Supplemental Tables and Figures

Table S1 Potential breath biomarkers for lung cancer based on literature review.

Volatile organic compounds	Molecular formula	Molecular weight	m/z values	PubChem CID
Acetaldehyde	C_2H_4O	44.05	44.05, 45.05	177
Ethanol	C_2H_6O	46.07	46.07, 47.07	702
Propionaldehyde	C_3H_6O	58.08	58.08, 59.08	527
Propanol	C_3H_8O	60.10	60.10, 61.10	1031
2-Hydroxyacetaldehyde	$C_2H_4O_2$	61.04	61.04, 62.04	756
Dimethyl sulfide	C_2H_6S	62.14	62.14	1068
Isoprene	C_5H_8	68.12	68.12	6557
Butanal	C_4H_8O	72.11	72.11, 73.11	261
Benzene	C_6H_6	78.11	78.11	241
Pentanal	$C_5H_{10}O$	86.13	86.13, 87.13	8063
Butyric acid	$C_4H_8O_2$	88.11	88.11, 89.11	264
Toluene	C_7H_8	92.14	92.14	1140
Phenol	C_6H_6O	94.11	94.11, 95.11	996
2, 5-Dimethylfuran	C_6H_8O	96.13	96.13	12266
Cyclohexanone	$C_6H_{10}O$	98.14	98.14	7967
Hexanal	$C_6H_{12}O$	100.16	100.16, 101.16	6184
Propyl acetate	$C_5H_{10}O_2$	102.13	102.13, 103.13	7997
Styrene	C_8H_8	104.15	104.15	7501
Benzaldehyde	C_7H_6O	106.12	106.12, 107.12	240
Heptanal	$C_7H_{14}O$	114.19	114.19, 115.19	8130
4-Hydroxyhexanal	$C_6H_{12}O_2$	116.16	116.16, 117.16	131022
Acetophenone	C_8H_8O	120.15	120.15, 121.15	7410
Propylcyclohexane	C_9H_{18}	126.24	126.24	15505
Octanal	$C_8H_{16}O$	128.21	128.21, 129.21	454
Benzothiazole	C_7H_5NS	135.19	135.19	7222
Nonanal	$C_9H_{18}O$	142.24	142.24, 143.24	31289
Decanal	$C_{10}H_{20}O$	156.26	156.26, 157.26	8175
2, 2-Dimethyldecane	$C_{12}H_{26}$	170.33	170.33	28459

We reviewed the original studies included in the following four reviews to select potential breath biomarkers of lung cancer. Lung cancer-related volatile organic compounds that had been reported in not less than two original studies were selected as potential breath biomarkers.

1. Ratiu IA, Ligor T, Bocos-Bintintan V, Mayhew CA, Buszewski B. Volatile Organic Compounds in Exhaled Breath as Fingerprints of Lung Cancer, Asthma and COPD. J Clin Med. 2020; 10(1). DOI: 10.3390/jcm10010032.

2. Marzorati D, Mainardi L, Sedda G, Gasparri R, Spaggiari L, Cerveri P. A review of exhaled breath: a key role in lung cancer diagnosis. J Breath Res. 2019; 13(3): 034001. DOI: 10.1088/1752-7163/ab0684.

3. Hanna GB, Boshier PR, Markar SR, Romano A. Accuracy and Methodologic Challenges of Volatile Organic Compound-Based Exhaled Breath Tests for Cancer Diagnosis: A Systematic Review and Meta-analysis. JAMA Oncol. 2019; 5(1): e182815. DOI: 10.1001/jamaoncol.2018.2815.

4. Campanella A, De Summa S, Tommasi S. Exhaled breath condensate biomarkers for lung cancer. J Breath Res. 2019; 13(4): 044002. DOI: 10.1088/1752-7163/ab2f9f.

Table S2 Performance of volatile organic compounds in diagnosing lung cancer patients from healthy individuals.

Volatile organic compounds	Diagnosis performance					
	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy
Acetaldehyde	0.563 (0.506-0.621)	27.4%	87.5%	48.3%	73.9%	69.5%
2-Hydroxyacetaldehyde	0.596 (0.542-0.649)	49.0%	69.3%	40.5%	76.1%	63.2%
Isoprene	0.859 (0.817-0.901)	77.7%	85.6%	69.7%	90.0%	83.2%
Pentanal	0.797 (0.756-0.838)	69.4%	79.9%	59.6%	86.0%	76.8%
Butyric acid	0.623 (0.574-0.671)	77.7%	48.6%	39.2%	83.6%	57.3%
Toluene	0.722 (0.671-0.773)	59.9%	76.4%	51.9%	81.7%	71.4%
2,5-Dimethylfuran	0.694 (0.642-0.745)	58.0%	78.8%	53.8%	81.5%	72.6%
Cyclohexanone	0.723 (0.675-0.770)	73.9%	59.0%	43.4%	84.1%	63.4%
Hexanal	0.843 (0.805-0.881)	73.9%	83.4%	65.5%	88.2%	80.6%
Heptanal	0.751 (0.706-0.797)	68.2%	70.4%	49.5%	83.8%	69.7%
Acetophenone	0.676 (0.623-0.728)	58.0%	73.9%	48.7%	80.5%	69.1%
Propylcyclohexane	0.797 (0.753-0.841)	70.1%	78.5%	58.2%	86.0%	76.0%
Octanal	0.723 (0.677-0.769)	85.4%	48.6%	41.5%	88.6%	59.6%
Nonanal	0.790 (0.745-0.834)	66.9%	81.0%	60.0%	85.1%	76.8%
Decanal	0.734 (0.685-0.783)	44.6%	92.4%	71.4%	79.6%	78.1%
2,2-Dimethyldecane	0.778 (0.732-0.824)	64.3%	80.4%	58.4%	84.1%	75.6%

AUC: area under the curve; CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

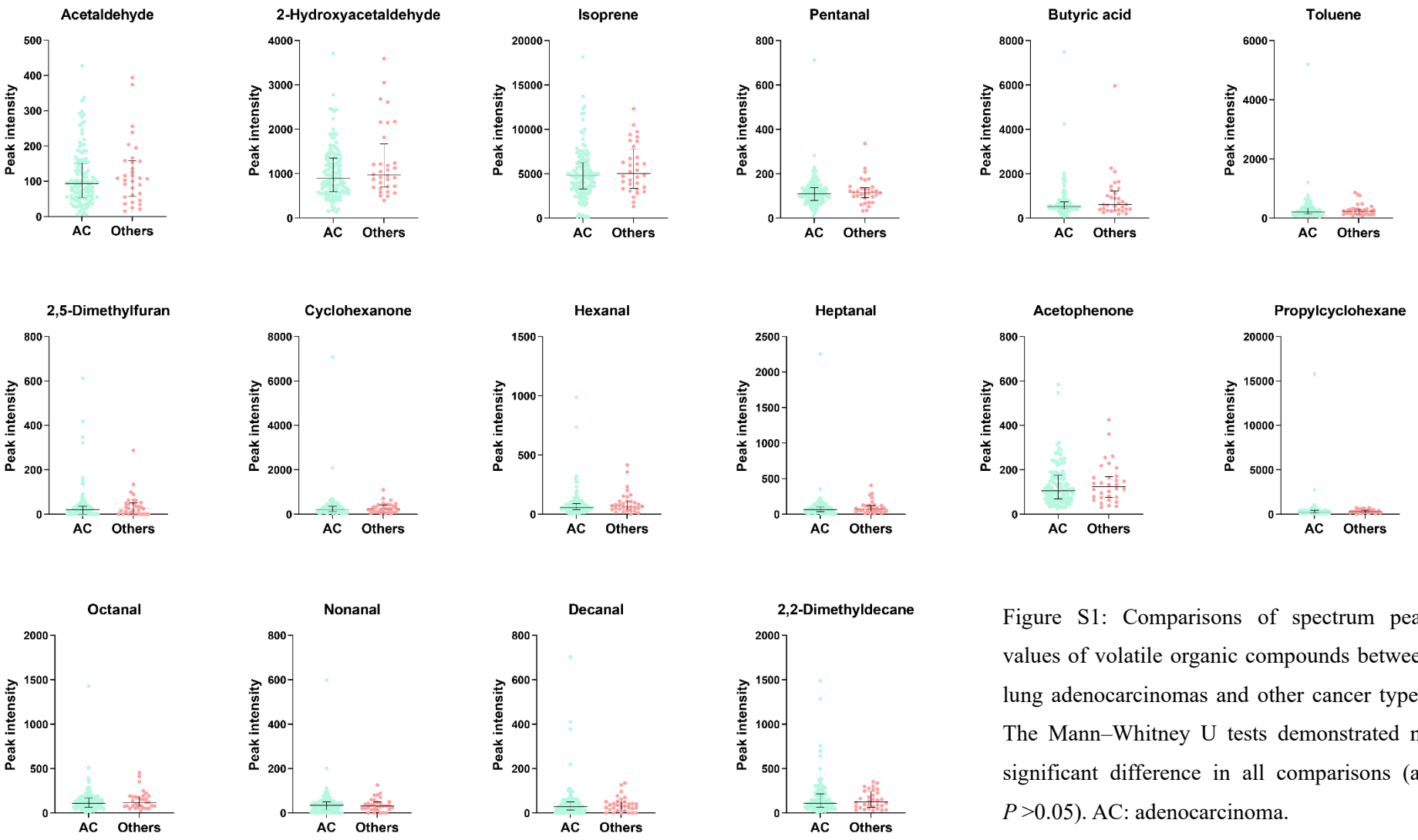

Figure S1: Comparisons of spectrum peak values of volatile organic compounds between lung adenocarcinomas and other cancer types. The Mann–Whitney U tests demonstrated no significant difference in all comparisons (all $P > 0.05$). AC: adenocarcinoma.

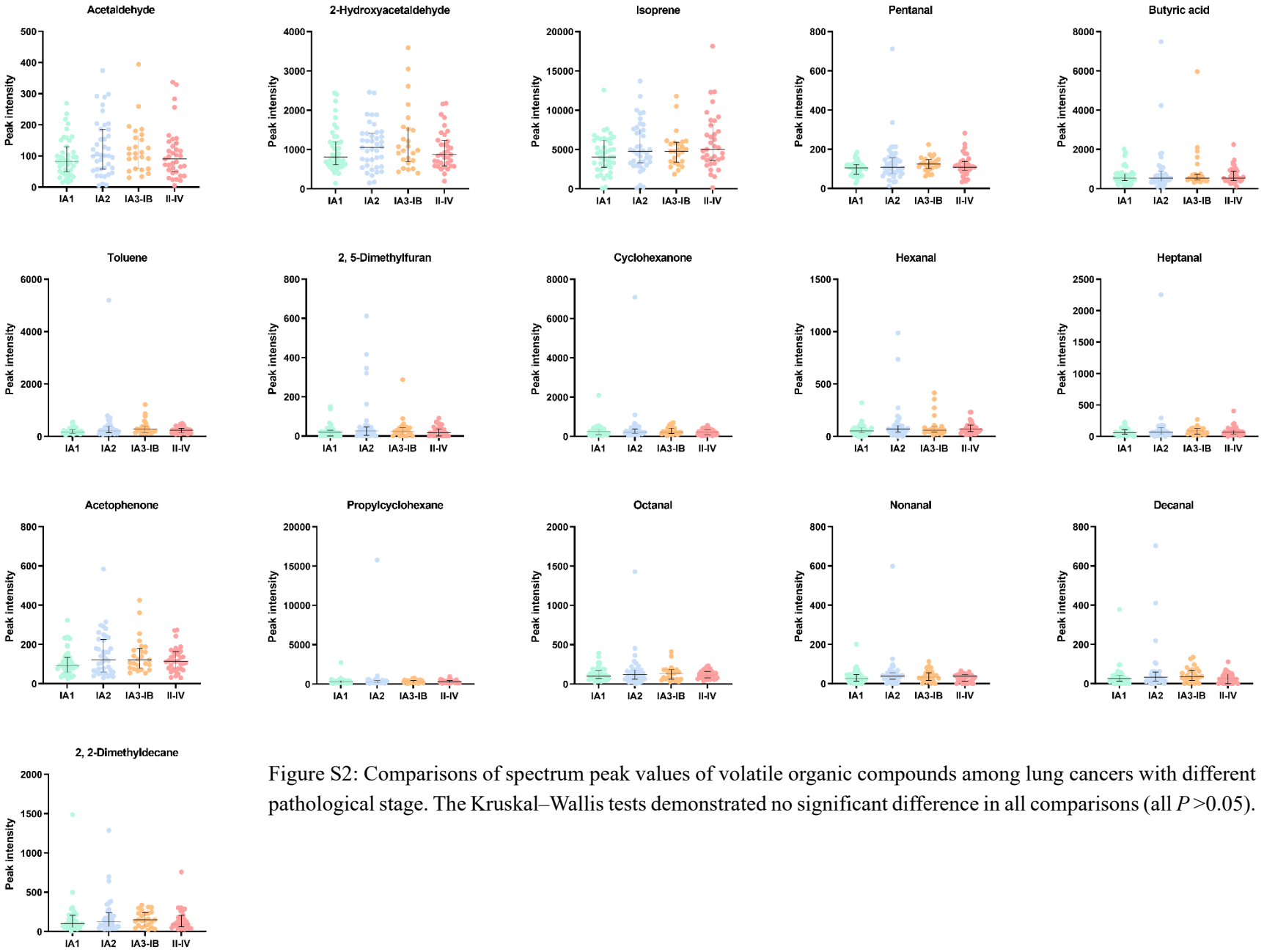

Figure S2: Comparisons of spectrum peak values of volatile organic compounds among lung cancers with different pathological stage. The Kruskal–Wallis tests demonstrated no significant difference in all comparisons (all $P > 0.05$).