Chemical signature of colorectal cancer: case-control study for profiling the breath print

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Background:

Effective screening for colorectal cancer can reduce mortality by early detection of tumours and colonic polyps. An altered pattern of volatile organic compounds (VOCs) in exhaled breath has been proposed as a potential non-invasive diagnostic tool for detection of cancer. The aim of this study was to evaluate the reliability of breath-testing for colorectal cancer screening and early diagnosis using an advanced breath sampler.

Methods:

Exhaled breath of patients with colorectal cancer and non-cancer controls with negative colonoscopy was collected using the ReCIVA® Breath Sampler. This portable device is able to capture the alveolar breath fraction without environmental contamination. VOCs were desorbed thermally and analysed by gas chromatography–mass spectrometry. The discriminatory ability of VOCs in detecting colorectal cancer was evaluated by receiver operating characteristic (ROC) curve analysis for each VOC, followed by cross-validation by the leave-one-out method, and by applying stepwise logistic regression analysis.

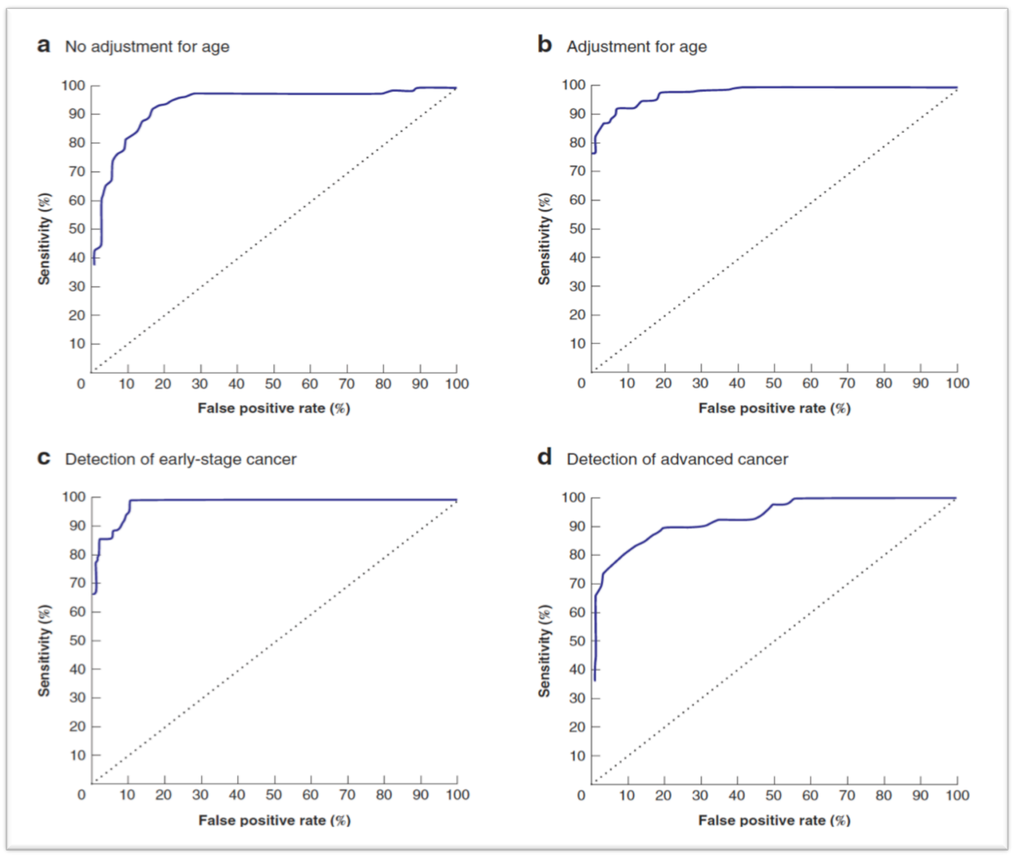
Demographics and co-morbidities in colorectal cancer and control groups

	Colorectal cancer group (*n* = 83)	Non-cancer control group (*n* = 90)	*P*†
Age (years)*	69·7(9·1)	58·7(13·4)	<0·001‡
Sex ratio (M:F)	43:40	49:41	0·937
Hypertension	50 (60)	38 (42)	0·033
Diabetes	14 (17)	9 (10)	0·175
Hypothyroidism	8 (10)	4 (4)	0·168
Cancer stage			
I–II	38 (46)		
III–IV	42 (51)		
Missing	3 (4)		
Smoker	7 (8)	11 (12)	0·415

Values in parentheses are percentages unless indicated otherwise; *values are mean(s.d.). †χ^2 test, except ‡Student's t test.

Results:

The study included 83 patients with colorectal cancer and 90 non-cancer controls. Fourteen VOCs were found to have significant discriminatory ability in detecting patients with colorectal cancer. The model with the diagnosis of cancer versus no cancer resulted in a statistically significant likelihood of discrimination of 173·45 (P <0·001), with an area under the ROC curve of 0·979. Cross-validation of the model resulted in a true predictive value for colorectal cancer of 93 per cent overall. Reliability of the breath analysis was maintained irrespectively of cancer stage.



Multivariable models: a with no adjustment for age (likelihood = 151·03, P <0·001, area under the ROC curve (AUC) = 0·963); b with adjustment for age class (model A) (likelihood = 173·45, P <0·001, AUC = 0·979); c for detection of early-stage cancer (model B) (likelihood = 113·63, P <0·001, AUC = 0·985); d for detection of advanced cancer (model C) (likelihood = 88·51, P<0·001, AUC = 0·933).

Volatile organic compounds identified in the exhaled breath of analysed patients

Peak no.	RT (min)*	Compound	Match (‰)	Probability (%)	Standard identity confirmation†	Frequency (%) Colorectal cancer	Frequency (%) No cancer
1	3·48(0·03)	Ethanol	919	87	Yes	30	64
2	8·58(0·03)	Acetic acid	959	69	Yes	100	83
3	10·88(0·04)	Methylbenzene	979	60	Yes	91	83
4	11·53(0·03)	Unidentified				100	100
5	11·60(0·02)	Dimethyl heptane	879	53		86	100
6	11·97(0·03)	Hexanal	989	65	Yes	31	58
7	12·54(0·03)	Octane, 4-methyl	905	51		83	91
8	12·77(0·03)	Butanoic acid		75	Yes	60	62
9	13·04(0·04)	Ethylbenzene	954	71	Yes	78	82
10	13·22(0·03)	Xylene	908	61	Yes	51	58
11	13·85(0·03)	Unidentified				69	74
12	14·40(0·03)	2-Butoxy ethanol	839	82		71	83
13	15·24(0·03)	Decane	913	54	Yes	52	50
14	15·74(0·02)	Benzaldehyde	930	92	Yes	77	88
15	16·07(0·02)	Octanal	888	60	Yes	71	84
16	16·31(0·02)	Undecane	922	57	Yes	58	55
17	16·42(0·03)	Unidentified				62	50
18	16·61(0·03)	2-Ethyl-1-hexanol	850	63		77	70
19	16·99(0·03)	Unidentified				65	70
20	17·07(0·02)	3,3-Dimethyl octane	907	55		74	91
21	17·91(0·04)	Nonanal	912	91	Yes	90	94
22	18·91(0·03)	Dodecane	934	55	Yes	91	100
23	20·00(0·02)	Decanal	879	51		97	91
24	20·58(0·02)	Benzoic acid	950	88	Yes	91	88
25	20·67(0·03)	4,6-Dimethyl dodecane	907	53		74	66
26	21·01(0·03)	Tridecane	911	63	Yes	94	100
27	21·39(0·04)	Benzene, 1,3-bis(1-methylethenyl)	917	67		69	91
28	22·01(0·04)	Nonanoic acid	879	78	Yes	56	71
29	22·75(0·04)	Unidentified				66	65
30	23·16(0·03)	Tetradecane	934	53	Yes	83	90
31	23·24(0·03)	Unidentified				78	80
32	23·63(0·03)	2,4,4,6,6,8,8-Heptamethyl-1-nonene	903	51		50	69
33	24·22(0·04)	Decanoic acid	867	77	Yes	53	59
34	24·40(0·02)	Ethanone, 1-[4-(1-methyl-ethenyl)-phenyl]	815	61		71	74
35	24·65(0·03)	Pentadecane	921	53	Yes	60	70
36	25·52(0·03)	Nonadecane	907	51	Yes	51	59
37	25·77(0·02)	5,9-Undecadien-2-one, 6,10-dimethyl (E)	896	58		51	58
38	27·00(0·04)	Butyl hydroxy toluene	922	51		57	78

Conclusion:

This study demonstrated that analysis of exhaled VOCs can discriminate colorectal cancer patients from non cancer subjects. This finding may eventually lead to the creation of a smart online sensory device, capable of providing a binary answer (cancer/no cancer) and directing to further screening.