

Kommentarer til:
Breath test for lung cancer screening

KOMMENTERET VARSEL – 1. ÅRG. – NR. 1 – JULI 2004

Teknologien

Det engelske National Horizon Scanning Centre udsendte januar 2004 en Technology Briefing om Breath test for lung cancer screening. I år 2000 påpegede en dansk klaringsrapport, at analyser af flygtige organiske stoffer i udåndingsluften synes at muliggøre påvisning af lungekræft, men at resultaterne da ikke var verificerede i større studier, og metoden derfor endnu ikke var anvendelig som screeningsredskab [1].

Imidlertid synes videnskabelige forsøg, publiceret i 2003, nu at bekræfte disse præliminære positive resultater [2].

Menssana Research, der udvikler metoden, har i februar 2004 fået FDA-godkendelse af en analyse af udåndingsluften til bestemmelse af sandsynligheden for, at et transplanteret hjerte udstødes [3]. Dette udstyr betragtes som forløberen for udstyr, der på tilsvarende vis diagnosticerer ikke alene lungekræft, men også fx brystkræft, svangerskabsforgiftning og halsbetændelse.

Menssana Research har desuden oplyst, at det tredje multicenterforsøg til påvisning af lungecancer i udåndingsluften er afsluttet og forventes publiceret til efteråret 2004, og at firmaet umiddelbart derefter vil søge godkendelse i USA og Europa.

Det danske patientgrundlag

Lungecancer er den hyppigste kræftform blandt mænd og er også ved at blive det blandt kvinder på grund af deres tobaksforbrug. I Danmark opstår ca. 3.500 nye tilfælde af lungecancer hvert år [4]. Langt størsteparten af disse patienter dør af sygdommen, kun få helbredes, og 5-årsoverlevelsen er kun 5 %. Prognosen for lungecancer er væsentlig bedre, hvis sygdommen påvises tidligt, her kan 5-årsoverlevelsen blive bedre end 50 % [5]. Den mulige gevinst ved screening er derfor meget stor [6]. Hvis man fx vælger at screene 50-65-årige danskere, der ryger over 20 cigaretter dagligt, drejer det sig om ca. 130.000 personer.

Nuværende screening i Danmark

I år 2000 kunne Den Nationale Kræftplan ikke anbefale screening for lungekræft [7], men en arbejdsgruppe under Dansk Lunge Cancer Gruppe forventer nu i år at starte forsøg med lavdosis, multislice spiral CT-scanning. Forsøget er planlagt at vare 6 år og at omfatte 4.000 rygere og tidligere rygere i alderen 50-65 år [8].

[*] angiver links til referencer på Internettet

New and Emerging Technology Briefing

***National
Horizon
Scanning
Centre***

**Breath test for lung
cancer screening**

January 2004



**THE UNIVERSITY
OF BIRMINGHAM**

Horizon Scanning Review

Early assessments of new or emerging technologies
contain time-limited information and should be
used with due caution.

Not to be used for commercial purposes

Breath test for lung cancer screening

Summary

Breath test for lung cancer is a non-invasive test that measures volatile organic compounds (VOCs) in the breath and predicts the probability of lung cancer in an individual. In a group of 178 people who had undergone bronchoscopy for the evaluation of symptoms of lung cancer, analysis of breath using this test detected lung cancer with a sensitivity of 90% and a specificity of 83%. A positive predictive value of 10.8% and a negative predictive value of 99.5% were calculated for this breath test as a screen for asymptomatic smokers by extrapolating data from this study. Currently the place of this test in the screening for lung cancer is unclear.

Developer – Menssana Research.

Regulatory status – Late clinical trials. Plan to apply for approval in Western Europe, including the UK, in 2004.

Unit cost – Not determined at present.

NHS or Government priority - Cancer is a NHS and Government priority.

Relevant Existing UK Guidance – No relevant guidance identified.

Burden of disease - Lung cancer is the most common cancer with 33,011 new cases of lung cancer in England and Wales in 1999. In 2001 there were 28,689 deaths from lung cancer in England and Wales.

Potential clinical benefit - Due to late presentation and the generally poor outcome of treatment, early detection by screening would be highly desirable. If its usefulness is confirmed and it is incorporated into a screening programme in the UK, this breath test could help reduce mortality and morbidity.

NHS or societal resource impact – No information on cost is currently available. The test could impact significantly with the cost of sample analysis by gas chromatography and mass spectroscopy. However, the test may ultimately be cost saving as its use as a primary screen would reduce the use of current diagnostics such as bronchoscopy. Training would be required.

The technology

Breath test for lung cancer – Menssana Research, is a non-invasive test that measures volatile organic compounds (VOCs) in exhaled breath and predicts the probability of lung cancer in an individual. Exhaled breath contains approximately 200 different VOCs some of which are known markers of lung cancer - predominantly alkanes and methylated alkanes. In this test a portable collection apparatus captures the VOCs in one litre of breath on an absorbent trap. Subjects wear a nose clip whilst breathing in and out of a disposable mouthpiece for 2

minutes. The absorbent traps are then analysed by gas chromatography and mass spectroscopy.

Menssana Research plans to apply for approval of the test in the USA and Western Europe (including the UK) during 2004.

Patient group

Lung cancer is the most common cancer in men and the third most common in women. In 1999 there were 33,011 new cases of lung cancer in England and Wales (20,445 men and 12,566 women)¹. In 2001 there were 28,689 deaths from lung cancer in England and Wales (17,564 men and 11,125 women)². The outlook for patients following diagnosis is poor; 80% die within one year with only 5% surviving 5 years.

This breath test for lung cancer could be used to screen a sub-population that are at high risk of lung cancer such as smokers over the age of 50 years. In England and Wales in 2001 there were approximately 3.6 million cigarette smokers over 50.

Current treatment and alternatives

Screening for lung cancer is not currently offered to the UK population³.

In the USA the National Cancer Institute is supporting a national lung screening trial: a controlled study of 50,000 people randomised to chest screening by computed tomography or X-ray⁴.

Diagnosis of lung cancer currently involves a variety of tests including chest X-ray, bronchoscopy, mediastinoscopy and lung biopsy⁵.

Cost

The cost of the breath test for lung cancer has not yet been determined.

Current research evidence

Effectiveness

A recent study⁶ recruited 178 people undergoing bronchoscopy from five academic pulmonary medicine services in the USA and the UK. An additional 41 healthy volunteers also enrolled into this combined case-control and cross-sectional study. Breath samples were collected and analysed by gas chromatography and mass spectroscopy to determine the alveolar gradients (abundance in breath minus the abundance in room air) of particular alkanes and monomethylated alkanes. Eighty-seven of the 178 patients had lung cancer – primary lung cancer (PLC) n=67; metastatic lung cancer (MLC) n=15; undetermined n=5. The case-control study involved patients with PLC and healthy volunteers in the development and initial cross-validation of a statistical prediction model. This model, employing nine

VOCs, identified PLC with a sensitivity of 89.6% (60 of 67 patients) and a specificity of 82.9% (34 of 41 patients). On cross-validation, the sensitivity was 85.1% (57 of 67 patients) and the specificity was 80.5% (33 of 41 patients). Based on these findings, it is possible to estimate the potential value of the breath test as a primary screen for lung cancer in apparently healthy subjects. Thus, in combination with previous findings from a study using chest CT scanning to screen a similar group, the expected outcomes of screening 1,000 asymptomatic smokers who were ≥ 60 years of age were determined and a positive predictive value (PPV^a) of 10.8% and a negative predictive value (NPV^a) of 99.5% calculated for the breath test.

The cross-sectional study involved two groups of people undergoing bronchoscopy in additional, independent cross-validations. Here the model predicted MLC with a sensitivity of 66.7% (10 of 15 patients) and classified the cancer-negative bronchoscopy patients with a specificity of 37.4% (34 of 91 patients). Thus patients with PLC, when compared to healthy volunteers, had abnormal breath test findings. The study authors concluded that the predictive model developed employing nine VOCs, exhibited sufficient sensitivity and specificity to be considered as a screen for lung cancer in a high-risk population. Stratification by smoking status and tumour type was not associated with unique patterns on breath analysis. The fact that there is no difference in the signal between patients with TNM staging of 1,2,3 or 4 means that the breath test is a unique marker for cancer because the signal does not vary with tumour mass.

Cost-effectiveness

No cost-effectiveness studies have been identified.

Ongoing or related research

Patient recruitment was terminated at the end of February, 2004 in a large multi-centre study in the US. The study is comparing the results of the breath test in patients with proven lung cancer to cancer-free controls. The patients with lung cancer were recruited when the cancer was proven with a tissue diagnosis (biopsy at bronchoscopy, thoracotomy or needle biopsy), but before definitive treatment commenced (surgery, RT, chemotherapy). The controls were recruited from a study of spiral CT in high-risk patients (smokers aged over 60); a negative image qualified the patient as cancer free. The target for data analysis is mid 2004.

Cost impact and projected diffusion

Lung cancer is the most common cancer and due to late presentation and the poor outcome of treatment, early detection by screening would be highly desirable. If the potential of this breath test is realised in the ongoing US trial, the optimal role of breath analysis in the NHS would need to be evaluated. If its usefulness is confirmed and it is incorporated into a screening programme in the UK this breath test could impact significantly on patient care and NHS resources, particularly with the associated cost of sample analysis by gas chromatography and mass spectroscopy. However, the test may ultimately be cost saving as a primary screen would reduce the use of current more-invasive diagnostics such as bronchoscopy.

^a NPV is the percentage of subjects testing negative who do not have lung cancer. PPV is the percentage of subjects testing positive who have lung cancer.

References

- ¹ Cancer Research UK, Incidence-UK, Cancer Stats, April 2003.
- ² Cancer Research UK, Mortality-UK, Cancer Stats, February 2003.
- ³ National Electronic Library for Screening available online at www.nelh.nhs.uk/screening/cancer.html
- ⁴ Swensen SJ. Screening for cancer with computed tomography (editorial). *BMJ* 2003;326:894-895.
- ⁵ Cancer Help UK at www.cancerhelp.org.uk
- ⁶ Phillips M, Cataneo RN, Cummin ARC, Gagliardi AJ *et al.* Detection of lung cancer with volatile markers in breath. *Chest* 2003; 123:2115-2123.

The National Horizon Scanning Centre is funded by the Research and Development Division
of the Department of Health, UK

The National Horizon Scanning Centre,
Department of Public Health and Epidemiology
University of Birmingham, Edgbaston, Birmingham, B15 2TT, England
Tel: +44 (0)121 414 7831 Fax +44 (0)121 414 2269 www.publichealth.bham.ac.uk/horizon