

LEGEND	
A (N=20)	Screening control
B (N=20)	Initial RADS4 Diagnosis
B1 (N=14)	Confirmed cases
B2 (N=6)	LNG-RADS4-False Positive
C (N=5)	Disease progression (LDCT/Death)

Source	miRNA	logFC	logCPM	F	P-value	Comparisons	Implicated in cancer (PMIDs)
EV	hsa-miR-10b-5p	-0.593	17.225	6.986	0.012	A vs B	32236623, 31798622, 30853516
EV	hsa-let-7b-5p	0.611	16.706	4.538	0.039	A vs B	33283713, 29017393, 33733556, 32300359, 30995921, 25611389
EV	hsa-miR-26a-5p	0.545	15.337	3.966	0.053	A vs B	34313719, 34149922, 34141617, 33898304, 33841514, 33795765, 33761638, 33744438, 33553298
EV	hsa-miR-184	-1.79	13.17	10.43	0.00	B1 vs B2	34328198, 34076278, 34055058, 34039407, 34000513, 33982217, 33816469, 33656787, 33354213
EV	hsa-miR-92b-3p	-2.19	11.44	6.73	0.01	B1 vs B2	34283053, 34136482, 34047469, 33984967, 33240410, 32864858, 32514152, 32256526, 31975504
EV	hsa-miR-574-5p	-1.29	12.94	5.07	0.02	B1 vs B2	34136389, 33989902, 33907569, 33869216, 33354213, 33317407, 33231826, 32832554, 32769887
EV	hsa-miR-203a-3p	-3.14	14.36	4.65	0.05	B1 vs B2	34316330, 34147083, 33664577, 33504224, 33080572, 32806571, 32708601, 3267869, 332672054
EV	hsa-miR-122-5p	3.899287	12.2346089	26.0619736	7.9417E-06	C vs A	34313924, 34053467, 33992764, 33760201, 33752480, 33738672, 33583123, 33531550, 33505957
EV	hsa-miR-200c-3p	5.125889	9.91150971	20.6179926	1.2535E-05	C vs A	34315420, 34259142, 34257614, 34071861, 34067060, 33911091, 33504224, 33465676, 33174523
EV	hsa-miR-31-5p	-5.44366	10.5156451	11.2580472	0.00105829	C vs A	34201353, 34082869, 34074322, 33867838, 33682215, 33531839, 33526040, 33510047, 33370717
EV	hsa-miR-100-5p	-4.88756	10.1486038	9.14525193	0.00301642	C vs A	34218800, 34102608, 33948855, 33911091, 33504224, 33465676, 33335853, 32911741, 32767323
EV	hsa-miR-148a-3p	2.146505	11.325399	9.04796255	0.00315259	C vs A	34324740, 34288373, 34257725, 34098776, 34082012, 34021072, 34007215, 33959508, 33922968
EV	hsa-miR-378a-3p	2.840503	9.80565516	8.21489885	0.00484017	C vs A	34222341, 34113564, 33823894, 33766217, 33751805, 33634974, 33634097, 33578293, 33531456
EV	hsa-miR-192-5p	1.65028	12.3389158	7.85517362	0.00583524	C vs A	34104082, 34042256, 33806966, 33735626, 33708127, 33256802, 33024199, 32914665, 32626956
EV	hsa-miR-363-3p	-3.7842	10.2131451	6.66152515	0.01094898	C vs A	34286520, 33950983, 33742335, 33640021, 33015780, 32779194, 32638620, 32561457, 32380791

EV	hsa-miR-4454	-3.97105	9.66192374	6.48518854	0.01206807	C vs A	34315950, 33003646, 32816024, 32422901, 32350057, 28571588, 28469417, 26576778
EV	hsa-miR-21-5p	1.196673	13.5532275	6.37311549	0.01277623	C vs A	34336825, 34316687, 34295456, 34288551, 34288231, 34254453, 34249905, 34201504, 34101749
EV	hsa-miR-141-3p	2.440423	9.90951629	6.09247612	0.01486065	C vs A	34136401, 34112774, 34086253, 33977869, 33866108, 33854632, 33845141, 33820555, 33784000
EV	hsa-miR-27a-5p	-3.25124	9.42401734	4.82880742	0.02979586	C vs A	34201504, 34160887, 34073426, 34007020, 33931086, 33675923, 33465676, 33161496, 32910366
EV	hsa-miR-4700-5p	-3.06506	9.34585606	4.72515738	0.03157331	C vs A	NA
EV	hsa-miR-7155-5p	-3.40754	9.51460762	4.70024454	0.03201701	C vs A	30128020
EV	hsa-miR-127-3p	-2.95369	9.32769432	4.49875803	0.03585731	C vs A	34295456, 33744851, 33732019, 33734890, 33468140, 33155194, 32742197, 32703147, 32538067
EV	hsa-miR-29c-3p	-2.83713	9.3066489	4.11911272	0.04448431	C vs A	34199886, 34035375, 33887587, 33798549, 33569427, 33536761, 33391354, 33314669, 33261630
EV	hsa-miR-155-5p	1.38374	11.4926268	4.088312	0.04521116	C vs A	34295456, 34277059, 34201504, 34192708, 34190442, 34131104, 34103994, 34024195, 33999777
Plasma	hsa-miR-184	-2.12128	8.81691171	7.05539364	0.01251046	A vs C	34328198, 34076278, 34055058, 34039407, 34000513, 33982217, 33816469, 33656787, 33354213
Plasma	hsa-miR-3976	-4.91	7.33	14.11	0.001	A vs B	27573701, 25388097
Plasma	hsa-miR-423-5p	1.05	13.70	9.81	0.003	A vs B	34283074, 34048164, 33924142, 33833530, 33505907
Plasma	hsa-miR-4259	-2.22	5.51	8.83	0.004	A vs B	NA
Plasma	hsa-miR-486-5p	0.83	19.85	8.25	0.007	A vs B	34323695, 34199766, 34165171, 34094949, 33955505
Plasma	hsa-miR-320a-3p	0.76	13.51	7.55	0.007	A vs B	30634628, 29803922, 32814878
Plasma	hsa-miR-185-5p	1.55	6.51	7.50	0.008	A vs B	34280472, 34270733, 34205829, 34084747, 33962174, 33885171, 33858489, 33817236, 33734890
Plasma	hsa-miR-598-3p	-1.80	5.69	7.04	0.010	A vs B	34069838, 27347136
Plasma	hsa-miR-7-5p	-1.42	7.47	6.76	0.011	A vs B	33283713, 29017393, 33733556, 32300359, 30995921, 25611389
Plasma	hsa-miR-223-3p	-1.59	6.46	6.25	0.015	A vs B	34320033, 34237309, 34205829, 34149922, 33986876, 33750388
Plasma	hsa-miR-99a-5p	1.70	5.44	5.99	0.017	A vs B	34200463, 34192880, 34038200, 33846533, 33575116
Plasma	hsa-let-7b-5p	0.66	14.03	5.42	0.023	A vs B	33283713, 29017393, 33733556, 32300359, 30995921, 25611389
Plasma	hsa-miR-16-5p	-1.25	11.53	7.46	0.011	B1 vs B2	34132358, 34101749, 33993193, 33975517, 33789312
Plasma	hsa-miR-22-3p	-0.89	11.01	6.27	0.017	B1 vs B2	34320711, 34239562, 34036905, 34019487, 33974352
Plasma	hsa-miR-425-5p	-1.49	9.55	5.44	0.025	B1 vs B2	34280472, 34204158, 33670246, 33633568, 33123581
Plasma	hsa-miR-146a-5p	-0.65	10.02	3.16	0.083	B1 vs B2	34293926, 34232111, 34073426, 34055487, 33948855
Plasma	hsa-miR-92b-3p	-0.65	10.09	2.96	0.094	B1 vs B2	34283053, 34136482, 34047469, 33984967, 33240410, 32864858, 32514152, 32256526, 31975504
Plasma	hsa-miR-423-5p	-1.08	13.56	17.29	0.000	AB2 vs B1	34283074, 34048164, 33924142, 33833530, 33505907
Plasma	hsa-let-7b-5p	-0.66	13.87	10.28	0.002	AB2 vs B1	33283713, 29017393, 33733556, 32300359, 30995921, 25611389

Plasma	hsa-miR-22-3p	0.70	11.48	8.45	0.006	AB2 vs B1	34320711, 34239562, 34036905, 34019487, 33974352
Plasma	hsa-miR-320a-3p	-0.62	13.44	7.48	0.009	AB2 vs B1	30634628, 29803922, 32814878
Plasma	hsa-miR-486-5p	-0.63	19.75	7.30	0.010	AB2 vs B1	34323695, 34199766, 34165171, 34094949, 33955505
Plasma	hsa-let-7i-5p	-0.43	12.21	6.14	0.017	AB2 vs B1	34009009, 33806966, 33775245, 33537093, 32799221
Plasma	hsa-miR-122-5p	1.48	12.06	5.02	0.031	AB2 vs B1	34313924, 34053467, 33992764, 33760201, 33752480, 33738672, 33583123, 33531550, 33505957
Plasma	hsa-miR-192-5p	3.46382	12.1063752	29.5907537	1.8992E-05	A vs C	34104082, 34042256, 33806966, 33735626, 33708127, 33256802, 33024199, 32914665, 32626956
Plasma	hsa-miR-148a-3p	3.23502	11.7392659	29.3569297	1.9988E-05	A vs C	34324740, 34288373, 34257725, 34098776, 34082012, 34021072, 34007215, 33959508, 33922968
Plasma	hsa-miR-122-5p	3.331167	12.9334566	18.0407132	0.00033661	A vs C	34313924, 34053467, 33992764, 33760201, 33752480, 33738672, 33583123, 33531550, 33505957
Plasma	hsa-miR-423-5p	1.295447	13.5276312	10.2355684	0.00323341	A vs C	34283074, 34048164, 33924142, 33833530, 33505907
Plasma	hsa-miR-320a-3p	1.145576	13.5353561	9.29090428	0.00475998	A vs C	30634628, 29803922, 32814878
Plasma	hsa-miR-486-5p	0.819955	19.6941712	6.78175629	0.01416047	A vs C	34323695, 34199766, 34165171, 34094949, 33955505
Plasma	hsa-miR-451a	-0.94834	12.7512907	6.05582553	0.01980453	A vs C	34345270, 34333815, 34257614, 34199766, 34183927
Plasma	hsa-miR-142-5p	-0.71891	10.968385	5.82535735	0.02207851	A vs C	34323174, 34321149, 34178135, 34163033, 34040437
Plasma	hsa-miR-21-5p	0.633327	11.8878778	4.97194941	0.03335729	A vs C	34336825, 34316687, 34295456, 34288551, 34288231, 34254453, 34249905, 34201504, 34101749
Plasma	hsa-miR-143-3p	1.231633	8.70671219	4.29172087	0.04695037	A vs C	34335889, 34322386, 34279157, 34202934, 34085707
Plasma	hsa-let-7c-5p	-1.71626	11.7255483	4.32640405	0.04952009	A vs C	34308851, 34026328, 33910598, 33461652, 33376529

Supplementary table 1. List of differentially expressed miRNAs from NGS analyses
Highlighted rows denote prioritized miRNAs that are significantly deregulated in at least two of the following groups comparisons: Lung-RADS2 versus Lung-RADS4; Lung-RADS4 false positive versus confirmed cancer patients; Lung-RADS2 combined with false-positive Lung-RADS4 patients versus confirmed cancer patients; any of the preceding groups versus patients who rapidly progressed (LDCT imaging). The last column shows PMID of prior reports implicating the corresponding miRNA in cancer biology.