

**DOGS CAN PREDICT CANCER?!**

**AN EXPLORATION INTO ADVANCEMENTS INTO BREATH  
ANALYSIS THROUGH NANOTECHNOLOGY WHICH MAY  
LEAD TO THE DETECTION OF CANCER**

**BY**

**KATHERINE DAVIDSON**

**PASS**

**RESEARCH PAPER  
BASED ON  
PATHOLOGY LECTURES  
AT MEDLINK 2010**

## **Abstract (190)**

Potential lung cancer patients undergo a series of lengthy, and occasionally painfully intrusive testing to detect the disease. These patients require a chest x-ray, a computerised tomography scan, and then possibly even a positron emission tomography scan to provide us with an indication of the presence of a growth; even then are we only provided with a computerised image of the interpretation of the activity of body tissues. But is there a means of protecting uninfected body cells in the process? To widen treatment options and cut down prognosis time? Is it possible to avoid the dangers of multiple doses of ionised radiation to a cancer patient? Is there perhaps a means of rendering radiation-for-detection unnecessary? The answer is yes, through the concept of nanotechnology. This paper consists of a collaboration of studies, both within humans and animals, in order to develop a possible breakthrough in detecting lung cancer through nanotechnology, and how to tailor precision in radiation to destroy cancer cells. It comprises of research for possible advancements, ethical issues, and the analysis of what steps to take in the future towards detecting and destroying lung cancer cells.

## **Introduction**

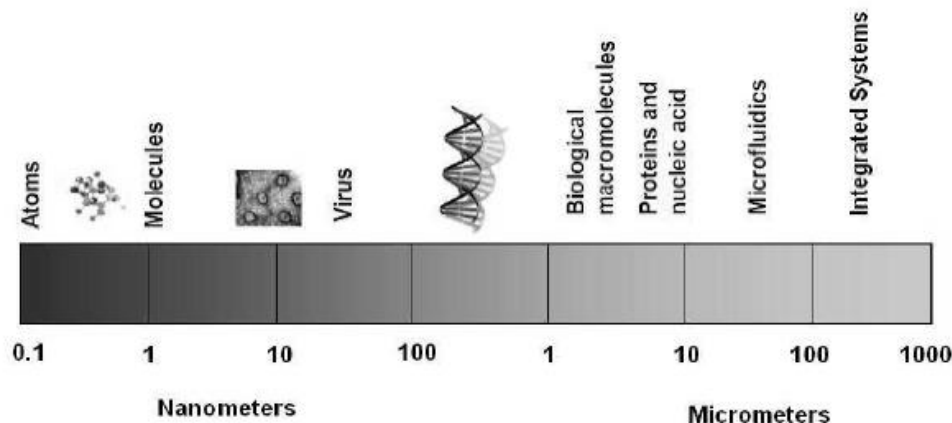
Before getting into the specifics of detecting lung cancer through breath analysis, the main focus of this paper, we must delve into the physics and practicalities of nanotechnology itself (the part where most Star Trek concepts come into play).

### ***CONCEPT OF NANOTECHNOLOGY AND ITS FUNCTION***

Nanotechnology is defined as the “intentional design, characterization, production, and applications of materials, structures, devices, and systems by controlling their size and shape in the nanoscale range (1 to 100 nm)”<sup>[1]</sup>. It may come across as naïve in stating that nanotechnology involves creating tiny ‘machines’ at the molecular level. The slightly more scientific approach to nanotechnology is somewhat more daunting; somewhere in the grey area between classical & quantum mechanics- controlling the motion of things we can, and cannot see.

The principle of nanotechnology is effectively emulating nature in building things up from the smallest molecules we can, atoms. Scientists wish to take this newfound technology and our abilities to manipulate it, and apply it to the medical field- thus ‘nanomedicine’ is born. The primary benefit from nanomedicine is its miniscule size. It is similar to that of a biological molecule, and due to this, opens a range of doors into treating at a molecular level. Seeming as most life threatening diseases stem from cell malfunction/ miscommunication due to mutated genes and infections<sup>[2]</sup>, being able to attack these molecules at their level- nanometres in size, protected by barriers and molecules nanometres in size, delivering agents, albeit for diagnostic or therapeutic purposes, such as these through this technology would become much more easy and effective. And seeming as the basic principle of medicine is diagnose and treat, diagnose and treat, scientists have effectively created a whole new generation of achieving this. To gain an idea of this concept of size with biological molecules, the diagram below shows a speculation on size comparison;

Fig. 1. [3] Size and compatibility- the benefits of nanotechnology are evident.



Expanding research could lead to scientists tailoring and fabricating nanotechnology from such a miniscule level that targeting molecules such as the individual cancer cells could be a possibility, as opposed to shooting radiation blindly.

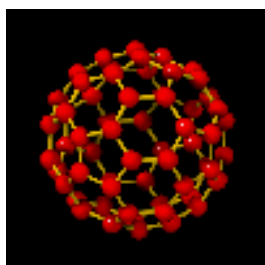
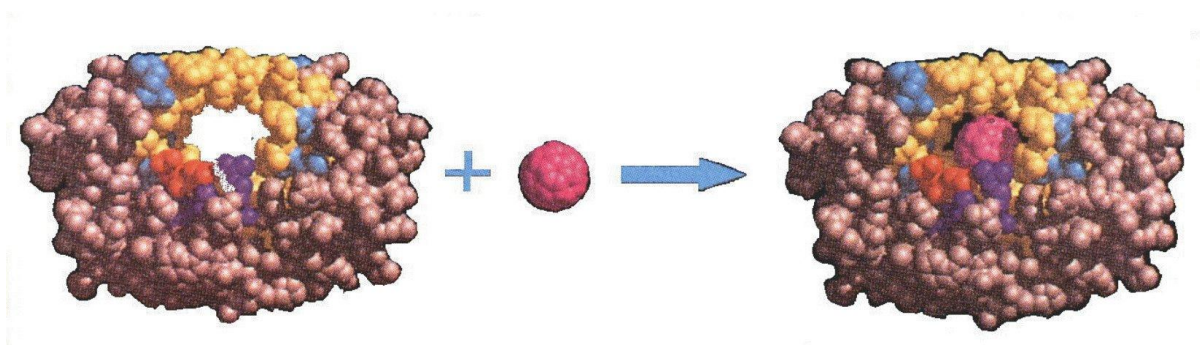


Figure 2  
Appearance of a Bucky Ball [4]

Up until 1985, only two allotropes of carbon were known; diamond and graphite. Then, a third, spherical allotrope of carbon was discovered,  $C_{60}$ . This resembling of R. Buckminster Fuller's work on buildings of this spherically based nature, thus Buckminsterfullerene (or more commonly known as 'Bucky Balls' due to their football-esque shape) was born. It is the most abundant form of carbon. The Bucky Ball discovery is extremely beneficial to us when treating cancer, for example, illustrated by the diagram below [4]:



Atoms can be caged and placed inside of the fullerene molecule, and then delivered to the patient in this manner, without damaging the surrounding cells in the process with the broader means of delivering radiation etc. whereas here the drug itself can be placed directly inside the body and controlled to specifically target the cell malfunction/infection.

## FORMATION OF NANOTUBES

Based upon this fullerene technology, we can create nanomolecules, most specifically relevant to this paper, the nanotube. Despite the fact that little is known about their creation, scientists can be certain that carbon nanotubes are made of cylinders of graphite, which in turn is made up of a lattice of hexagonally arranged layers of carbon atoms. The layers between are held together with the weakest intermolecular force, Van der Waals, and the entire formation resembles that of figure 3.

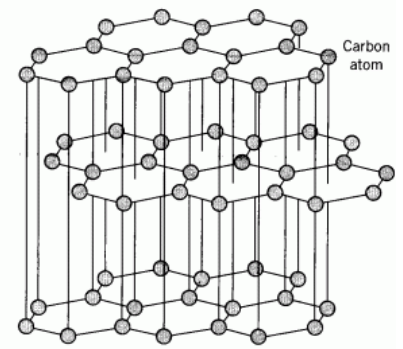


Figure 3- Structure of graphite- hexagonally formed layers of carbon with Van der Waals forces between each layer<sup>[5]</sup>

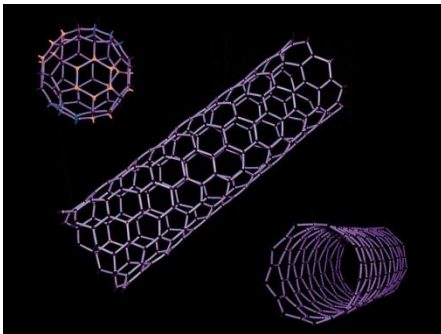


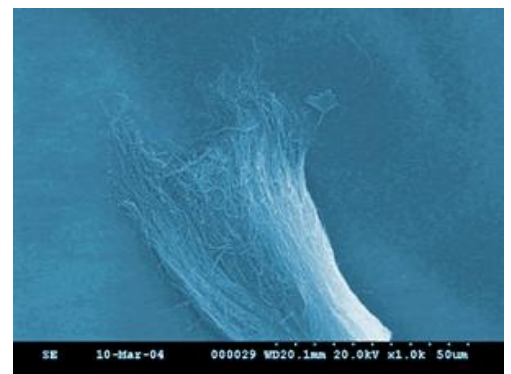
Figure 4-Structure of a carbon nanotube compared to Robert F. Curl, Harold W. Kroto and Richard E. Smalley's 'Bucky Ball'<sup>[6]</sup>

Bending this layer formed of hexagonally arranged carbon atoms, into a tube, scientists can obtain what Nobel Prize winner Richard Smalley described as "in one direction . . . the strongest damn thing you'll ever make in the universe".

Nanotubes range from '2 to 10nm is size- roughly the width of 50 atoms'<sup>[7]</sup>. To get an idea of the size of this technology, according to the Institute of Medicine; 'one nanometre is  $10^{-9}$  metres, by comparison, a human hair is approximately

70,000 nm in diameter, a red blood cell is approximately 5,000 nm wide and simple organic molecules have sizes ranging from 0.5 to 5 nm'.<sup>[8]</sup>

Despite the fact we know little about the techniques in creating them, nanomolecules (being molecules of a few nanometres in length), or more specifically nanotubes consist of long thin cylinders of graphite and are possibly the most common building blocks of nanotechnology<sup>[9]</sup>. The fact that there are so many variations of nanotubes has the potential to open up a world of new uses, the variations including 'long, short, single-walled, multi-walled, open, closed, with different types of spiral structure'<sup>[10]</sup>.



[11]Figure 5-Nanoparticles include carbon nanotubes, metal nanowires, semiconductor quantum dots and other nanoparticles produced from a huge variety of substances.

The properties of nanotubes include an intense strength, around one hundred times that of steel, and its sensitivity and conductivity- much higher than that of copper, and a thermal sensitivity of all the purest diamond<sup>[12]</sup> However, working at such a miniature level, and the potential uses one could consider with nanotechnology, a number of ethical issues are raised.

## **DISCUSSION**

Being dubbed as possibly the greatest revolution to industry since plastics, and the hype built up by the scientists who wish to embrace it, searching for the drawbacks to nanotechnology is a challenge. It is impossible to predict the enormous potential of this technology, and we can only speculate upon the ethical considerations to be borne in mind.

The human race is constantly in fear of the idea of nuclear weapons being misused or falling into the wrong hands, so regulators must remain watchful or whom this technology is exposed to. The principle of nanotechnology is quite the same. Despite the fact that nanotechnology is so recent in terms of its potentials being reached, regulations and cautionary procedures must remain watchful over how it is used and expanded upon. Although these may be taking the concept a little too far, There are ideas floating around of weapons and explosives at the miniscule level, the idea of self-replicating machines, and most disturbingly ideas of tracking and surveillance.<sup>[13]</sup> This may be more along the lines of possible Orwell 1984 dystopia re-enactment, but it is still a point to be taken into consideration when facing the prospects of nanotechnology.

A more realistic means of scrutinising nanotechnology in the field of medicine is slightly less exciting; one must revise the rules of current standards and ethics within European law to decide where the proverbial 'line' should be placed, and where it cannot be crossed.

Sensitivity in issues such as genetic engineering also comes into play here. This is one of the most controversial factors when exploring nanotechnology. In the midst of brain chips and implants, is there a point where we can go to far into the ideals of 'playing god'?

And then religious elements open up a whole new range of concerns for the potential cancer patient- what would God say about forming new machines at the molecular level?

It can be agreed that interpretations of nanomedicine's usage are based solely on the opinions its potential usage comes down to.

And then, ideas of equality could come into consideration. Do we really want to spend millions on research for smokers who have probably brought this illness on themselves?

Having considered the ethics of nanotechnology, this paper can now launch into its main focus. But first one must consider reasons why we should continue research into this field of medicine, or more specifically, how nanotechnology would benefit the health care system compared to current methods of lung cancer detection, before creating the boundary between what is right and wrong when handling a topic which can provoke some major ethical concerns.

This paper is targeting lung cancer specifically because it is the second most common cancer in men and women. In 2010 about 222,520<sup>[15]</sup> new lung cancers were diagnosed, 116,750 men and 105,770<sup>[16]</sup> women. Most disturbingly, 157,300 people will die of lung cancer. It has one of the lowest survival rates of all cancers. Obviously, the best means to reduce this number is to detect cancer quickly and correctly from the moment symptoms occur.

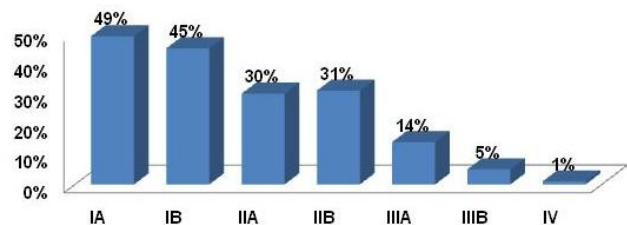
The main point of all this research is in order to detect cancer in its earliest stage possible, with the least discomfort for the patient. The reason research is being done into nanotechnology in the treatment and diagnosis is due to of lung cancer

The graphs on the right convey a strong correlation between detecting cancer early and a higher survival rate. When lung cancer is detected in early stages, surgical resection alone can achieve 5-year survival rates as high as 50%<sup>[17]</sup> Nevertheless, currently, the drawbacks of using the current methods of detecting cancer are evident. One of the most common means of detecting cancer is the chest X-ray. However, the effectiveness of the chest X-ray is compromised due to its high false- negative rate and due to this is hindered in its ability to detect early stage cancer.<sup>[18]</sup>

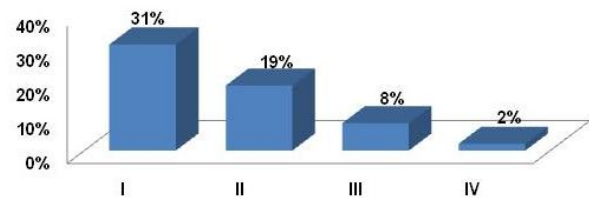
The other method of detecting lung cancer is through CT Scans. These perform the opposite of chest X-rays; can detect lesions as small as 1mm in diameter, and because of this can produce false positives- which draws up many controversy with its ethical issues- naturally learning you have cancer is devastating, and having to deal with this- and then hearing the test was a false positive is unnecessary stress for the patient, not to mention followed with needless surgery.

Therefore this paper urges research to continue with the detection of lung cancer through a means of certainty, to protect the patient and save time avoiding pointless surgeries.

**Chart 1. 5-year survival rate: non-small cell lung cancer**



**Chart 2. 5-year relative survival rate: small cell lung cancer**



<sup>[14]</sup> Figure 6- Chances of survival compared to various stages in lung cancer development show an obvious correlation; the later the stage, the less likely a patient is to survive.

The main dilemma is that it is so difficult to detect lung cancer in its early stages. Symptoms often occur in the later stages, and so this can mean that potential cancer patients must effectively wait for symptoms to physically occur without feeling the necessity to visit a doctor/ GP. Not only with this as a drawback, lung cancer can be confused with many other conditions, and the symptoms are similar to a lot of chronic obstructive pulmonary disease()<sup>[19]</sup>, bronchitis, pneumonia and asthma. On top of this, it could also be completely overlooked if a patient already has one of these. A frightening statistic is that it ranks fourth in malpractice lawsuits in America.

The aim of this paper, and the entire theory of medicine, is to prolong peoples lives by detecting this devastating cancer earlier than we could have before to increase this survival rate.

Imagine your colleague had really bad breath. So bad that you could actually physically detect what they had eaten to cause to subject you to the stench. The suggestion this paper is making is practically the same, as you are effectively analysing that person's breath, and finding the culprit of the stench!

## DOGS DETECTING CANCER

The idea of 'sniffing out cancer' stemmed first from a cancer patient's dog persistently smelling a point of the patient's leg- a point which, once tested, was discovered to be a melanoma. Since then, the idea of dogs having an acute sense of smell has been tried and tested; studies have documented dogs' abilities to identify chemicals that are diluted as low as parts per trillion<sup>[20]</sup>. Most notable being that of Micheal McCulloch<sup>[21]</sup>, in an experiment in which dogs were familiarised with the scent of lung and breast cancer, and then allowing the dogs to sniff the captured breath of 86 untreated cancer patients, and showed "specificity between 88% and 97%- accuracy"<sup>[22]</sup> hindered by the patients being current smokers- most likely masking the scent.

Since this moment, the idea of detecting gases connected to cancer through breath analysis has plagued scientists. This paper is going to offer a solution. Through the concept of Nanotechnology.

The analysis of exhaled breath has led scientists to believe that there are certain chemicals or 'markers' present which are evidentiary for different diseases.<sup>[23]</sup>

Disease	Gas
Asthma	Nitric Oxide
Diabetes	Acetone
Renal Disease	Trimethylamine
Lung Cancer	VOCs

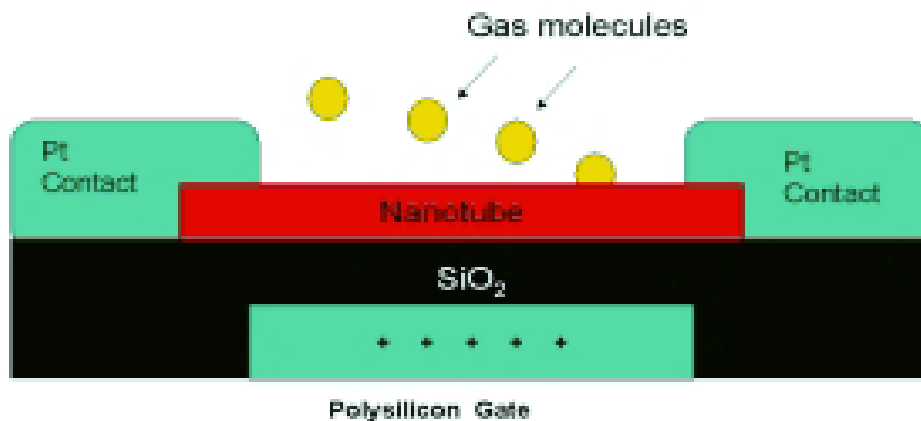
Figure 7- illnesses and the gases indicative of said illnesses in analysed breath

The idea that VOCs (Volatile Organic Compounds) are distinctly present to lung cancer patients is a myth; VOCs are present in our surroundings, and therefore in an average persons breath as well as a cancer patients. Nevertheless, techniques have been developed showing complex analysis using computers to detect specific concentrations of VOCs which are related to lung cancer patients and not in an average exhalation of a healthy person.

### HARNESSING THESE SPECIFIC MARKERS

In order to harness the presence of VOCs in exhalation, this paper proposes a sub-category of nanotechnology- nanotubes. As explained in the introduction, these are particularly useful in industry due to their immense strength and conductivity.

Due to nanotubes being miniscule in size, they are extremely sensitive. This means they have a strong ability to detect minor changes in their environments. Suppose the gas molecules in the illustration below were VOCs from a sample of a potential cancer patient's breath.



[22] Figure 8- proposed mechanism of nanotubes in detecting VOCs

The principle of detecting gas; in this case, VOCs, is through chemical based sensors, like the ones above. The conductivity of the nanotubes (red) changes as chemicals bond to the red area on the diagram, and this can be measured. The bonds formed between the chemicals and the nanotube alter the 'band structure of the tube'<sup>[24]</sup>

The fact that nanotubes can conduct effectively has led to its usage in the formation of electronic wire, and conducting between electrodes, which can be measured. As a strong function of their structure, 'mechanical deformations or chemical doping can induce strong changes in conductance'<sup>[25]</sup>

Thus, when specific gas has bonded with the nanotubes, we can measure this by the ability the nanotubes have to conduct.

Nevertheless, few experiments have been done to test out the theory of this.

One of the most modern methods of achieving this is through the work of Tran, V.H. Hiang, Ping Chan, Thurston, M. Jackson, P. Lewis, C. Yates, D. Bell, G. Thomas, P.S. Centre for Infection & Inflammation Res., Univ. of New South Wales, Randwick, NSW, Australia <sup>[26]</sup>, which showed promising results in the sense that using ‘electronic noses’ containing this nanotechnology, as they are becoming ‘rapid detectors of an array of gaseous markers’ for detecting even the smallest amounts of what a subject’s breath comprises of or, rather aptly named ‘smellprint’. Their methods were simple; 89 subjects were recruited, of these 33 nonsmokers, 11 ex-smokers, 18 smokers, 11 respiratory disorders, and 16 lung cancer patients. They exhaled into gas-impermeable bags, and then the results were analysed. Effectively, significant differences were shown between those with lung cancer and those without. Nevertheless, and the experimenters claim this themselves, more research needs to be done in increasing the sensitivity of these tests, and specificity.

## **CONCLUSION**

Despite the fact that this method is purely in its infancy stages, and predominantly speculation on this paper’s part, using this method can avoid uncomfortable procedures such as a needle biopsy, and can vastly decrease the average waiting time for a patient, and the certainty of the presence of cancerous cells will be a certain diagnosis, avoiding potential lawsuits for misdiagnosis.

Due to the main audience susceptible to lung cancer being older adults of ages 40-70 <sup>[27]</sup>, This paper’s target ideas for the future would include something of a routine, standardised test for anyone over 40, in which they will spend a few minutes breathing out which could potentially save their lives.

The fact of the matter is, when it comes to nanotechnology, there is not conclusion one can draw. From this paper’s research, the use of nanotechnology through breath analysis could be a means of preventing the onset risks of cancer. Research suggests that, when perfecting this method, the benefits of improving patient care in diagnosis could potentially outweigh the ethical concerns with nanotechnology. Only when we delve into the deeper, considerably more ambitious of nano-robots and brain implants must we chalk out a line, and really delve into whether the benefits of what we are attempting to create and master will help or hinder humanity for years to come.

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