University of Glasgow
GLASSENSE
SENSUS 2024

TEAM RESULTS DOCUMENT

University of Glasgow

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09 AUGUST 2024

SensUs

ACUTE KIDNEY INJURY SENSUS 2024

Contents

Abstract

To address acute kidney injury (AKI), GLAsense will target the intensive care units (ICUs) in hospitals where more than **100,000 patients** in the UK alone are affected.

The **Acute** kidney injury **Monitoring** in **Intensive** care units sensor, **AMI** shown in Figure 1, is a continuous wearable biosensor for near real-time monitoring of creatinine levels in AKI patients, dramatically accelerating decision support for nephrologists who currently wait up to four hours for test results. Not only does our biosensor eliminate the need for frequent blood tests (every 1–2 hours), but also reduces patient discomfort and strain on hospital resources, importantly freeing healthcare professionals to address other critical tasks in the wards. The sensor utilises molecularly imprinted polymers (MIPs) that alter the physical properties of a hydrogel in response to creatinine levels in interstitial fluids (ISF), which will be obtained passively using microneedles. Our device employs an ultrasonic measurement at 20 MHz to detect these changes, providing real-time data on kidney function.

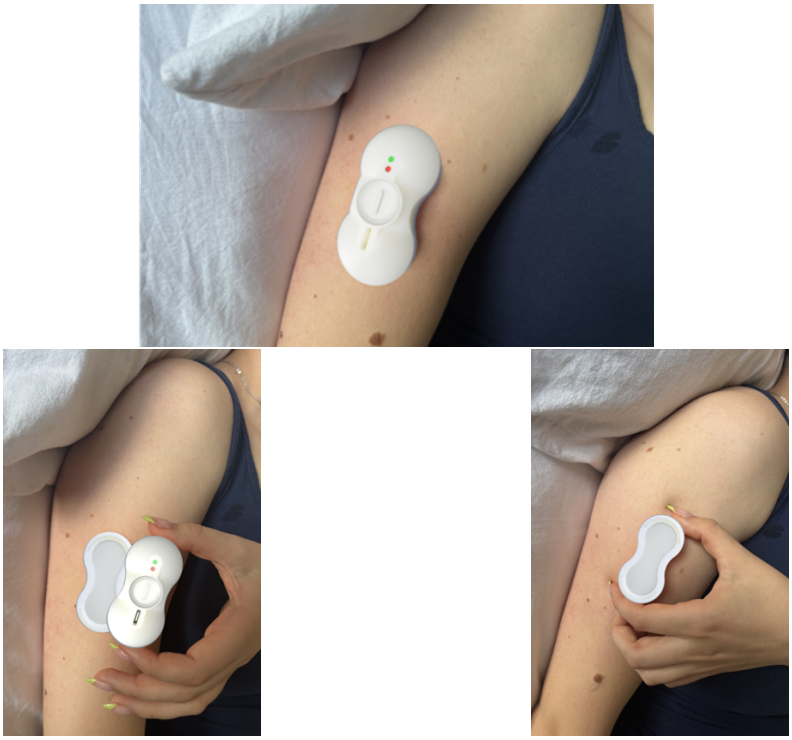


Figure 1: AMI in use

1 BIOSENSOR

1.1 Molecular Recognition

For the detection of the analyte, the molecular recognition component is essential and also plays an important role in the analyte's specificity and sensitivity. In this study, the diffusion behaviour of fluorescein isothiocyanate (FITC) was studied as a model for creatinine using agarose gel and polyacrylamide gel, to understand the behavior of small molecules like creatinine with different types of gels. We used 0.5% agarose gel with a thickness of 2 mm to analyse movement of molecules in an out of the gel. The intensity of fluorescence provided us with a measurement of diffusion, which reach equilibrium after ca. 50min, which is too long for a fast continuous measurement. Decreasing size (thickness to 1.5mm) and using 3% polyacrylamide enabled us to accelerate the diffusion, as well as to build specific molecular recognition elements in the gel, with Molecularly Imprinted Polymers (MIPs). These results are important to understand how creatinine would interact with the polyacrylamide gel matrix. These results also justify the use of polyacrylamide for precise molecular recognition in the design of our biosensor.

Analysing interstitial fluid (ISF) for biomarkers provides a promising approach for continuous and non-invasive monitoring of kidney function [2]. The epidermal accessibility to ISF has been utilised for the development of convenient wearable biosensors [3]. Moreover, the metabolic similarity between ISF and blood, alongside the absence of clotting factors in ISF make it a preferable sampling route for developing continuous biosensors, which tend to foul and fail in other samples [4]. While there are multiple methods to sample interstitial fluid, hydrogel microneedles are the most preferred due to their minimal invasiveness, high mechanical strength, and their ability to be fabricated with recognition molecules such as enzymes [5], aptamers [6], and molecularly imprinted polymers [7]. Compared to enzymes and aptamers, the fabrication of hydrogel microneedles with MIPs provides higher stability and biomarker flexibility [7]. MIPs are synthetic polymers that provide recognition to molecules of interest based on their size, shape, and chemical properties [8]. They are created by imprinting a polymer using the target molecule of interest as a template during the polymerisation, as shown in Figure 2. This is achieved by promoting the polymerisation of functional monomers in the presence of a target molecule, utilising the target molecule as a template for printing cavities in the polymer for molecular recognition of the target upon template removal [8].

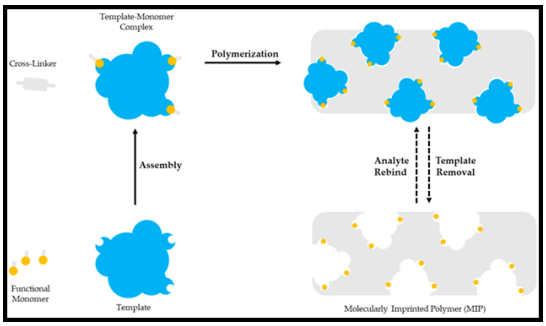


Figure 2: The process of developing MIPs. (Adopted from [1])

In our device shown in figure 3, we will use a setup similar to electrophoresis to actively push creatinine out of the gel with small DC currents in sequences, akin to systems that elicit sweat generation in wearable patches [9]. This way, we create an electric field that encourages the migration of creatinine molecules out of the MIPs embedded in the gel towards anodes, ensuring that the sensor is continuously reset and ready to detect new creatinine molecules. Nevertheless, this also suggests a strong binding to the MIPs which holds promise for sensitivity.

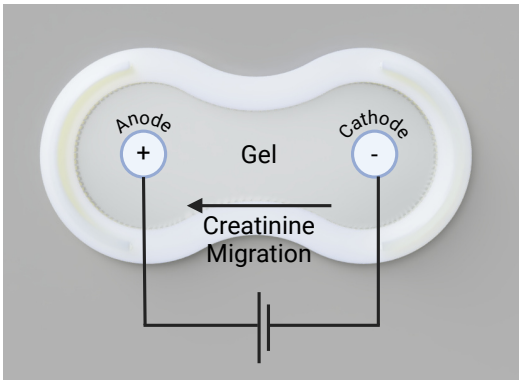


Figure 3: Sensor configuration showing the position of anode and cathode used for electrophoresis to remove creatinine out of the gel.

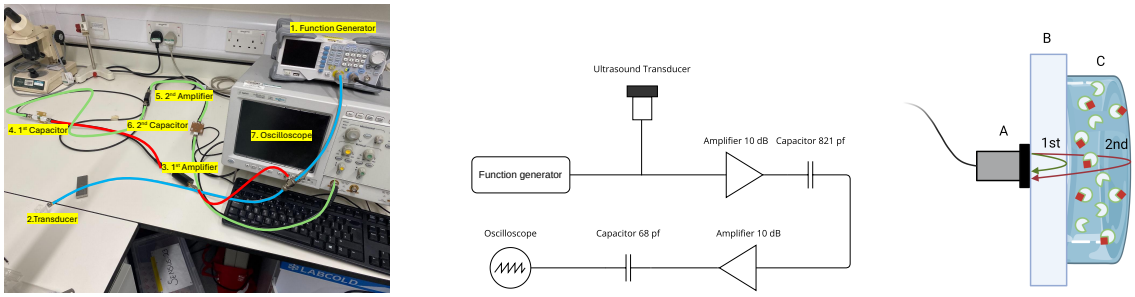
As the analysis utilised pure creatinine solution, the diffusion of off-target molecules can affect the signal when testing the biosensor in a complex mixture such as interstitial fluid. Therefore, the acoustic response of creatinine MIPs upon subjecting them to ISF samples with known creatinine concentrations must be measured and compared to the measurements

observed for pure creatinine solutions.

1.2 Physical Trasduction

The quantification of creatinine is based on the change in the acoustic response of the polyacrylamide gel, specifically by detecting the change in the speed of sound reflecting back from the sample. The gel contains MIPs for creatinine which will alter the speed of sound depending on creatinine concentration.

As shown in Figure 4b, the measurement setup consisted of a function generator to produce a single pulse sine wave signal with a frequency of 20 MHz. This signal is then transmitted from an ultrasound transducer into the gel medium. Upon transmission, the signal first reflects off the inner surface of an acrylic sheet back to the transducer followed by another reflection which bounces back from the backside of the gel, as illustrated in Figure 4c. The reflected signal is then passed through two stages of amplification, with each amplifier having a gain of 10 dB, making the total gain equal to 20 dB. After amplification, the signal is stabilised by capacitors with capacitance of 821 pF and 68 pF. The processed signal is then displayed on an oscilloscope. By analysing the signal on the oscilloscope, the speed of sound in the gel can be determined through appropriate signal processing techniques.



(a) (b) (c)

Figure 4: **(a)** Real measurement setup. **(b)** Circuit diagram of (a): The function generator drives the transducer, emitting ultrasound waves. The reflected is signal is amplified with amplifiers and displayed on an oscilloscope. **(c)** Gel-Transducer interface: The transducer (A) sends sound waves through an acrylic sheet (B) into a gel medium (C) with MIPs and creatinine. The '1st' path shows the initial reflection; the '2nd' reflects from the back of the gel.

1.3 Reader Instrument & User Interaction

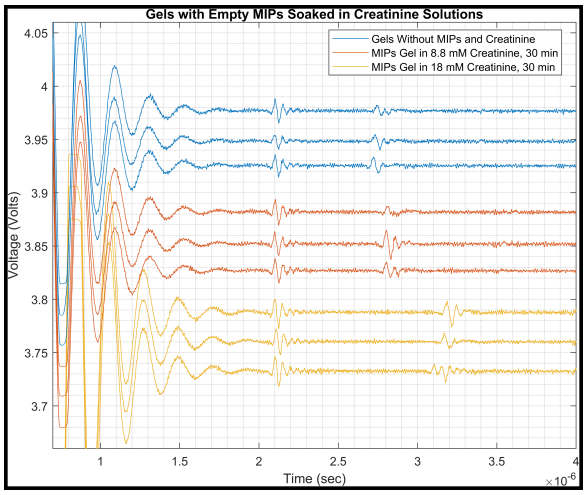
The AMI sensor is designed to be a compact and easy-to-use solution for achieving continuous creatinine monitoring in AKI patients in the ICU. The body of the sensor is split into two major parts, a top half containing the electronics, and the bottom hydrogel cartridge which acts as an interface between the sensor and the patient. The top half contains most of the major hardware components including the transducer, processor, battery, WiFi repeater, and LEDs, as well as a central button for inputting power and recording commands. This piece can be reused for the entire product life cycle. The hydrogel cartridge is the smaller piece, and comprises of the hydrogel patch for creatinine absorption, housed in an outer plastic scaffold. On the side which is interfacial to the skin, adhesive hydrogel microneedles help attach it to the arm of the user and access the interstitial fluid layer. On the opposing side, there is a snap-fit clip to easily attach the two parts, and ensure the correct relative contact and orientation. The recommended process for the first use of the product involves:

- The removal of the hydrogel cartridge from its protective film.
- Pressing the microneedle side of the cartridge into the cleaned skin surface of the user, ensuring a secure and uniform contact.
- Ensure the upper half of the device has battery charge, and turn on with the central button.
- Align the upper half with the hydrogel cartridge, securing it with the snap-fit mechanism.
- At this stage, the device should begin recording automatically, indicated by the green LED lighting, and data is sent via WiFi to the hospital or clinic patient database, and outputted live on the clinician's electronic device.
- Once the recording is completed, the red LED lights, and notification is sent to a graphical user interface on the clinician's PC or portable device.

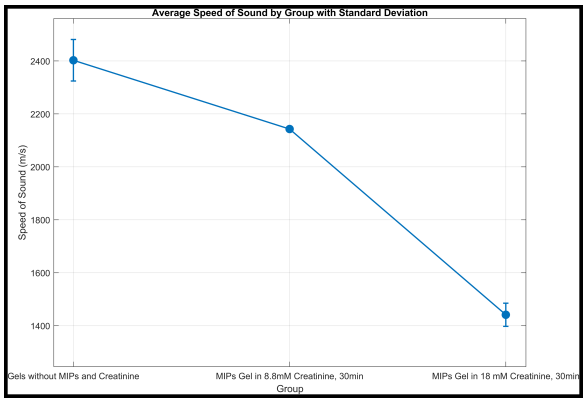
2 TECHNOLOGICAL FEASIBILITY

2.1 Physical Transduction

The signal in figure 5a represents the response for polyacrylamide gel soaked in varying concentrations of creatinine solution. The comparisons were made within three conditions including without MIPs and creatinine (blue), MIPs gels soaked in 8.8 mM creatinine solution for 30 minutes (red), and MIPs gel soaked in 18 mM creatinine solution for 30 minutes (yellow) in each condition was measured three times. It is consistently shown that the second reflection, which is due to gel, is delayed further as the concentration of creatinine increases, indicating the change in the physical characteristics of gel with MIPs. While the tested concentrations are above the clinical range, it proves the concept of the biosensor to be applicable for detecting and quantifying creatinine. However, further testing with creatinine concentrations within the clinical range is essential for assessing the biosensor sensitivity at the required range for clinical monitoring. Focusing on the speed of sound within the gel in figure 5b, the 'Gels without MIPs and creatinine' groups showed the highest speed of sound at 2,402.56 m/s followed by the 'MIPs gel soaked in 8.8 mM creatinine solution for 30 minutes' group at 2,142.86 m/s and lastly the 'MIPs gel soaked in 18 mM creatinine solution for 30 minutes' group at 1,441.31 m/s.



(a) Signal response of polyacrylamide gel soaked in Creatinine solution: no MIPs with no creatinine (blue), MIPs with 8.8 mM creatinine for 30 minutes (red), and MIPs with 0.018 M creatinine for 30 minutes (yellow). The results illustrate how the presence and concentration of creatinine in the gel medium affect the voltage response of reflected signals.



(b) Average speed of sound across three experimental groups: 'Gels without MIPs and Creatinine,' 'MIPs Gels in 8.8mM Creatinine 30 mins,' and 'MIPs Gels in 18 mM Creatinine 30 mins.' The plot displays mean values with standard deviations.

Figure 5

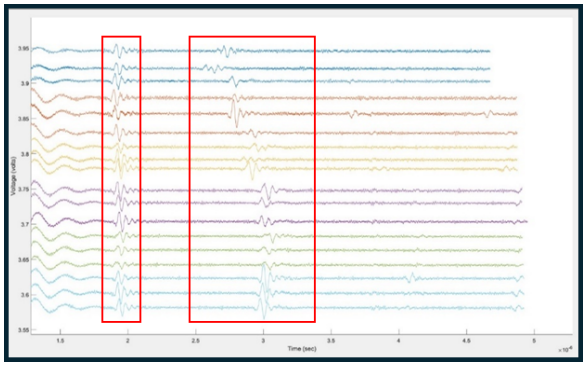
2.2 Calibration and Display

For calibrating the biosensor, taking a measurement of standard creatinine solutions with known concentrations must be done. This is done to confirm the association between the acoustic response of the biosensor with varying creatinine concentrations, alongside confirming the precision of the creatinine concentrations calculated by the biosensor. To do the calibration, the user will be provided with three bottles of standard creatinine solutions with concentrations of 30 µM, 150 µM, and 300 µM. The user will be required to subject the microneedles to a few drops of the solutions using a glass dropper and compare the readings of the device to the concentrations of each solution.

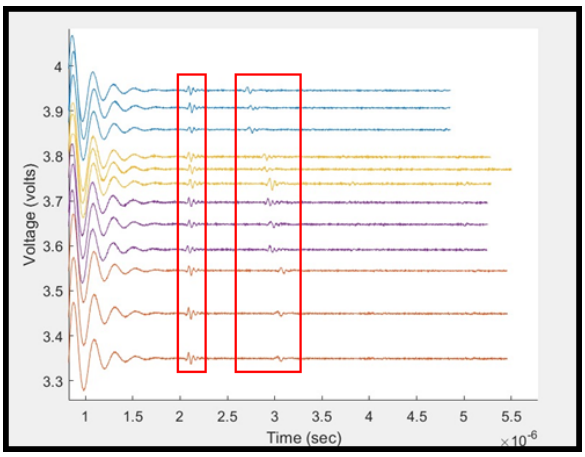
2.3 Molecular Recognition

Monitoring creatinine in MIPs using acoustics to test the ability of the developed MIPs-based creatinine biosensor for the continuous monitoring of creatinine, the acoustic response of polyacrylamide gel imprinted with creatinine MIPs was measured after subjecting the gel to different concentrations of creatinine for different durations. A delay was observed upon incubating the imprinted gel in 8.8 mM creatinine solution, suggesting creatinine diffusion to the gel Figure 6b and modification of its acoustic properties. However, the gel was observed to uptake creatinine even when subject to low concentration of creatinine, showing a further delay in the second reflection upon placing the gel in 442µM creatinine solution for 15 minutes as shown in Figure 6b. A further delay in the second reflection was observed when incubating the gels in a high creatinine concentration of 17.7 mM, followed by exposure to a lower creatinine concentration of 442 µM.

This suggests that the gels continued to uptake creatinine even in the presence of a concentration gradient, as illustrated in Figure 6a. Assessing the effect of varying creatinine concentrations on the acoustic response of polyacrylamide gel to assess the suitability of utilising acoustics to detect and quantify creatinine in a MIP-based biosensor, the acoustic response of polyacrylamide gel containing different concentrations of creatinine was measured. Figure 6b illustrates the analysis of the acoustic response of all the gels, revealing the presence of two peaks irrespective of the creatinine concentration. These peaks represent the reflection of the acoustic wave as it propagates in the device as shown in Figure 7. The first reflection was observed to occur at the same time in all the gels, indicating equal distance between the start of all the gels and acrylic glass holding them on the transducer as shown in Figure 6b.



(a) Acoustic response of polyacrylamide gel imprinted with creatinine MIPs when subjected to various creatinine concentrations.



(b) Effect of varying creatinine concentration on the acoustic response of polyacrylamide gel.

Figure 6: Combined acoustic response data for polyacrylamide gel imprinted with creatinine MIPs at different creatinine concentrations. Colours indicate creatinine concentrations: Dark blue (no creatinine), Orange (8.8 mM), Yellow (442 µM), Purple (17.7 mM), Green (442 µM), and Light blue (water).

However, the second reflection varied among the gels, with those containing higher creatinine concentrations exhibiting a greater delay compared to gels with lower or no creatinine. This suggests that creatinine concentration influences the acoustic response of the polyacrylamide gels, as shown in Figure 6b. Due to the change in the acoustic response observed to occur according to varying creatinine concentrations, acoustics were utilised to detect and assess creatinine diffusion to the MIPs of biosensor gel.

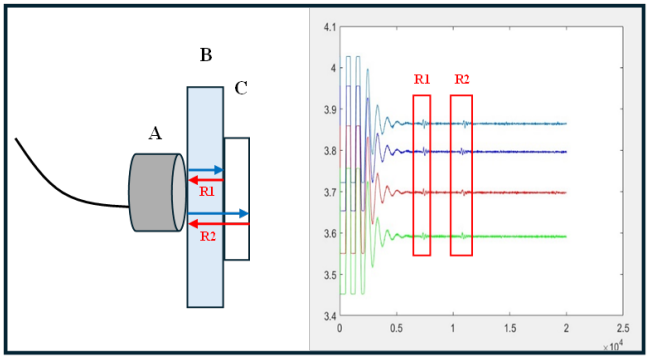


Figure 7: An illustration of the reflections of the acoustic waves observed upon analysing the gel's acoustic response. The transducer (A) was placed on a layer of acrylic glass (B) to assess the acoustic response of the gels (C). The acoustic waves generated by the function generator are shown in blue (Blue), while the waves reflected at the interfaces are shown in red (Red). The first and second reflections (R1, and R2 respectively) are highlighted on the time domain plot (D) by red boxes.

The polyacrylamide gel containing creatinine MIPs is expected to have high specificity to creatinine in interstitial fluid. Such specificity is due to the nature of molecular recognition of the MIPs, which relies on the shape of the target molecule [10]. Moreover, functional monomers can be incorporated during MIPs synthesis that can promote higher creatinine specificity based on its chemical properties [10].

3 ORIGINALITY

3.1 Team Captain

Our biosensor represents a groundbreaking advancement in the management of creatinine levels, not only for AKI patients but also for any individual with kidney issues who needs to monitor and control their creatinine levels in the future, such as those with chronic kidney disease (CKD), diabetic nephropathy, or patients undergoing dialysis.

The core innovation lies in our sensor's ability to continuously monitor creatinine levels in ISF using a combination of MIPs and ultrasonic measuring techniques. This continuous monitoring capability addresses a significant gap in current medical technology and uniquely combines a well-known technique (ultrasound sensing) that many of us have studied in our courses (for industrial applications as well as for medical imaging), with a robust, yet flexible molecular recognition element (MIPs). Although MIPs have been used in many biosensing situations [[11],[12]], we are not aware of any combination with acoustics, potentially due to the difficulties in finding the right material to both enable small molecules to diffuse and provide enough contrast for sensitive measurements. We also believe that such materials could be multiplexed in future (spatially with different gels in arrays) but also potentially acoustically (with different structures responding to different frequencies, for example), opening up wider applications.

In our development phase, we systematically assessed biosensing technologies, including electrochemical, magnetic, and optical methods in addition to acoustics. The latter became interesting to us as it allowed for the use of thicker gel structures that could be embedded with microneedles and would also be easier to handle than a thin surface [13]. We calibrated our transducer extensively and optimised gel formulations, transitioning from agarose to acrylamide to enhance performance. This was done in parallel with our device design team crafting custom 3D-printed holders and test rigs to support the sensor. Moreover, regarding human factors, we are pushing boundaries by transforming our sensor into a wearable device. This is being done using micro-needles which will be minimally invasive and therefore painless for the patient. The whole sensor will be encased in a small, ergonomic, manually applied system, designed with input from users and utilising the gel as a conformable interface. I believe our team has done amazingly well in all aspects of this competition.

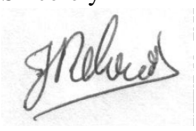
3.2 Team Supervisor

I can confirm that the team has developed their idea **completely independently**. Some of the team members took a course on biosensors as part of their curriculum, that both Chunxiao (SensUs coach) and I teach in. The course covers the basics of biosensing and provides examples of different sensor systems and strategies. Members of the team were thus exposed to optical sensors and sandwich assays, along with concepts of microfluidics. However, I should stress that they were not exposed to MIPs and only superficially to acoustics (although other courses discuss this for different applications, including medical imaging for example). They indeed started their work from scratch, through literature searches of possible strategies and used a thorough and systematic analysis to determine their preferred sensing strategy.

They realised that acoustic sensing could penetrate deeper into materials and thus could be useful with materials interfaced with the human body as a wearable, as they did not want to consider implants. They also found the idea of microneedles in literature and although Professor Gadegaard has worked on them in Glasgow, he was not involved with the team and his research did not use hydrogels. Given the costs and complexity associated with using antibodies or enzymes in assays (which the team members coming from life sciences were very familiar with), they also decided to minimise the use of labels (which eventually could lead to a wash-free device). This led them to devise the MIPs-based assay scheme, after calculations on the changes in mechanical properties that creatinine binding could potentially yield. This is akin to photonic sensors developed by Lowe at Imperial College (with beads in gels that change their plasmonic properties upon swelling) but it has not been used with acoustics or with MIPs to my knowledge. Our wider research group certainly has not researched this at all.

My role was kept at an advisory level (outlining potential challenges in their strategies), as well as to guide access to existing equipment in the wider campus and directing the team to potentially useful expertise in Glasgow. However, I must stress that no active research is taking place in the group at the moment on these topics. All in all, I am very proud of how the team focused on a difficult challenge and provided a workable solution for such an arduous task.

Sincerely



Julien Reboud	Tasneem Khodair	Najaree Janjerdsak
Team Supervisor	Team Captain	Team Captain

4 TRANSLATIONAL POTENTIAL

4.1 Introduction

Acute kidney injury (AKI) is a common condition affecting millions of patients worldwide. It is defined as an increase in serum creatinine to 1.5 times the baseline value, which is considered the patient's usual creatinine level when clinically well [14]. Additionally, it is limited to a duration of seven days and anything longer than that is defined as acute kidney disease (AKD) [15]. Early identification and treatment of AKI could avoid up to 42,000 deaths from AKI yearly [16].

Despite the high incidence of AKI, current monitoring methods are largely reliant on intermittent blood tests, which are invasive and provide delayed results. This approach can lead to suboptimal patient management and increased healthcare costs. Moreover, the intermittent nature of these tests often results in the early signs of kidney deterioration being missed, exacerbating the condition and leading to worse outcomes for patients.

GLAsense addresses this critical gap in healthcare with its innovative biosensor **AMI**v(Acute Kidney Injury Monitoring for Intensive Care Unit), designed to detect creatinine levels in the ISF of AKI patients. Our minimally invasive wearable device employs micro-needles to allow ISF flow, where creatinine diffuses into a hydrogel, causing a change in density detectable using an ultrasound transducer. This breakthrough technology promises to revolutionise AKI monitoring by offering continuous insights into kidney function in the near future, thus enabling healthcare providers to intervene promptly and effectively.

4.1.1 Business Model Canvas

Figure 8: Business Model Canvas

4.2 Market Description & Stakeholder Desirability

4.2.1 Target Customers

AKI is a common incident in critically ill patients, especially those who have been admitted to the ICU. According to the study in 2022 [17], 53.3% of patients in the ICU have developed AKI. This is a huge number considering the mortality rate of AKI can range from 20% to 90% [18]. In the UK alone, an average of 250,000 patients is recorded to be admitted to the critical care [19]. This means that at least 125,000 people will experience AKI, annually.

In clinical settings, ICU patients routinely undergo blood tests to monitor their response to treatment [20]. Creatinine, a key biomarker for kidney function, is frequently measured and can indicate early signs of AKI. Patients suspected of having AKI often undergo repeated blood tests, with nephrologists or nurses monitoring creatinine levels every hour for 24 to 72 hours, followed by less frequent monitoring until the patient is well [21]. In one week, the number of blood test needed can range from 50 to 80 times per patient, depending on their severity.

In GLAsense, our sensor AMI aimed to lessen this rigorous process of blood testing to monitor creatinine level in ICU patient from doctors and nurses. However, in order to reach this goal, we have to develop a thorough business plan to reach the end-users as efficiently as possible.

As a smaller, researcher-based start up, our customer base for **AMI** is divided into two segments: Primary and Secondary customer. Through B2B approach, our primary customers are medium to large medical device and biosensor manufacturers. This approach will help us to speed up the process of acquiring recognition and credibility to sell our sensor to the market.

Our secondary customers are the UK NHS and other organisations that will purchase our sensor from the primary customers. Local hospitals, general practitioners (GPs), and other healthcare providers are also supplemental customers, whose purchasing decisions will largely depend on the NHS's choice. Other prospective customers, such as public and private insurance companies, are not our primary focus at this stage. However, their decisions will be affected by our financial strategies and the actions of our primary and secondary customers.

Our customers require a solution that offers continuous monitoring of kidney function, minimally invasive, and ICU-friendly to prevent and manage AKI patients in the ICU setting effectively. These factors will be discussed in the following sections

4.2.2 Stakeholders & their needs

At GLAsense, we recognise that our stakeholders are integral to the success of our mission. Our stakeholders include a diverse array of individuals and organisations, such as patients whose health and quality of life we aim to improve, doctors and hospital administrators who integrate our technology into their clinical practices, and insurance companies who benefit from reduced costs and enhanced data accuracy.

Table 1 provides a detailed overview of each stakeholder's sector, role, and needs. Understanding these factors is crucial for strategic planning, compliance, and overall stakeholder satisfaction, all of which are vital for maintaining positive relationships and ensuring the long-term success of GLAsense. The insights presented in Table 1 were gathered through literature reviews and interviews with nephrologists and patients, see Appendix A.

The rules and regulations required vary for each sector. The first regulatory focus is on the government sector, which is pivotal for validating the usability of our product. Our device will pass a safety assessment before proceeding to clinical trials. Data from these trials, along with technical information, will be used to obtain conformity assessments such as CE marking for European countries, UKCA marking for the UK, and FDA approval for the USA, all of which must comply with the ISO 13485 and ISO 10993 standard. Additionally, our medical device must secure marketing authorisation (e.g., from the MHRA in the UK) to be available to the healthcare, public, and private sectors. Ensuring compliance with data privacy laws is also critical for maintaining confidentiality across sectors.

To streamline the certification process for our medical sensor, we will begin by obtaining ISO 13485 certification, followed by the ISO 10993 to ensure our processes meet international quality standards. Subsequently, we will leverage clinical data from the Queen Elizabeth University Hospital (QEUH) and the Royal Infirmary in Glasgow to support our CE marking application. In the UK, we need approval from the Research Ethics Committee in NHS West of Scotland to conduct clinical trials involving human participants [22]. This requires submitting our clinical trial protocol and other necessary documentation for review.

Key steps include:

- Implement ISO 13485 and ISO 10993: Obtain certification for our quality management system.
- Regulatory Submissions: CE marking (EU), UKCA marking (UK), and FDA (US)
- Clinical Trials: Conduct trials in the UK once REC approval is secured.

After securing the CE mark, we will apply for UKCA marking using the same data. The equivalence is currently in place and is expected to continue, although we will need to involve a UK Approved Body as well as an EU Notified Body in the process to enable this. We will follow with FDA approval for the US market. This phased approach will facilitate early market entry (and revenue generation) while ensuring compliance with essential regulatory standards. Although the US market is larger and thus would be a better fit for first entry, our product does not have a predicate device that could facilitate approval, limiting this advantage, whilst our project and team are embedded into the vibrant Glasgow innovation ecosystem, facilitating acquiring local data and the regulatory process in the UK, thus tilting the balance for an initial market entry closer to the UK.

Table 1: Stakeholders, their roles, and needs

Stakeholder	Sector	Role	Needs
Licensee Companies	Public	Primary customer, Decision-maker	Accurate: Ground-breaking technology User-friendliness: Compact design that does not impact other monitoring or treatment Cost-effective Efficient.
AKI patients in ICU	Public	End user	Efficiency: Significantly improve health and prevent death User-friendliness: Compact design that does not impact other monitoring or treatment.
Doctors (mainly nephrologists)	Healthcare	Direct user, key opinion, endorsement	Efficiency: Reduce the testing frequency, easy-to-analyse readouts, reduce mortality rate Reliability: Accurate real-time monitoring with more data points User-friendliness: Seamless integration into clinical workflow
Nurses	Healthcare	Direct user, key opinion	Efficiency: Reduce the testing frequency User-friendliness: Seamless integration into workflow, easy to set up and read
Healthcare systems (i.e. NHS)	Government, Healthcare	Secondary customer, decision maker	Cost-effectiveness: Reduce spending Efficiency: Allow doctors and nurses to perform up to the standard and regulations, reduce mortality rate
Hospitals, GPs, and other healthcare providers	Government or private	Supplemental customer, decision maker	Cost-effectiveness: Reduce spending Efficiency: Allow doctors and nurses to perform up to standards and regulations, reduce mortality rate
Patient's family and friends	Public	Influencer	Efficiency: Significantly improve health and prevent death
Public and private insurance companies	Private	Other prospect customer	Information: Complement data from the test

4.3 Value Proposition

GLAsense's value proposition is clear: by providing a faster, minimally-invasive, and ICU-friendly method of monitoring kidney function in AKI patients, our biosensor enhances patient care, optimises hospital operations, and contributes to better overall healthcare outcomes. This allows AMI to address the critical needs of both patients and healthcare providers.

Currently, continuous sensors specifically designed for monitoring creatinine levels are not commercially available. While continuous monitoring technologies exist for biomarkers such as glucose, glutamate, and lactate, and are commercialised by large companies such as Abbott, research on continuous creatinine monitoring is ongoing [23], as existing technologies are not easily adaptable to this marker. This highlights a substantial market opportunity for a device like AMI. However, it also suggests that securing the required certifications and approvals may be more complex due to the lack of a predicate device in this field.

Moreover, to the best of our knowledge, the technology underlying our product and its specific application in continuous creatinine monitoring are not covered by any existing intellectual property rights. This gives us a strategic advantage to secure strong intellectual property protection for our innovative MIPs technology and microneedle integration. By doing so, we can safeguard our innovation and maintain a competitive edge in the market, ensuring that GLAsense remains a leader in advancing AKI patient care.

4.4 Business Feasibility

4.4.1 Key Resources, partners, and activities

Aiming to help increase the survival rate of AKI patients in the intensive care unit (ICU), AMI needs to go through several development and classification processes to ensure safety and required performance.

Our sensor uses the properties of ultrasound waves to detect changes in creatinine-imprinted polymer gel. This approach is new, requiring significant investment in the research and development process to demonstrate analytical and clinical performance in particular. We will also need key opinion leaders (KOLs), nephrologists and nurses who work closely with AKI patients in the ICU setting, to ensure the usability and integration of our product. As students from the University of Glasgow, we have consulted KOLs through our university's connections with QEUH and will include them in our Advisory Board. Our Student Enterprise Team also offers business and marketing advice, an incubator and mentorship programme, as well as networking and funding opportunities, such as the SantanderX competition.

Although research and development is an ongoing process, clinical trials can begin after the minimum viable product (MVP) is achieved. The MVP manufacturing process will be outsourced as our parts can be produced using existing capabilities such as injection moulding and standard electronics. We will assemble the devices initially in-house to keep the process under control. After obtaining approval from the Research Ethics Committee in Scotland, the clinical studies will be conducted at our local hospitals, Queen Elizabeth Hospital and the Royal Infirmary which host 5,334 patients in ICU, with 1217 patients diagnosed with AKI [24]. We expect to manufacture at least 100 sensors for the later stage of the clinical trials to be conducted. With regulatory approvals, this data, along with technical information, will be submitted for conformity assessments: CE mark, EU MDR, and UK MDR. We expect to get funding to support this process through government funding, Kidney Research UK, accelerator programs and initial (limited) venture capitals (high-risk angels for example). For patenting, we will consult an IP-specialised lawyer to apply for utility and design patents. The University of Glasgow can provide initial support through the Student Entreprise structures.

Once the product is recognised as safe and marketable, we will prepare to enter our pilot market, ICU patients in the UK. As a small start-up made up primarily of researchers and engineers, we have limited capital to successfully enter the market on our own. As a result, we decided to mitigate the risk by selling a non-exclusive IP license to bigger medical device manufacturers such as Abbott, Roche, or Dexcom. We plan to offer a 5-year licensing agreement that includes an upfront fee, a minimum annual guarantee, and a royalty fee. This approach enables us to avoid manufacturing and marketing costs, allowing us to concentrate on enhancing the efficiency and value of our product.

We aim to increase our company's visibility to our potential licensees through academic conferences (e.g. IEEE EMBS and BioMedEng) and Trade shows (e.g. MEDICA and Med-Tech Innovation Expo). Targeted campaigns and initiating pilot trials in QEUH and the Royal Infirmary will also be conducted, along with product demonstrations and easy-to-access educational online content to highlight our features and value. Once the deal is signed with the licensee, we will also offer the possibility of a training scheme for doctors and nurses to integrate our sensor into their clinical pathway more efficiently. This will allow us to take some pressure off of the licensee and allow us to have direct contact with the customer in case of technical issues.

Another advantage of adopting a licensing approach is the ease with which it allows us to scale our market presence. Licensing provides a steady revenue stream from various manufacturers without the need for us to relocate or directly enter different markets. This strategy is also the most efficient way to rapidly reach a large patient population, as partnering companies would already have access to established distribution channels and marketing resources. By leveraging these networks, we can deliver the value of our devices to those who need them more quickly.

With a solid understanding of our biosensor's role in the UK, our pilot market, we can effectively demonstrate our market potential to EU-based manufacturing companies. While we are also considering the US market, we plan to focus on the EU first, as FDA approval is more time-consuming, and our clinical trials currently do not reflect the US population.

4.4.2 Sustainability

As mentioned above, GLAsense will pursue a licensing approach to sell our product's know-how rather than the physical sensors. The sensors will be produced using the existing manufacturing facilities, storage, and offices that the licensee company already has in place. Moreover, the licensing strategy enables the sensors to be manufactured near the local market, minimising the need for logistics and shipping. This approach significantly reduces CO2 emissions compared to manufacturing or outsourcing the sensors ourselves. Although our sensor is designed to be disposable and single-use, its lifespan is expected to last 7 days, which aligns with the average length of stay for AKI patients in the ICU. This means there will be only one piece of waste compared to the waste generated by 50-80 laboratory creatinine tests [21] in one week. Some parts of the sensor—such as the casing, ultrasound transducer, and other electronic components—are intended to be retrieved and recycled. However, more studies are needed to safely and efficiently dispose of the microneedles, as they come into contact with the patient's skin and the MIPs gel. A specialised bin with complimentary waste collection services is a good way to manage the sensor waste while also mitigating the risk of

infectious disease and preventing contamination of non-biodegradable polyacrylamide-based MIPs in land and water.

4.5 Financial Viability

4.5.1 Costs projection

The main materials and components used in the biosensor were identified to determine the material costs. Costs associated with manufacturing were then evaluated along with labour costs, which were calculated based on the required production time and hourly wages based on the Scottish industry average. From these elements, the cost of goods sold was determined. Following this, initial research and development expenses were assessed, along with testing, and quality control procedures were analysed to determine their associated costs. Packaging and distribution expenses were included to account for the delivery of the product to end-users. Additionally, regulatory compliance costs were reviewed. General overhead costs, such as utilities and administrative expenses, were also considered, and conservative economies of scale savings were factored throughout. With these fixed and variable costs considered, the cost of goods sold (£16.08) and conservative intended profitability (20%) were factored to determine a suitable sales price of £19.30. With this the accumulative sales could be plotted with each unit and compared against the development cost to find a break-even value of 49,606 units sold, giving insight into the economic feasibility of the product. Please see Figure 10 for our cost breakdown analysis and Figure 11 for our Labour & Overhead Analysis in Appendix B.

In a hospital setting, a single test costs approximately £6, covering staff and equipment expenses. According to our interview with a nephrologist and NHS Rotherham's guidelines, tests are conducted hourly in the ICU during the first 24-72 hours. The frequency is then reduced based on the patient's condition. Over seven days, creatinine testing can be performed 50 to 80 times, resulting in a total cost of £300-£480 per patient.

4.5.2 Market analysis

The global market for AKI treatment is set to experience substantial growth, with an anticipated compound annual growth rate of 8.2% from 2022 to 2029. By 2029, the market is expected to reach approximately £2.8 billion [25]. This presents an excellent opportunity for us to introduce our continuous sensor, which facilitates early detection and treatment of AKI. Additionally, further proving the market availability for our sensor, the hospitalisation rates for AKI patients across Europe are as follows: 19.3% in Northern Europe, 25.2% in Southern Europe, 23.2% in Eastern Europe, and 20.8% in Western Europe [26]. Moreover, AKI occurrence in these areas is predominant in ICUs and is treatable and reversible, which shows that there is market availability for our sensor [26].

Given the innovative and pioneering nature of our technology, finding a direct comparison in the market is challenging. Comparing to the huge glucose sensing application where wearables exist, is useful but does not address the same situation. Instead of relying on external benchmarks, we prioritise our internal performance metrics and feedback from healthcare professionals. This approach allows us to stay at the forefront of innovation and tailor our solutions to meet the unique needs of AKI patients, ensuring we deliver cutting-edge and effective diagnostic tools.

The current gold standard for monitoring kidney function, especially in AKI patients in ICUs, is serum creatinine testing via regular blood draws, combined with urine output measurement. These methods are well-established and widely used due to their clinical reliability and extensive historical data supporting their efficacy. Urine output measurement involves collecting and quantifying urine over a specific period, providing additional data on kidney function.

4.5.3 Revenue

In establishing our business intelligence framework, we have decided to adopt a strategy centred around licensing our innovative continuous biosensor technology for measuring creatinine levels in AKI patients to other diagnostic companies. This approach allows us to leverage the established market presence and distribution networks of existing diagnostic companies rather than investing heavily in building our own brand from scratch. By doing so, we can focus on our core strengths in research and development, ensuring our technology remains at the cutting edge. Our business intelligence efforts will be geared towards identifying potential licensing partners, understanding market trends, and continuously improving our product based on feedback and performance data. This strategic decision not only accelerates our market entry but also maximises our reach and impact in the healthcare industry. In addition to upfront licensing fees, we will receive ongoing royalty payments based on the sales of diagnostic products that incorporate our technology. For the first five years after regulatory approval, we will have a fixed royalty rate of 5%, which will allow for a predictable budget plan. However, once we have reached the break-even point (between year 6 and 7), we will switch to a variable royalty rate, depending on each company's sales performance and market conditions. Please see Appendix B.

We estimate signing 5 licensing agreements at £1,500,000 each, with milestones payments over five years. We will also offer subscription-based services for software updates, maintenance, and advanced analytics, with an estimated 100 subscribers paying £1,000 annually, totalling £100,000 in the early days. Licensees will also benefit from those.

5 TEAM & SUPPORT

Table 2 provides an overview of each team member's roles and contributions to the project.

Table 2: Team members' contributions

Name	Role & contribution
Adam Peat	Member of the Business Team. Focused on mapping the user journey and conceptual design.
Adi Karni	Member of the Business Team. Played a crucial role in securing sponsorships.
Aleksandar Zahariev	Developed the team website from scratch.
Ally Nicolas	Managed all our social media posts, keeping our followers updated and engaged.
Farid Mohammed Farid Bahada	Created and tested the MIPs.
Hamna Khalid	Member of the Business Team focusing on biosensor market research.
Himaja Machiraju	Member of the Business Team. Took charge of applying for accelerator programmes.
Najaree Janjerdsak	Served as co-captain and played a major role in the Business Team. Worked on designing the test-rig.
Olivia Skinner	Made significant contributions in designing and 3D printing the test-rig for the detection setup.
Pongnarit Plengsangsri	Member of the Detection Team, focusing on data acquisition and analysis.
Riddhi Papnai	Worked on optimising the MIPs.
Tasneem Khodair	Served as co-captain and member of the Business Team. Played a major role in various aspects of the project.
Zihao Pan	Member of the Detection Team. Played an essential role in the ultrasound measurement setup and data analysis.

We are very grateful to the individuals who have supported us throughout the year, see Table 3. Their help and invaluable contributions have significantly enhanced our project's success. Their support has been instrumental in achieving our goals, and we extend our heartfelt thanks to each of them for their dedication and generosity.

Table 3: Supportive contributors to the team

Name	Role and contribution
Julien Reboud	Team Supervisor – Provided essential guidance and support throughout the project.
Chunxiao Hu	Team Coach – deputised for Julien when unavailable for team meetings and discussions and provided advice on analytical characterisation.
Andriejus Demcenko	Lecturer in Cell Tissue Mechanics – Coached us on expert data analysis.
Andrew Philips	Electronics Technician – Guided us in making informed electronics design decisions.
Andrew Glidle	Research Technologist – Assisted with practical organisation and ordering components.
Marion Anderson	Student Enterprise Manager – Provided crucial advice on our business model and pitch potential.
Olga Chashchina	**CTO of Metyos – Delivered insightful feedback on our business strategy.**

Finally, we are incredibly thankful to Diagnostic Healthcare for their generous sponsorship of our team. Their support has been invaluable in our journey and is deeply appreciated.

We also extend our heartfelt thanks to the University of Glasgow for enabling access to facilities.

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A Appendix A - Interviews

A.1 Interview with Dr Adisorn Pathumarak - Nephrologist

Key takeaways

"AKI is gradually reversible. Blood is drawn from patients daily at the hospital and when they get discharged, creatinine levels are checked weekly or monthly depending on the patient's condition. You can use standardised equipment in one area, but other areas might be quite expensive and you can use some processes which might be quicker and then other companies might have slower versions. Maybe half of the time is consumed by the logistic process, but the test is not long - it may be 10 or 15 minutes."

A.2 Dr Nuttasut Thanakornyothin - Nephrologist

Key takeaways "AKI was called Acute Renal failure in the past. The percentage of the kidney starts to decline and acute refers to it happening in a **few hours or days** compared to chronic kidney failure which happens in at least 3 months. Creatinine is the widely used test at the moment. Doctors have to check each individual's **baseline creatinine levels**. For the first 72 hours, when AKI is suspected, blood and urine tests are done every hour. **If we can measure a biomarker from the plasma it would be useful for the doctors.** We do not want the patient to go into a state of shock which lowers their blood pressure, therefore preventing their kidney from requiring dialysis which is expensive. Since creatinine levels are limited by muscle mass, it would be beneficial to add another biomarker to be measured. "

Doctors would like a sensor that is:

- Easy to use
- Fast result
- Accurate - explainable result
- Not harmful to the patient - not good if you have to puncture every time

A.3 Interview with Mrs Marion Anderson - Student Enterprise Manager

We received feedback on our business strategy and had discussions about intellectual property, focusing on licensing our ideas. This has helped us refine our approach and ensure our innovations are properly protected and monetised.

B Appendix B - Cost Analysis

Component	Low Estimate (£)	High Estimate (£)	x̄ Value (£)	Quantity	Total (£)
Upper Structure	0.15	0.24	0.195	1	0.195
Battery	0.38	0.75	0.57	1	0.57
Circuit Board	0.75	2.25	1.5	1	1.5
Button	0.04	0.08	0.06	1	0.06
LED	0.02	0.08	0.05	2	0.1
Microprocessor	0.75	3.75	2.25	1	2.25
USB-C Port	0.15	0.38	0.27	1	0.27
Ultrasonic Sensor	0.75	2.25	1.5	1	1.5
WiFi Transmitter/Receiver	0.75	2.25	1.5	1	1.5
			Upper subtotal		7.945
Lower Structure	0.15	0.24	0.195	2	0.39
Hydrogel Patch	0.08	0.38	0.23	2	0.46
Microneedle Patch	0.38	1.13	0.76	2	1.52
			Lower Subtotal		2.37
		Total unit component cost (£)			**10.315**
Labor and Overhead			Gross Cost (£)	Quantity	Net Cost (£)
Technician Wage per hour			15	0.33	4.95
Equipment and Utilities per day			36	0.014	0.504
Quality Control and Testing per day			22	0.014	0.308
		Total Manufacturing and Overhead Costs (£)			**5.762**
		Cost of Goods Sold per unit (£)			**16.077**

Figure 10: Cost Breakdown Analysis

Revenue Model for 1 company

			Year 1	Year 2	Year 3	Year 4	Year 5
Revenue		Selling price/unit	£24	£24	£24	£24	£24
		no. of unit sold	750	2,500	6,500	13,000	25,000
		Total Revenue	£18,000	£60,000	£156,000	£312,000	£600,000
Cost	fixed	Upfront fee	£1,500,000	-	-	-	-
	fixed	Minimum Annual Guarantee	£75,000	£75,000	£75,000	£75,000	£75,000
	variable	Royalty rate (5%)	£900	£3,000	£7,800	£15,600	£30,000
		Manufacturing cost	£12,058	£40,193	£104,501	£209,001	£401,925
		Total Cost (What we'll get)	£1,587,958	£118,193	£187,301	£299,601	£506,925
		Net profit (for the licensee)	**-£1,569,958**	**-£58,193**	**-£31,301**	**£12,399**	**£93,075**

Figure 13: Example Revenue Model for Licensee

Research and Development (R&D)		Overhead and Facilities		Preclinical Testing and		Materials and Equipment		Regulatory Compliance and		Clinical Trials		Manufacturing Setup		Marketing	
2 PhD Candidates (1 year at £19,988/year)	£ 39,976.00	University/Institution Overheads (20%)	£ 18,227.00	In-vitro Testing	£ 40,000.00	Lab Equipment	£ 30,000.00	Regulatory Consultant Fees	£ 40,000.00	Small-Scale Clinical Trials	£ 150,000.00	Pilot Manufacturing Setup	£ 60,000.00	Marketing Campaigns	50000
Lab Technician (1 year at £25,579/year)	£ 25,579.00	Facilities (Rent, Utilities) (2 years)	£ 30,000.00	Validation Studies	£ 20,000.00	Prototyping Materials	£ 15,000.00	MHRA Fees (UK Class II device)	£ 10,000.00	Ethics Committee Fees	£ 10,000.00	Initial Batch Production	£ 50,000.00		
Project Manager (1 year at £48,000/year)	£ 48,000.00					Specialised Biosensor Materials	£ 25,000.00	Clinical Trial Insurance	£ 20,000.00	Participant Logistics	£ 30,000.00	Quality Assurance and Control	£ 40,000.00		
2 BioChemists (1 year at £40,225/year)	£ 80,450.00					Documentation and Submission Costs	£ 10,000.00	Clinical Trial application fees	£ 4,100.00	Clinical Investigations (NHS)	£ 15,078.00				
Software Engineer (1 year at £43,326/year)	£ 24,326.00							ISO 13485 Certification Fees	£ 15,000.00	Participant Compensation (100 participants)	£ 800,000.00				
								ISO 10993 Certification fee	£ 70,000.00						
								Scientific advice meetings	£ 5,000.00						
Total Personnel Costs	**£ 218,331.00**	**Total Overhead and Facilities Costs**	**£48,227**	**Total Testing Costs**	**£60,000**	**Total Materials and Equipment Costs**	**£80,000**	**Total Regulatory Costs**	**£164,100**	**Total Clinical Trial Costs**	**£ 1,005,078.00**	**Total Manufacturing Setup Costs**	**£150,000**	**Total Marketing and Distribution Costs**	**£50,000**
Total Estimated Cost	£1,775,736														

Figure 11: Labour and overhead costs analysis

Total no. of licensees	Year	Annual cost	Total cumulative comparison development costs	Licensee #1	Licensee #2	Licencess #3	Total revenue	Net profit	
0	1	- 2,000,000	- 2,000,000				0	- 2,000,000	
0	2	- 1,000,000	- 3,000,000				0	- 3,000,000	Break-even point
0	3	- 1,000,000	- 4,000,000				0	- 4,000,000	
1	4	- 500,000	- 4,500,000	2,007,200			2,007,200	- 2,492,800	
1	5	- 500,000	- 5,000,000	536000			536,000	- 2,456,800	
2	6	- 500,000	- 5,500,000	620000	2,007,200		2,627,200	- 329,600	
3	7	- 500,000	- 6,000,000	704000	536000	2,007,200	3,247,200	2,417,600	
3	8	- 500,000	- 6,500,000	800000	620000	536000	1,956,000	3,873,600	
2	9	- 500,000	- 7,000,000		704000	620000	1,324,000	4,697,600	
2	10	- 500,000	- 7,500,000		800000	704000	1,504,000	5,701,600	
1	11	- 500,000	- 8,000,000			800000	800,000	6,001,600	

Figure 12: Break-even Analysis