

Smelling the diagnosis

A review on the use of scent in diagnosing disease

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ABSTRACT

For centuries, our sense of smell has been used as a diagnostic tool in the practice of medicine, be it for recognising gas gangrene on the battle field or diabetic ketoacidosis in the emergency room. In recent decades, many scent detection studies have been performed with human, animal and electronic noses. The ability of humans to diagnose disease by smelling has only rarely been the subject of quantitative studies. Scent detection by animals, on the other hand, has been addressed in several diagnostic studies, which all suggest similar or even superior accuracy compared with standard diagnostic methods. Examples include, amongst many others, the use of dogs for the detection of lung cancer in breath samples, or rats for *Mycobacterium tuberculosis* detection in sputum. Studies using different types of electronic noses in conditions such as pulmonary disease and cancer have also shown promising results with high overall sensitivity and specificity. However, results of different types of noses are not easily generalisable and independent confirmation studies are generally lacking, which should be a focus for future research.

In conclusion, scent detection by animals and electronic noses holds promise for the future and should receive higher priority in terms of research effort and funding.

KEYWORDS

Electronic nose, detection dog, odours, scent detection, smell

INTRODUCTION

As early as 2000 BC, the ancient Greek and Chinese used scent to diagnose infectious diseases such as tuberculosis.¹ Ever since, our sense of smell has been used as a

diagnostic tool in the practice of medicine. Well-known examples include fetor hepaticus surrounding patients with liver failure, and the fruity smell of ketones in exhaled breath of patients with diabetic ketoacidosis.

The sense of smell depends on the ability of specialised sensory cells of the nose to perceive volatile compounds. Diseases such as infections and malignancies can be associated with changes in host metabolism, accompanied by production of different metabolic compounds, and thus a different odour. In the late 1980s, a dog handler became increasingly suspicious of a mole after her dog constantly kept sniffing at the lesion on her leg and eventually even tried to bite it off.² The consulted dermatologist subsequently diagnosed a melanoma. Since then, several studies have addressed animal scent detection as a diagnostic technique. Attempts to mimic the biological olfactory system resulted in several types of electronic noses (Enoses),³ which are also increasingly used in the medical field.

In this clinical review, we discuss different types and applications of scent detection and their potential as diagnostic tools in modern medicine.

METHODS

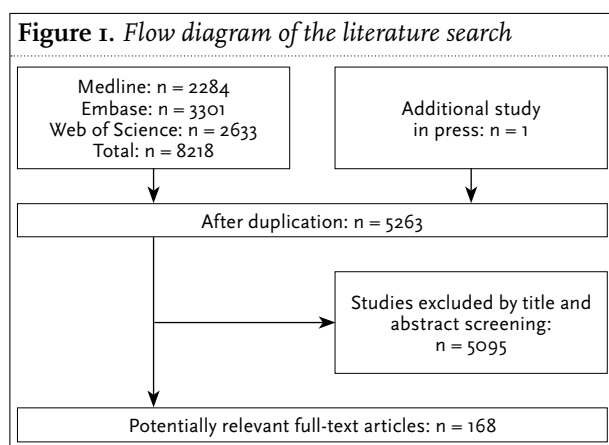
Two systematic literature searches were performed. One included scent detection by animals and humans, the other focused at scent detection by Enose. We followed the PRISMA statement as a guideline for the systematic search.⁴ Search terms such as “volatile organic compound”, “detection dog”, “scent detection”, “electronic nose” and “olfactory detection” were used in the following databases: Medline, Embase and Web of Science. For a detailed description of the search strategies, see *appendix I*. We use the term ‘Enose in the broadest sense of the word, including applications such

as chemical gas sensors, gas chromatography, optical sensor systems, infrared spectroscopy, and mass spectrometry. The electronic search was supplemented by hand searching of references cited in available literature.

Studies were included if human, animal, or electronic noses were used for diagnostic analyses of patient material (e.g. breath, faeces, urine, and tissue) and written in English. Duplicates and case reports were excluded. Using the remaining potentially relevant research articles, we then aimed to give a narrative review of the key studies in scent detection per medical field.

RESULTS

Figure 1 shows a flow diagram of the literature search. A total of 168 studies were included, of which the key studies in scent detection per medical field are reviewed here.



Cancer

Scent detection for the diagnosis of cancer has the benefit of being non-invasive and could therefore have great potential as a screening tool. As mentioned in the introduction, the first time an animal was described to detect a disease was in fact a case of cancer (melanoma).² Enoses have been used for a few decades now, but their application in diagnosing cancer is rather new. Here we describe several types of cancer for which animals and Enoses were used as a diagnostic tool. The main findings are summarised in table 1. No studies on scent detection of cancer by humans have been reported.

Lung cancer

Trained dogs perform well in detecting lung carcinoma in breath samples. Recently, in one of the largest animal scent detection studies to date, breath samples of 220 participants (healthy individuals, patients with lung cancer, and patients with chronic obstructive pulmonary disease – COPD) were presented to sniffer dogs. Lung cancer was identified with an overall sensitivity of 71% and a specificity of 93%, independent of the presence of COPD or tobacco smoke.⁵ Studies in which exhaled breath is analysed by Enose were first conducted in 1971.⁶ In 1985, it proved possible to use this type of breath analysis as a non-invasive marker of lung cancer.⁷ Since then, many reports studying VOCs in lung cancer have appeared, showing a fair overall sensitivity (71-85%) and good specificity (92-100%).⁸⁻¹¹ Moreover, both dogs and Enoses are able to discriminate between lung cancer and COPD.^{5,12}

Ovarian cancer

Dogs performed extremely well in identifying ovarian carcinoma in both blood and tissue samples, reaching a

Table 1. Characteristics of key scent detection studies by dogs and electronic noses (Enoses) for different types of cancer

Cancer	Type of nose	Type of sample	Sensitivity / Specificity (95% CI when available) or success rate	Sample size (diseased/healthy)
Lung ⁵	Dog	Breath	71% (51-88%) / 93% (87-98%)	60 / 160
Lung ⁸	Enose	Breath	71% / 100%	65 / 31
Lung ⁹	Enose	Breath	85% / 100%	56 / 36
Lung ¹⁰	Enose	Breath	94% success rate	35 / 25
Lung ¹¹	Enose	Breath	71% (42-92%) / 92% (82-97%)	14 / 62
Ovarian ¹³	Dog	Tissue and blood	Tissue : 99% / 97% Blood : 100% / 98%	40 / 200
Ovarian ¹⁴	Enose	Tissue	84% / 87%	15 / 15
Breast ¹⁷	Dog	Breath	88% (75-100%) / 98% (90-99%)	6 / 17
Breast ¹⁶	Enose	Breath	94% / 74%	51 / 147
Breast ¹⁸	Enose	Breath	75% / 85%	54 / 204
Bladder ¹⁹	Dog	Urine	41% success rate (23-58%)	9 / 54
Bladder ²⁰	Enose	Urine	100% / 100%	25 / 18
Colorectal ²¹	Dog	Breath and faeces	Breath: 91% / 99% Faeces: 97% / 99%	Breath: 33 / 132 Faeces: 37 / 148
Melanoma ²⁶	Dog	Tissue	75-86% success rate	7 / 98
Melanoma ²⁷	Enose	Tissue	70% / 90%	10 / 47

sensitivity of 100% and a specificity of 98%.¹³ The same research group tested an Enose for the detection of ovarian carcinoma in tissue samples. In keeping with the lower sensitivity of Enoses compared with the dog's nose, the Enose study suggested a somewhat lower overall sensitivity and specificity, of 84% and 87% respectively, compared with the dog's performance.¹⁴

Breast cancer

Breast cancer is the most prevalent malignancy amongst women in the Western world.¹⁵

Both dogs and Enoses have been tested for the detection of breast carcinoma in breath samples. The study using an Enose identified five volatile organic compounds (VOCs) in exhaled breath that could predict the presence or absence of breast cancer.¹⁶ A few years later, a study including detection dogs was performed, where sensitivity and specificity of dog detection was 88% and 98%, and Enose reached 94% and 74%, respectively.^{16,17} A more recent Enose study analysed 258 breath samples and found a sensitivity of 75% and a specificity of 85%, supporting the notion that Enoses do not reach the same diagnostic accuracy as dogs.¹⁸

Bladder cancer

Bladder cancer was the first disease for which the diagnostic accuracy of animal scent detection was systematically analysed. In this study, dogs were trained to recognise bladder cancer in urine samples; the subsequent formal evaluation study showed a diagnostic success rate of 41%, whereas based on chance a success rate of only 14% was anticipated.¹⁹ Another study found that an Enose was also able to discriminate urine samples of healthy patients from those of patients with bladder cancer, with a diagnostic accuracy of 100%.²⁰

Colorectal cancer

Dogs have also been trained to identify colorectal carcinoma. In 350 stool and breath samples, the dogs' diagnostic accuracy was very high, with a sensitivity of 91% and 97% in breath and faecal samples, respectively, and a specificity of 99% for both sample types.²¹ In comparison, the sensitivity of the haemocult test ranges from 25-44%.²²⁻²⁴ Only one sizeable study for the detection of colorectal carcinoma using an Enose has been performed. The Enose was able to discriminate breath samples of patients with colorectal carcinoma (n= 26) from samples of healthy controls (n= 22) by means of characteristic VOC patterns, but a diagnostic accuracy analysis was not included in this work.²⁵

Melanoma

After the first anecdotal report of a dog detecting melanoma,² a study using a dog as a diagnostic tool for this type of cancer was performed. This was the first study

in which dogs were trained to sniff actual patients in the clinic, rather than a sample of patient material (e.g. faeces, urine, breath, etc.). Melanoma samples were hidden in bandages on volunteers and the dogs were correct in their assessment in 75-86% of the cases.²⁶ Three years later, an Enose study addressed the ability to detect melanoma in tissue samples (n=57), and found a sensitivity and specificity of 70% and 90%, respectively.²⁷

Infections

The odour of infectious diseases has fascinated mankind for many years. For example, the typical smell of gas gangrene, a severe skin and soft tissue infection caused by *Clostridium perfringens*, was described as early as in the Middle Ages.²⁸ Throughout history, infectious diseases have played a major role in battles and wars. In both the First and Second World War, many soldiers suffered from gas gangrene, to which 50% succumbed. Since no other diagnostic tools were available, physicians solely relied on their senses, particularly smell.

Bedside diagnosis by smelling is still applied. For example, wound infections caused by *Pseudomonas aeruginosa* are characterised in textbooks and by clinicians as having a 'fruity' odour, and bacterial vaginosis has its distinctive 'fishy' smell. In recent years, studies have attempted to assess the superior smelling characteristics of animals, and newly developed scent detection tools have made earlier recognition of specific infectious diseases possible. *Table 2* shows the characteristics of the key studies.

Pulmonary infections

The ancient Greeks and Chinese had an interesting method of detecting *Mycobacterium tuberculosis*. The doctor set fire to the patient's sputum and diagnosed tuberculosis by recognising the specific smell in the fumes.²⁹ Nowadays, sputum is examined under a microscope (e.g. with an acid-fast stain), but this method has only limited sensitivity. Polymerase chain reaction is more sensitive, but also more expensive. Culturing is a sensitive method of detecting tuberculosis, but generally takes at least three weeks.³⁰ Could scent detection offer a solution?

After an interesting study on rats being able to detect landmines,³¹ the same research group studied the accuracy of trained rats for detecting tuberculosis. It turned out that rats can detect these bacteria in sputum samples with an accuracy of 74% and process 1680 samples a day, whereas a lab clinician has a limited capacity of 40 samples a day.³² A more recent study on rats detecting TB showed a sensitivity of 68% and a specificity of 87%.³³ Bees may be able to detect tuberculosis as well.³⁴

A study using Enoses suggested that *M. tuberculosis* can be detected in sputum with an accuracy of 85%.³⁵ *P. aeruginosa* can be detected in exhaled breath by Enose with a sensitivity exceeding 90% and a specificity of 88%.³⁶

Table 2. Characteristics of key scent detection studies by human, animal, and electronic nose (Enose) for different infectious diseases

Infection	Type of nose	Type of sample	Sensitivity / Specificity (95%CI when available) or Success rate	Sample size (diseased/ healthy)
<i>Mycobacterium tuberculosis</i> ³²	Rat	Sputum	80% / 72%	28 / 111
<i>Mycobacterium tuberculosis</i> ³³	Rat	Sputum	68% / 87%	162 / 748
<i>Mycobacterium tuberculosis</i> ³⁵	Enose	Breath	84% / 65%	65 / 161
<i>Pseudomonas aeruginosa</i> ³⁶	Enose	Breath	90% / 88%	32 / 40
Rotavirus ³⁷	Human	Faeces	38% / 88%	26 / 42
<i>Clostridium difficile</i> ³⁸	Human	Faeces	55% (33-77%) / 83% (76-90%)	37 / 81
<i>Clostridium difficile</i> ³⁹	Dog	Faeces and hospitalised patients	Faeces: 100% / 100% (91-100%) Patients: 83% (65-94%) / 97% (95-99%)	Faeces: 50 / 50 Patients: 30 / 270
<i>Clostridium difficile</i> ⁴⁰	Enose	Faeces	95% success rate	22 / 30

We found no studies addressing scent detection in other types of pulmonary infection, particularly not for common pathogens such as *S. pneumoniae*.

Intestinal infections

In 1987, the human nose was tested in distinguishing diarrhoea caused by rotavirus infection from diarrhoea caused by other organisms (i.e. adenovirus, *E. coli*, *Campylobacter*, or no isolated organism). Nurses were asked to classify stool samples by smell. Specificity was good (88%), but sensitivity was very low (38%).³⁷

Clostridium difficile infections (CDI) are a common cause of diarrhoea in hospitals and other healthcare facilities. Humans are able to recognise *C. difficile* diarrhoea by its smell. Trained nurses reach a sensitivity and specificity of 55% and 83%, respectively.³⁸ Recently, a dog proved capable of detecting *C. difficile* both in faecal samples and at the patients' bedside on hospital wards. Sensitivity and specificity for stool samples were 100% and 94-100%, respectively. Sensitivity and specificity for identifying CDI patients on the hospital ward were 83-93% and 97-98%, respectively.³⁹ When tested by Enose, faeces of CDI patients has a significantly different VOC pattern from faeces of asymptomatic volunteers, patients with *Campylobacter jejuni* infection, and patients with ulcerative colitis.⁴⁰ Furthermore, the Enose is able to discriminate between different aerobic bacteria such as *Helicobacter pylori*, *Escherichia coli*, and *Enterococcus* species on the basis of differences in volatile compounds.⁴¹

Metabolic and other diseases

Normal human metabolism generates countless VOCs that can generate a specific odour. Pathological processes influence the VOC composition by producing different VOCs, or by metabolic consumption of VOC substrates that are normally present. Notorious examples include the smell of acetone on the breath of patients with diabetic ketoacidosis and the 'musty' smelling breath of patients with hepatic encephalopathy.

There are several rare metabolic diseases that are accompanied by such a distinct smell that they owe their name to it; e.g. trimethylaminuria (also known as 'fish odour disease') is due to abnormal excretion of trimethylamine in breath, urine, sweat, saliva and vaginal secretions. The odour consists of sulphur and nitrogen compounds (amines) and resembles the smell of decaying fish. Another example is maple syrup urine disease, or MSUD. It is caused by a deficient enzyme, branched-chain alpha-keto acid dehydrogenase. Patients have been reported to smell like caramel, maple syrup, or to spread a 'malty' odour.

Although no formal diagnostic studies have been done, there are case reports that suggest that dogs are able to detect hypoglycaemia. In these cases, the dog acts in a stereotypical way to alarm the handler before he or she suffers from hypoglycaemic symptoms. It is unclear what triggers the dog's reaction, but the detection of specific VOCs has been proposed as the most plausible explanation.⁴² A similar phenomenon was described in the 1980s when a woman with epilepsy reported that her dog could predict her seizures. Since then, there has been great interest in 'seizure dogs', but their reliability remains unknown due to the lack of formal studies. Seizure alert dog owners have reported improvements in seizure rates which they attributed to their dogs.^{43,44}

Table 3 shows the characteristics of scent detection studies by Enoses in the group of metabolic and other diseases. No studies were found testing humans or animals.

Metabolic diseases

Enoses have found a significantly different VOC pattern in breath from people with diabetes and healthy controls (sensitivity 90%, specificity 92%).⁴⁵ Besides that, a breath marker for oxidative stress has been described that could potentially identify diabetic patients at increased risk for complications.⁴⁶

The characteristic smell of patients with liver failure, fetor hepaticus, is caused by increased levels of sulphur-

Table 3. Characteristics of key scent detection studies by electronic nose (Enose) in metabolic – and other diseases

Disease	Type of nose	Type of sample	Sensitivity / Specificity	Sample size (diseased/healthy)
Diabetes ⁴⁵	Enose	Breath	90% / 92%	21 / 26
Liver cirrhosis ⁴⁸	Enose	Breath	100% / 70%	52 / 50
Asthma ⁴⁹	Enose	Breath	-	20 / 20
Asthma & COPD ⁵⁰	Enose	Breath	85% / 90%	60 / 40
COPD ⁵¹	Enose	Breath	-	12 / 16

containing compounds.⁴⁷ Breath analyses by Enose reportedly discriminate patients with liver cirrhosis from healthy individuals with a sensitivity of 100% and specificity of 70% (n=102).⁴⁸

Other diseases

Both asthma and COPD are common respiratory diseases characterised by airway obstruction. Patients can be differentiated from each other and from healthy controls by breath analysis using Enose.^{49,50} Moreover, a recent study in COPD patients suggested that different stages of disease severity can also be identified by Enose.⁵¹

Finally, breath analysis by Enose has reportedly been able to recognise schizophrenia, in which pentane and carbon sulphide seem to be increased.⁵²

CONCLUSION AND DISCUSSION

Physicians have always used their sense of smell as a diagnostic tool, be it for wound infections on the battle field or the patient with diabetic ketoacidosis in the emergency room. The human nose is still a valuable instrument in times when bedside diagnostic skills are losing ground to modern analytical techniques. The ability of humans to diagnose disease by smelling has only very rarely been the subject of quantitative studies. Still, our senses come free of charge, and are among the most readily available diagnostic tools we have. As over years of practice we become experienced clinicians, we literally develop ‘a nose’ for the medical profession.

The smelling ability of animals holds promise as a detection tool. The studies reviewed here suggest that animals are often as accurate as or even superior to standard diagnostic methods. For example, trained rats are at least as sensitive as the conventional Ziehl-Neelsen stain for detecting *M. tuberculosis* in sputum; moreover, they are able to process over 40 times more samples per day than a lab clinician.³²

The potential of animals appears to be underestimated, understudied and, consequently, underused in the

medical field. Several studies discussed in this review show promising and sometimes even spectacular results. In the six cancer studies with dogs reviewed here, for example, median sensitivity and specificity were 94% and 98%, respectively. Although no direct comparison studies have been performed, dogs appear to outperform Enoses, since median sensitivity and specificity of the Enoses in the seven cancer studies was only 75% and 92%, respectively. It is surprising and unfortunate that independent follow-up studies are generally lacking. One of the explanations could be that the use of animals in healthcare is unconventional and physicians might consider it to be unhygienic. Also, each animal needs special training, which requires specific expertise and can be time-consuming. For instance, the training of detection dogs can take months before they are ready for practice; rats on the other hand can be trained very quickly.³¹ After this training phase, animals need individual performance assessment, and regular practice to maintain their skills. Enose studies have mainly focused on lung diseases and malignancies such as ovarian, bladder, and lung cancer. The overall sensitivity and specificity of Enoses is high in the published studies, but again few confirmation studies are available. Enoses are not widely implemented in daily practice. There are many types of Enoses with a large variety of underlying techniques; results from one type of Enose are not (easily) generalisable to another. Also, Enoses are relatively expensive, but they could prove cost-effective in the long-term.

It remains to be seen, however, if Enoses will ever be able to match the smelling capacity of animals. Dogs, for example, require an average VOC concentration of less than 0.001 part per million.⁵³ Enoses on the other hand have a detection threshold of 5 to 0.1 parts per million (ppm),⁵⁴ although like animals different types of Enoses have different affinity for different volatiles. In comparison, humans have a detection threshold, on average, ranging from 0 to 80 ppm, again depending on of the type of substance. For example, ammonia can not be perceived by humans until it reaches 50 ppm.⁵⁵ Taken together, many animals smell up to 100 times better than humans and Enoses, and it may well be worth making appropriate use of this superior technology.⁵⁶

Lately, the main focus of scent detection studies has been on pulmonary diseases (COPD, asthma and lung cancer). For other malignancies, such as colorectal cancer, imperfect (faecal occult blood) or invasive (colonoscopy) screening methods are currently used. Scent detection by animals or Enose could be of considerable value here. Diagnosis of several infectious diseases including tuberculosis could be improved by rapid and accurate animal-assisted screening, particularly in low-resource settings. Scent surveillance by animals or Enoses for transmissible diseases such as *Clostridium difficile*

infections could prevent and contain outbreaks. What are mainly needed are confirmatory studies, as the collective literature, although promising and occasionally spectacular, mainly consists of isolated studies. In conclusion, scent detection holds promise for the future and should receive higher priority in terms of research effort and funding.

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APPENDIX I:

Search performed on scent detection by animals & human and electronic noses (March 2012)

PUBMED – SEARCH STRATEGY

Period: 1966 to March 2012

Animals & Human

("Dogs"[Mesh] OR Dog*[tiab] OR canine*[tiab] OR detection dog*[tiab] OR sniffer dog*[tiab] OR "Nurses"[Mesh] OR nurse*[tiab] OR "Physicians"[Mesh] OR Physician*[tiab] OR "Humans"[Mesh] OR Human*[tiab] OR animal*[tiab] OR "Animals"[Mesh])

AND

("Carcinoma"[Mesh] OR carcinoma*[tiab] OR "Disease"[Mesh] OR disease*[tiab] OR "Infection"[Mesh] OR infection*[tiab])

AND

("Smell"[Mesh] OR smell*[tiab] OR "Odors"[Mesh] OR odor*[tiab] OR "Pheromones"[Mesh] OR pheromone*[tiab] OR "Volatile Organic Compounds"[Mesh] OR volatile organic compound*[tiab] OR volatile*[tiab])

AND

(scent detection[tiab] OR olfactory detection[tiab] OR detection*[tiab])

Enoses

(electronic nose*[tiab] OR bioelectronic nose*[tiab] OR substance class specific sensor*[tiab] OR infrared spectroscop*[tiab] OR infrared spectrometr*[tiab] OR "Spectrophotometry, Infrared"[Mesh] OR gas chromatograph*[tiab] OR "Chromatography, Gas"[Mesh] OR mass spectrometr*[tiab] OR ion mobility spectrometr*[tiab] OR "Mass Spectrometry"[Mesh] OR optical sensor*[tiab])

AND

("Volatile Organic Compounds/analysis"[Mesh] OR volatil*[tiab]))

AND

(humans[mesh] OR human[tiab] OR humans[tiab])

EMBASE – SEARCH STRATEGY

Period: 1980 to March 2012

Animals & Humans

('detection dog':ab,ti OR 'sniffer dog':ab,ti OR 'dog'/de OR canine*:ab,ti OR 'animal'/de OR 'physician'/exp OR physician*:ab,ti OR 'nurse'/exp OR nurse*:ab,ti OR 'rat'/exp OR rat*:ab,ti OR dog*:ab,ti OR animal*:ab,ti OR 'human'/exp OR human*:ab,ti)

AND

('scent detection':ab,ti OR 'olfactory detection':ab,ti OR detection*:ab,ti)

AND

(scent:ab,ti OR 'odor'/de OR odor*:ab,ti OR 'pheromone'/de OR pheromone:ab,ti OR smell:ab,ti OR 'volatile organic compound'/de OR volatile organic compound*:ab,ti)

AND

('carcinoma'/exp OR 'diseases'/exp OR 'infection'/exp OR carcinoma*:ab,ti OR infection*:ab,ti OR disease*:ab,ti)

Enoses

((electronic NEAR/3 nose*):ab,ti OR (bioelectronic NEAR/3 nose*):ab,ti

OR (('infrared spectroscopy'/de OR (infrared NEAR/3 spectroscop*):ab,ti OR ('infra red':ab,ti AND spectroscop*):ab,ti) OR 'infrared spectrometry'/de OR 'infrared spectrophotometry'/de OR (infrared NEAR/3 photospectroscop*):ab,ti OR (infrared NEAR/3 spectrophotometr*):ab,ti OR (infrared NEAR/3 spectrometr*):ab,ti OR (infrared NEAR/3 photospectrometr*):ab,ti OR 'gas chromatography'/exp OR (gas NEAR/3 chromatograph*):ab,ti OR 'mass spectrometry'/exp OR (mass NEAR/3 spectrometr*):ab,ti OR 'ion mobility spectrometry'/de OR (ion:ab,ti AND (mobility NEAR/3 spectrometr*):ab,ti) OR (optical NEAR/3 sensor*):ab,ti)

AND

('volatile organic compound'/exp OR volatil*:ab,ti)).

AND

('human'/exp OR human*:ab,ti)

WEB OF SCIENCE – SEARCH STRATEGY

Period: 1988 to March 2012

Animals & Human

(Carcinoma* OR Infection* OR Disease*)

AND

(Olfactory detection OR scent detection)

AND

(Sniffer dog OR detection dog OR dog* OR canine* OR human* OR physician* OR nurse*)

AND

(Scent* OR smell* OR odor* OR pheromone* OR volatile organic compound*)

Enoses

((Infrared near/3 spectroscop* OR infra red AND spectroscop*)

OR (Infrared near/3 spectrophotomet* OR infra red AND spectrophotomet*) OR (infrared near/3 spectrometr* OR infra red AND spectrometr*) OR (gas near/3 chromatograph* OR mass near/3 spectrometr*) OR (mobility near/3 spectrometr* OR optical near/3 sensor*) OR (bioelectronic near/3 nose* OR electronic near/3 nose*)

AND (volatile*)) AND (human*))

OR

((Infrared near/3 spectroscop* OR infra red AND spectroscop*)

OR (Infrared near/3 spectrophotomet* OR infra red AND spectrophotomet*) OR (infrared near/3 spectrometr* OR infra red AND spectrometr*) OR (gas near/3 chromatograph* OR mass near/3 spectrometr*) OR (mobility near/3 spectrometr* OR optical near/3 sensor*) OR (bioelectronic near/3 nose* OR electronic near/3 nose*)

AND volatile*) AND (disease*))

OR

((Infrared near/3 spectroscop* OR infra red AND spectroscop*)

OR (Infrared near/3 spectrophotomet* OR infra red AND spectrophotomet*) OR (infrared near/3 spectrometr* OR infra red AND spectrometr*) OR (gas near/3 chromatograph* OR mass near/3 spectrometr*) OR (mobility near/3 spectrometr* OR optical near/3 sensor*) OR (bioelectronic near/3 nose* OR electronic near/3 nose*)

AND volatile*) AND (cancer* OR onco* OR respirator* OR pathol*))