‘CHIP’ING AWAY LUNG CANCER

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Every member of the team contributed to an aspect of this poster. The diversity of our team allowed each member to demonstrate their knowledge in their respective discipline. Ahmad Shahid took advantage of his knowledge of economics to evaluate the feasibility of the chip and its long-term success in the public domain. Ngoni Mandeya, with his physics and engineering knowledge, as well as Mumo Mwandia, with his understanding of biochemical systems, focused on understanding and applying biochip technology to our project. Ammar Ahmed and Talal Shaikh (biology and chemistry students) researched our chosen biomarkers and the associated concerns. Faith Leal applied her artistic skills in producing illustrations to bring the biochip to life.

INTRODUCTION

Having caused **1.8 million deaths** worldwide in 2020[1], lung cancer is one of the most fatal cancers. It results from uncontrolled cell division in the trachea, bronchi or lung tissue, leading to the formation of a malignant tumour. The main symptoms include a long-standing cough, persistent breathlessness and lethargy, coughing up blood and recurrent chest infections. Some common causes are smoking, radon exposure and pollution. Since lung cancer is usually asymptomatic in its early stages, it **often goes undiagnosed**, resulting in a worse prognosis when finally identified.

DEFINITION & SIGNIFICANCE OF PROBLEM

Around 48,500 people are diagnosed yearly in the UK[2] with survival rates dependent on the stage at which the condition is identified. The cure rate can be as high as 80% to 90%[3] for early-stage lung cancer, but treatment delays lead to a significant decrease as the tumour spreads throughout the body. These delays result from a record **7.2 million individuals on the NHS waiting list** for hospital treatment this year (2023)[4]. Unlike other diseases that affect older individuals, there is **no national screening program** for lung cancer; so there is a **need for a tool to identify** it before it spreads to other parts of the body. Chemotherapy becomes the only treatment option after this point.

OUR PROPOSAL & TARGET DEMOGRAPHIC

We aim to introduce the use of microtechnology in the early diagnosis of lung cancer. **Biochips**, often called ‘miniaturised laboratories’, are a biotechnology used for molecular analysis, with particularly promising prospects in medical diagnostics and monitoring. The use of microtechnology through the employment of an implantable protein-based biochip serves as a potential solution to the lack of ways to monitor people at risk of health conditions and complications that work outside of a hospital setting. Our chip will track the levels of different indicators (biomarkers) of cancer in the blood of **individuals who are at risk of developing lung cancer**. These include: people over 40, smokers, cancer patients in remission, those exposed to high levels of radon and those with a family history of lung cancer.

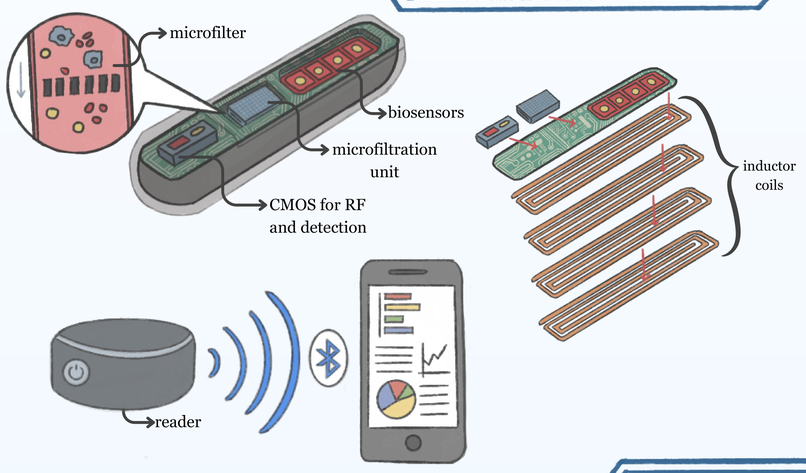
HOW IT WORKS

Our biochip is made up of **two components**: the reader and the transponder. The **reader** contains two coils; one which remotely provides the energy to ‘‘activate’’ the biochip and a separate coil to receive the information sent from the chip about levels of analyte (our chosen biomarkers) in the blood plasma. The **transponder** will be implanted under the skin (subcutaneously) on the arm or leg and would be activated by the reader, which is held up to the site of the implant. This triggers it to analyse the levels of biomarkers and relays this to the reader.

The transponder is the implanted component that monitors the levels of specific analytes in the blood plasma. These are:

- **Cyclin D1, Cyclin A2 and Cyclin E1**
- **Carcinoembryonic Antigen (CEA)**
- **Circulating Tumour Cells (CTCs)**

Our chip uses **microarrays** in the biosensors for the Cyclins and CEA and **microfiltration** for the detection of CTCs. The incorporation of both of these systems creates a micro total analysis system, often called a lab-on-a-chip (LOC) system[5].



Levels of the Cyclins and CEA will be identified through proteomic analysis performed by a **protein microarray** (a surface covered with miniaturised biosensors specific to different molecules). These biosensors are composed of bioreceptors, which are biological molecules that interact with the analyte, and biotransducers, which measure this interaction and output a signal of the presence of an analyte in the sample. High levels of the **Cyclins** in the blood plasma would indicate **cumulative radon exposure**[6], whilst an increased concentration of **CEA** highlights **possible tumour growth**[7]. However, it is already high in the blood of smokers[8], thus, **CTCs** serve as an **alternative** marker that is not elevated in these individuals[9].

Levels of CTCs will be identified through **microfiltration** techniques, whereby an array of micro ellipse filters will precisely separate the CTCs from the surrounding white and red blood cells (WBCs and RBCs). This is made achievable due to the differing sizes between CTCs and surrounding blood cells. Sizes of CTCs average between 17-52μm, which is approximately 9μm larger than RBCs and 2μm larger than WBCs[10].

We have taken measures to ensure **biocompatibility** (preventing rejection) and **biostability** (resistance to degradation after implantation) by emulating Cavallini *et al.* in their subcutaneous biochip design[11]. Through the use of non-toxic and inert materials, such as silicon, we can ensure the immune response is minimised, limiting inflammation and cell death. This is further achieved through entrapping bioreceptors and carbon nanotubes in a chitosan matrix and then sealing them behind a porous polycarbonate membrane. Biostability is improved by a conformal coating of Parylene C, which prevents the corrosion of electronic components and the leakage of potentially hazardous substances into surrounding tissue.

CLINICAL INVESTIGATIONS

We will conduct an investigation consisting of a pre-clinical trial followed by a three-phase clinical trial testing the efficacy of our biochip in improving the health outcomes of individuals at risk of lung cancer, as well as those who are in remission.

During the **pre-clinical trial**, we will assess the biocompatibility and biostability of our biochip *in vivo* by implanting it into mice and then monitor the immune response and levels of cell death at the site of implantation. We will also determine the accuracy of the chip in identifying and measuring concentrations of our chosen biomarkers *in vitro* in a solution that mimics blood plasma. Once this yields favourable results we will move on to the clinical trial.

The **first phase** of the clinical trial will involve two small groups of volunteers whose cancer is **in remission**. These are the control group and the experimental group. The experimental group will have our biochip implanted while the control will not. Both groups will continue with current preventative measures for cancer patients in remission, such as regular chest CT scans and blood tests. The trial will last for five years and the data will be collated and analysed afterwards. Granted that the chip is shown to improve patient outcomes through early detection (leading to diagnosis), we will continue onto the second phase of the investigation.

The **second phase** of the clinical trial would include a larger sample size made up of volunteers who are determined to be **at risk of developing lung cancer** (smokers, those with a family history, etc.). We will, once again, collect the health outcomes of the volunteers of the two groups to validate the effectiveness of the chip in improving rates of diagnosis and allowing for earlier treatment. The larger trial groups will allow us to gather data about rates of recurrence, diagnosis, etc. within **different demographic categories**, such as ethnicity and sex, which will allow for measures to be developed and implemented to decrease levels of inequality between these groups.

If the biochip is not found to significantly improve health outcomes, research would be conducted to improve its efficacy. Alternative biomarkers would be identified and the accuracy of the sensor technology would be increased, for example, by having multiple sensors specific to the same analyte. If implantation resulted in adverse health effects, then measures would be taken to review the safety of the chip in regards to vulnerability to corrosion and rejection.

Should the biochip be successful in the prior phases, we would then move to **mass production** of the chip for the general public whilst continuing to monitor its success and gather relevant data.

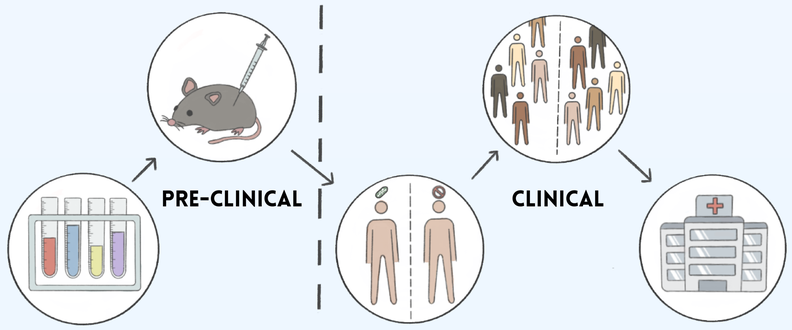
SHORTCOMINGS & ETHICS

The main drawback of our biochip is the nature of our biomarkers. Levels of **CTCs** and **CEA** are high in **breast and liver cancer** patients (among other conditions), which hinders our goal of making a chip dedicated to detecting lung cancer growth in particular. However, this is also a positive, as the biochip would be capable of referring people who may be developing other cancers to medical professionals for a diagnosis too. It is vital that users are aware that the chip is not a diagnostic tool, rather, it advises them to seek medical attention as early as possible for a better prognosis.

Another limitation is the price of the biochip. Due to biotechnology being a relatively novel and developing field of study, there are very few products available to the market that implement it for clinical use. Our estimated cost for the chip ranges from £60 to £600 as figures vary between companies[12]. Thus, **no set price** can be established for our device.

Some individuals may **reject the concept** of an implanted chip, perhaps because of fears surrounding the collection and selling of personal data. We will combat this by publicly outlining how their data is gathered and processed so that they have a better understanding of how it is handled. This will provide reassurance, allowing for a more positive reception of the chip.

There are also some **ethical concerns** that must be addressed with our proposal, one of which is the **use of mice** in the pre-clinical trial. The benefits that the trial will yield for human health justify their use for *in vivo* tests and all regulations on the use of animals in research will be followed. Another concern is the **withholding of the biochip** from volunteers in the control group which could negatively affect their health. However, this aligns with the principle of equipoise, where a drug or intervention can be withheld if there is no decisive evidence that it is superior to existing measures. Once there is sufficient evidence to prove that the chip is effective we will no longer involve control groups. Finally, we will ensure that we obtain informed consent from all volunteers involved and that we maintain confidentiality as well as the right to withdraw from the trial.



AFFORDABILITY & FEASIBILITY

Initial production, pre-clinical and clinical trials for our biochip would result in a relatively high short-term cost. However, this would be offset by the **long-term benefits** which **justify the investment**.

Lung cancer currently costs the UK economy £2.4 billion annually, with care totalling over £9,000 per patient for the NHS[13]. Although diagnosis and treatment in the first year is expensive, terminal care (care during the final 12 months of life) accounts for a much larger proportion of the overall expenditure[14]. Hence, by reducing the number of cases in the terminal stages, we aim to **reduce the expense per patient** through earlier diagnosis, allowing for more effective treatment and therefore a greater chance of survival. Earlier diagnosis would also lead to a decrease in the disparity between 18 to 64-year-olds and ≥65s. The latter, who make up the majority of lung cancer patients in the UK, receive only around half as many surgeries within 12 months of their diagnosis, leading to a lower survival rate[14]. The decreased requirements for terminal care will **ease pressures on the NHS** by increasing the availability of beds in hospitals, as well as decreasing its financial burden.

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REFERENCES