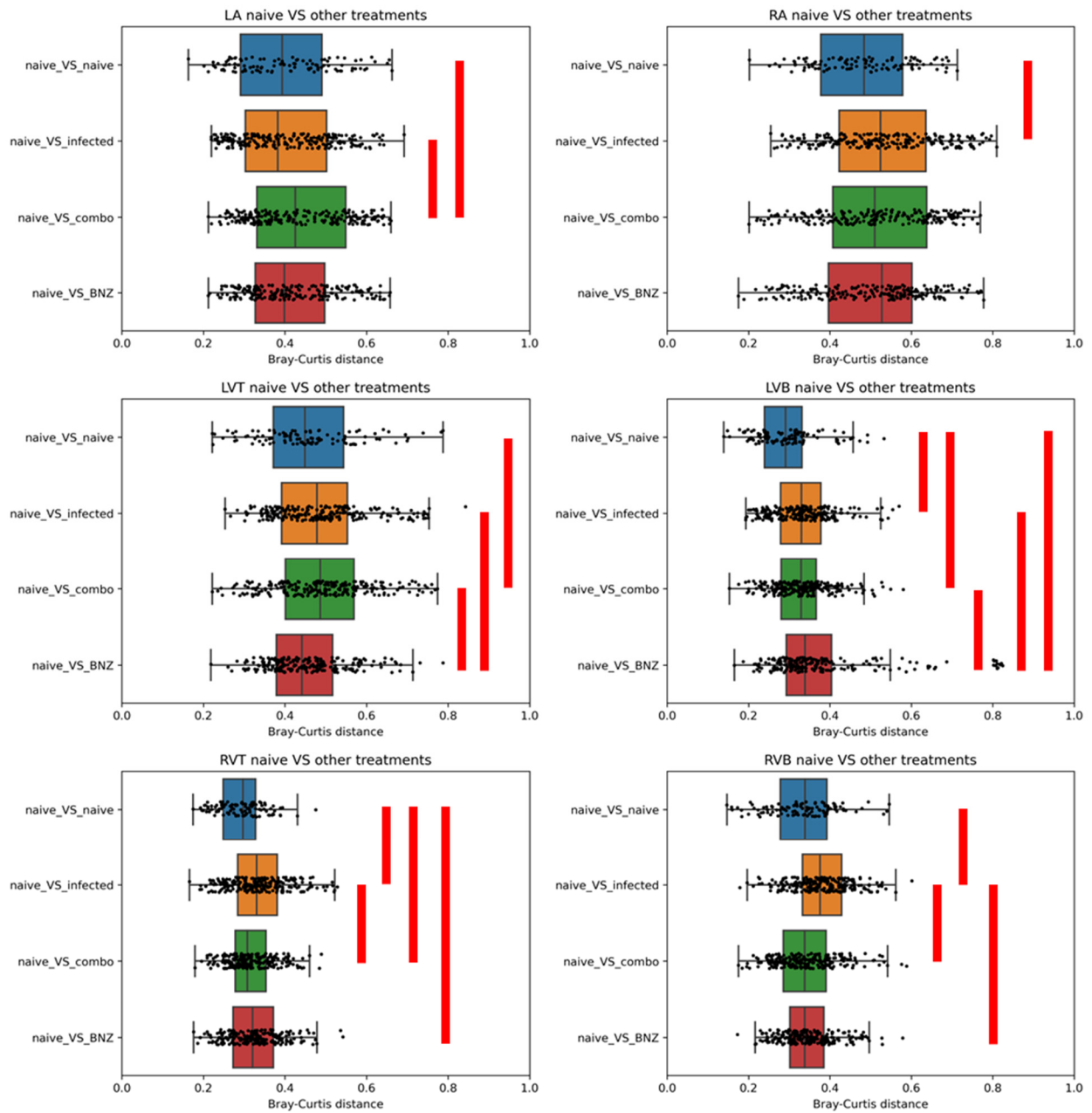


Figure D. Distance analysis boxplot between naïve groups and other experimental groups at 142DPI without high parasite burden post-BNZ treatment outlier mouse. Red line, p-value <0.05 by Mann-Whitney U Test, FDR-corrected.

Table H. Kruskal-Wallis with FDR-corrected post-hoc Dunn's test between infected no treatment group and other treatment groups at 142 DPI without high parasite burden post-BNZ treatment outlier mouse.

Heart section	Pair1	Pair2	FDR-corrected p value
LA	infected_VS_BNZ	infected_VS_infected	0.63264802
	infected_VS_BNZ	infected_VS_combo	0.09687013
	infected_VS_infected	infected_VS_combo	0.14182864
RA	infected_VS_BNZ	infected_VS_infected	0.7682509
	infected_VS_BNZ	infected_VS_combo	0.4544656
	infected_VS_infected	infected_VS_combo	0.6159846
LVT	infected_VS_BNZ	infected_VS_infected	0.060225950
	infected_VS_BNZ	infected_VS_combo	0.003792884
	infected_VS_infected	infected_VS_combo	0.587838689
LVB	infected_VS_BNZ	infected_VS_infected	0.02481829
	infected_VS_BNZ	infected_VS_combo	0.91364429
	infected_VS_infected	infected_VS_combo	0.03603772
RVT	infected_VS_BNZ	infected_VS_infected	0.5520473
	infected_VS_BNZ	infected_VS_combo	0.4810231
	infected_VS_infected	infected_VS_combo	0.4777285
RVB	infected_VS_BNZ	infected_VS_infected	4.311688e-02
	infected_VS_BNZ	infected_VS_combo	4.854801e-09
	infected_VS_infected	infected_VS_combo	6.522770e-03

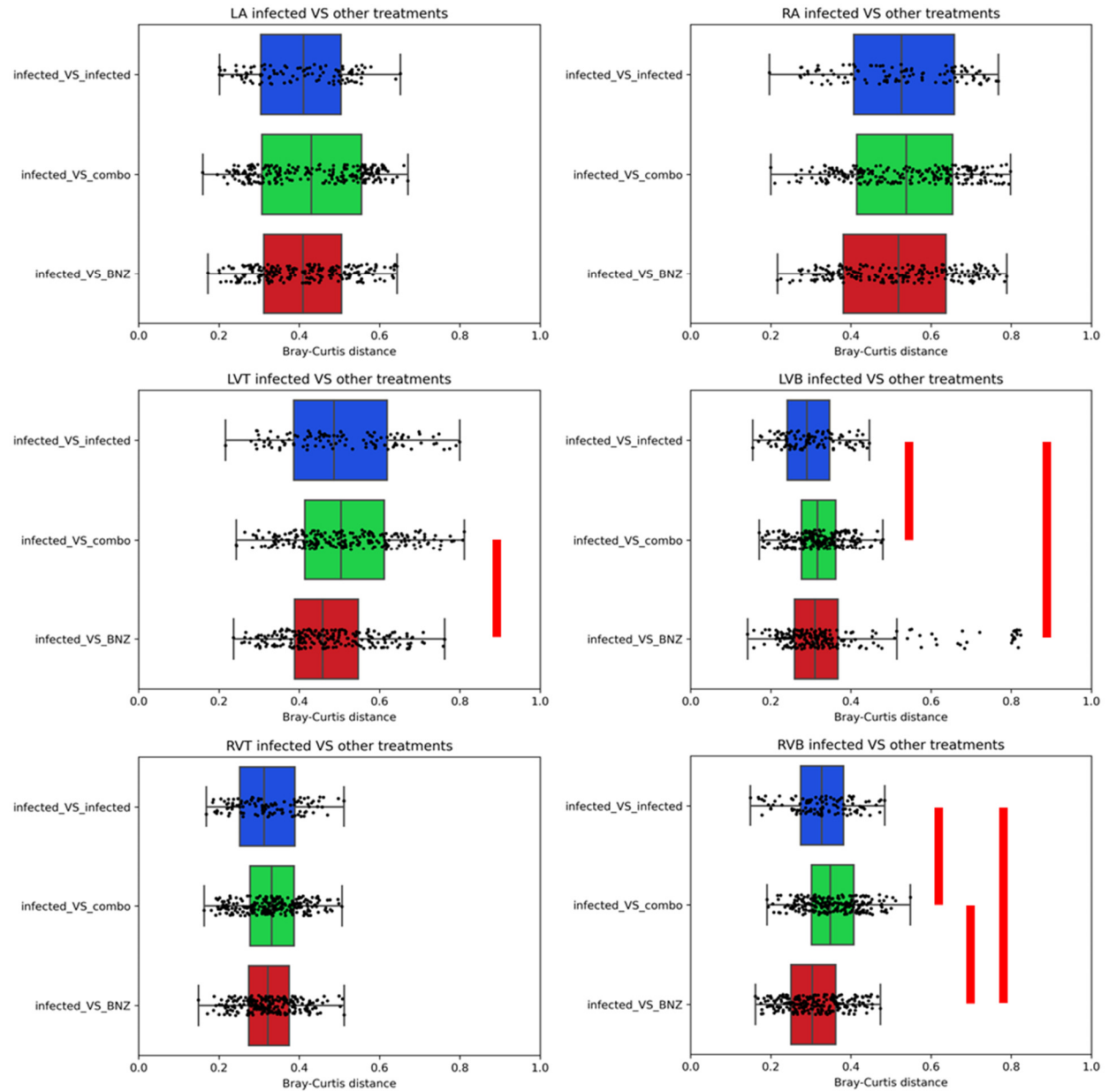


Figure E. Distance analysis boxplots between infected no treatment group and other treatment groups at 142DPI without high parasite burden post-BNZ treatment outlier mouse. Red line, p-value < 0.05 by Mann-Whitney U Test, FDR-corrected.