SensASH Scientific Paper

By SensASH of the American School of the Hague

Members:
Abhishek Gopal Ramshanker, Jaiden Grimminck, Olivia Ike,
SeongYun Lee, Jurgen Westerhof, Sophia Williams

Abstract

Kidney failure is a significant risk for many individuals with various conditions such as diabetes and hypertension (high blood pressure). Early detection of kidney failure and monitoring for this, as well as monitoring individuals with continuous kidney failure (CKD) is essential, as it provides crucial time for healthcare professionals to intervene with medication and lifestyle modifications, thereby mitigating any further kidney damage. This paper explores the development of a novel urine analysis device designed for at-home creatinine detection, with the goal of facilitating early diagnosis and continued monitoring, especially in underdeveloped settings.

1. Introduction

The diagnosis of continuous kidney disease is performed by monitoring the level of creatinine to urea in a patient's urine. Creatinine is a waste product from a muscle's metabolic process from the conversion of creatine to creatine phosphate, releasing energy. The creatinine enters the bloodstream and is excreted through urine after being filtered by the kidneys. Creatinine excretion outside of the normal rate may signify a loss of kidney function, particularly kidney failure or continuous kidney disease. Mount Sinai established normal creatinine levels in urine in separate studies, with 14 to 26 mg per kg of body mass per day for men and 11 to 20 mg per kg of body mass per women ("Creatinine Urine Test"). An increase in creatinine levels in the body is considered harmful and toxic. Hence, creatinine is used as a biomarker to predict the condition of the kidney.

Urea is also produced from the breakdown of proteins into amino acids. Ammonia is produced from the leftover amino acids, and through a process of enzymes is converted to urea (Hurst). In renal urea handling, urea allows the kidneys to create hypertonic urine, allowing for water that is crucial for the body to be retained, while excreting more waste in the process. In the final urine, a large amount of urea is found, allowing it to be used as an additional biomarker due to this process (Boron).

Various groups of people may experience AKI when they experience sudden failure due to injury, medication or illness. As time goes on, there will be potassium buildups to a high level in the blood– in severe cases, this leads to muscle weakness, paralysis and heart rhythm problems (“Acute Kidney Injury”) and hence it is important to monitor creatinine and urea levels in high-risk individuals for potential diseases such as AKI (Acute Kidney Failure) or CKD (Chronic Kidney Disease) . The sensor, acting as a continuous monitor with daily measurements, allows for patients and users to understand when critical events are occurring and to understand one’s current condition for patients to consider and choose their best options.

AKI can be detected in various ways, such as testing eGFR(estimated glomerular filtration rate, see Appendix A), BUN (Blood Urea Nitrogen), and more (“Acute Kidney Injury”).

2. Influential creatinine level factors

Creatinine is a waste product from a muscle’s metabolic process from the conversion of creatine to creatine phosphate, releasing energy. As kidneys filter creatinine out of the bloodstream, if there are issues with the kidney such as (acute) kidney failure, the amount of waste creatinine will be reduced, resulting in a measurable decrease of creatinine levels in the urine (Ronco, et al.).

Post-renal conditions also lead to influencing the creatinine levels in urine due to conditions such as bladder stones, cancer in the bladder, and more (Raup, Chang, Eswara). Additionally, various other factors in the diet can also cause a decrease in the creatinine and urea levels. For example, more fiber in the diet has been found to lower serum creatinine levels in patients with chronic kidney disease (Salmean, et al.).

3. Synopsis of Sensor

Our full sensor device is a small, rectangular design that can be mounted with two hooks onto the side of any toilet bowl, with the box hanging on the outside. On top, the box features a small hole that allows a retractable guide to enter the toilet and take any sensor readings of biomaterial that may be present. The sensor also acts as a disposal tool for water, with a tube attached to the side that allows for a water connection from any water piping, whether it be the freshwater used for the toilet, or some other water source if one is not available. Additionally, a plug is featured, allowing for the sensor’s internal battery to be charged from any power source if needed. Bluetooth is built into the device, allowing for anyone to use their phone to connect to the device, allowing for quick readings and understanding of one’s data, as well as to alleviate the amount of processing that is required by the device and to reduce costs. A small screen is available on the device for setup and to display readings if a phone cannot be used.

Figure 1, Mockup concept of the sensor (self-made)

The extension in the device that extends into the toilet features two tubes on the end and an electrode to know when the device reached the sample. Using a servo, the extension can be easily extended and retracted. Once the electrode is triggered, one tube will begin collecting the sample, bringing it to the various electrical components inside the rectangular container of the device and to be processed.

To process the sample, first the amount of sample is measured using a transducer underneath a small container inside the bigger, larger shell that encompasses the entire device. Assuming that the density is still similar to water, the volume of the water can be calculated using the bend of the transducer, which can be used to find the weight and therefore the volume. This number can be used to adjust any sensor readings to lead to an accurate measurement of the concentration of various substances in the urine sample, such as creatinine, urea, and more.

Once the mass is measured and volume is calculated, the sample is then moved to the creatinine sensor and urea sensor. The creatinine sensor is a self-powered biosensor. Using modified zinc oxide wires in a piezo-enzymatic reaction with a substance with creatinine, energy is produced in correlation to the concentration of creatinine in the substance (Wang, et al.). By measuring the magnitude of the voltage produced from the wires and comparing the volume of the urine, the concentration of the creatinine in the urine can be determined. In a study done by Northeastern University in Shenyang, China, the method of synthesizing zinc oxide nanowires through growing zinc oxide seeds and a process of annealing and immersing it in zinc acetate and zinc nitrate hexahydrate was able to successfully create the zinc oxide nanowires that could detect creatinine in sweat. Due to sweat containing unmetabolized drugs and various waste products, at times greater in concentration than urine (Chen, et al.), this therefore could in theory work similarly for urine to detect the creatinine levels in an easy, fast, and reliable way.

The urea is measured by the urea sensor via the reaction between urea and diacetyl monoxime in the presence of strong acids like sulfuric acid and phosphoric acid. A mixed acid reagent containing sulfuric acid and phosphoric acid provides the strongly acidic medium. A color reagent solution contains diacetyl monoxime, thiosemicarbazide, and ferric chloride (Langenfeld, et al.).

When the sample is mixed with these reagents and heated, diacetyl monoxime breaks down into diacetyl which condenses with urea to form a yellow diazine product. [source] Thiosemicarbazide stabilizes this diazine, which then forms a pink-colored complex. The intensity of this pink color is directly proportional to the urea concentration. By measuring the absorbance and comparing it to a calibration curve prepared with urea standards, the unknown urea concentration in the sample can be quantified over a linear range of 0.4 to 5.0 mM. In the device, to measure the urea, the urine sample will first have a small separate sample to be separated from the rest of the urine sample, then have that small sample to be diluted by 100x before the urea analysis. After, the small sample will go through the process of adding reagents stored in the device (that can also be restocked when needed) and heating. Once these measurements are made for both urea and creatinine, the data from the readings and the mass/volume is then sent to the nearby phone via Bluetooth or stored in temporary storage until a phone is connected to the device.

To complete the process, the separate urea and diacetyl monoxime solution is outputted via a separated tube to a secure waste container that can be safely disposed of instead of being flushed. The rest of the sample that was not mixed with the diacetyl monoxime is then ejected from the device via a second tube on the extension back into the toilet, then water from the outside water source is brought in to clean any remaining sample that might be still in the device, then is ejected from the device via the tubes (the water does not enter the urea measurement area does not go through this process to keep any potential residue of diacetyl monoxime from being flushed). One of the tubes also has an exit by the electrode, allowing it to rinse and clean the electrode. The extension with the tubes then retracts back into the device as it begins to heat up to remove any leftover samples via vaporization.

4. Target Implementation Setting

The proposed biosensor aims to be implemented as a commercial product for at-home use, focusing on patients who are at risk for acute kidney injury (AKI) but do not necessarily have it yet. This target audience includes individuals who may benefit from early detection and preventive measures before the onset of kidney failure.

Due to the nature of the sensor taking measurements over time, being able to have access to the device at home would allow for a continuous evaluation of one’s state and understand when there were any significant irregularities in one’s creatinine and urea levels.

5. Problem Addressed and Affected Population

5.1. Kidney Failure and Its Impact

Our biosensor can help detect kidney failure before it is clinically diagnosed, addressing a critical need for early intervention and prevention. Kidney failure, or acute kidney injury (AKI), is a significant health concern that affects various populations, including:

- Individuals aged 60 and above, who are at an increased risk due to age-related factors.
- Younger individuals who may be predisposed to kidney failure due to underlying conditions or risk factors.
- Obese individuals, as obesity is a known risk factor for kidney disease.
- Individuals with pre-existing heart disease, as cardiovascular conditions can contribute to kidney dysfunction.
- Individuals who have experienced past kidney damage or have a history of kidney-related issues.

5.2. Vulnerable Populations

Certain minority populations are disproportionately affected by kidney failure due to higher rates of risk factors such as hypertension (high blood pressure). These vulnerable groups include:

- Black or African American individuals
- Hispanic or Latino individuals

Early detection and preventive measures facilitated by our biosensor can potentially mitigate the impact of kidney failure on these vulnerable populations.

6. Business Strategy & Market Analysis

6.1 Problem Identification

We understand the problem to be one of providing a convenient and hygienic method for urine analysis at home, specifically focusing on the measurement of creatinine levels in urine. Elevated creatinine levels can indicate impaired kidney function, thus enabling early diagnosis and monitoring of kidney disease. Our team recognizes the significant health benefits and the convenience this device offers, particularly for individuals with chronic conditions such as kidney disease, as well as for those interested in general health monitoring. By facilitating regular, at-home testing, our biosensor aims to empower users to manage their health proactively and to provide critical data for healthcare providers.

6.2 Stakeholder Analysis

Consumers

The primary users of our biosensor are patients with kidney disease or those at risk of developing it, as well as health-conscious individuals interested in proactive health monitoring. By providing a user-friendly and accessible tool for regular urine analysis, we aim to empower individuals to take control of their health and facilitate early detection of kidney disease.

Healthcare Providers

Doctors and healthcare facilities play a key role in interpreting and acting on the data generated by our biosensor and using it for patient monitoring and diagnosis. By providing healthcare professionals with accurate and timely information on creatinine levels, our biosensor enables early intervention and personalized treatment plans for patients with kidney disease.

Insurers

Health insurance companies have a strong vested interest in preventive health solutions that can help reduce healthcare costs associated with chronic diseases like kidney disease. By offering a cost-effective and efficient method for kidney disease detection, our biosensor may appeal to insurers seeking to incentivize proactive health management among their policyholders.

Manufacturers

Companies involved in the production of medical devices are essential stakeholders in the manufacturing and distribution process of our biosensor. Collaborating with reputable manufacturers ensures the quality and scalability of our product, allowing us to meet the growing demand for home-based health monitoring solutions.

6.3 Market Analysis

The market for home urine analysis devices, particularly those targeting creatinine detection for kidney diagnosis, is poised for significant growth due to several converging factors. Chronic Kidney Disease (CKD) is a widespread health problem affecting around 10% of the global population, with early detection being crucial for effective management and treatment. Detection in its early stages is important, and later diagnosis can only lead to effective management and treatment. The growing prevalence of CKD — driven by such factors as aging populations, and increasing cases of diabetes and hypertension — alongside greater awareness of kidney health underscores the demand for easily accessible diagnostic tools. Economic considerations further amplify this demand. National healthcare systems worldwide have been struggling with rising costs — putting more focus on preventive care rather than expensive treatment for advanced CKD would otherwise be cost-effective, reducing the need for frequent clinical visits and enabling earlier interventions.

The transformative impact of our sensor would be most pronounced in developing countries. The healthcare systems in these regions are often characterized by instability and insecurity, rendering advanced diagnostics expensive and scarce. Our relatively portable, easy-to-use kidney failure sensor offers a practical solution in this area, enabling early detection and continuous monitoring of kidney health at a fraction of the cost of traditional methods. Not only does our sensor help reduce the economic strain on overburdened healthcare systems, but it also aligns with global health initiatives aimed at quelling the inequality between access to essential medical services in underdeveloped nations. The potential market in developing countries is profuse; ample opportunities for the adoption of our sensor are provided by the constant need for affordable healthcare solutions.

7. Appendix A: eGFR

eGFR (estimated glomerular filtration rate) is a measure of how well the kidneys are working. eGFR is an estimated number based on the blood test and your age, gender, and body type. Glomeruli in the kidneys function as the filters to remove toxins from our body and is the measure of how much these filters can clean based on the size of your body. Those with kidney disease filter less blood, and toxins build up in the blood. Normal eGFR range taking into account the age, in general, is shown below.

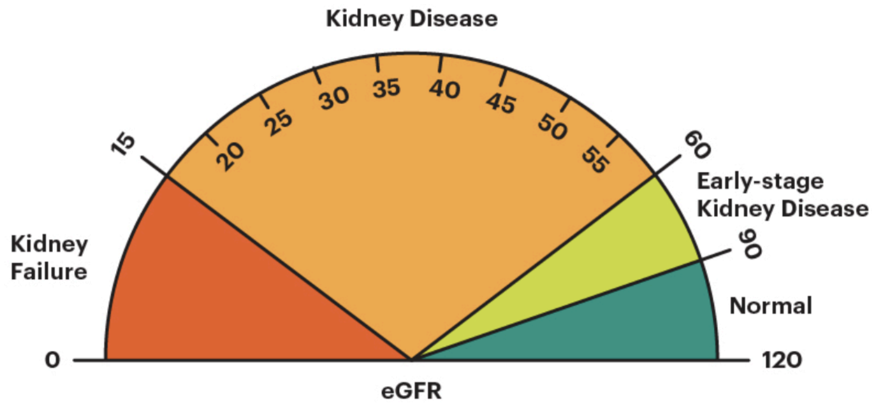

Figure 2, normal creatinine levels (credit to National Kidney Foundation, "Estimated Glomerular Filtration Rate")

8. Works Cited

Jones, C., McQuillan, G., Kusek, J., Eberhardt, M., Herman, W., Coresh, J., … Agodoa, L. (1998). Serum creatinine levels in the US population: Third National Health and Nutrition Examination Survey. American Journal of Kidney Diseases, 32(6), 992–999. doi:10.1016/s0272-6386(98)70074-5

Verhave, J. C., Fesler, P., Ribstein, J., du Cailar, G., & Mimran, A. (2005). Estimation of Renal Function in Subjects With Normal Serum Creatinine Levels: Influence of Age and Body Mass Index. American Journal of Kidney Diseases, 46(2), 233–241. doi:10.1053/j.ajkd.2005.05.011

Boron, Walter. "Medical Physiology: A Cellular And Molecular Approach." *Elsevier/Saunders*. ISBN 1-4160-2328-3. Page 791

Ronco, Claudio et al. “Acute kidney injury.” Lancet (London, England) vol. 394,10212 (2019): 1949-1964. doi:10.1016/S0140-6736(19)32563-2

Raup, V.T., Chang, S.L. and Eswara, J.R. (2018) ‘Post-renal acute kidney injury: Epidemiology, presentation, pathophysiology, diagnosis, and management’, Core Concepts in Acute Kidney Injury, pp. 247–256. doi:10.1007/978-1-4939-8628-6_16.

Salmean, Y. A., Segal, M. S., Langkamp-Henken, B., Canales, M. T., Zello, G. A., & Dahl, W. J. (2013). Foods With Added Fiber Lower Serum Creatinine Levels in Patients With Chronic Kidney Disease. Journal of Renal Nutrition, 23(2), e29–e32. doi:10.1053/j.jrn.2012.04

Chen, Yi-Lang, et al. “Comparative Study of the Composition of Sweat from Eccrine and Apocrine Sweat Glands during Exercise and in Heat.” *International Journal of Environmental Research and Public Health*, U.S. National Library of Medicine, 12 May 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7277079/.

“Creatinine Urine Test.” *Mount Sinai Health System*, www.mountsinai.org/health-library/tests/creatinine-urine-test. Accessed 24 May 2024.

“Estimated Glomerular Filtration Rate (Egfr).” *National Kidney Foundation*, 9 Apr. 2024, www.kidney.org/atoz/content/gfr.

Hurst, Anna. “Hereditary Urea Cycle Abnormality: Medlineplus Medical Encyclopedia.” *MedlinePlus*, U.S. National Library of Medicine, 31 Dec. 2023, medlineplus.gov/ency/article/000372.htm.

Langenfeld, Noah James, et al. “Colorimetric Determination of Urea Using Diacetyl Monoxime with Strong Acids.” *National Library of Medicine*, U.S. National Library of Medicine, 8 Nov. 2021, www.ncbi.nlm.nih.gov/pmc/articles/PMC8575183/.

Wang, Meng, et al. “Self-Powered Biosensor for Specifically Detecting Creatinine in Real Time Based on the Piezo-Enzymatic-Reaction Effect of Enzyme-Modified Zno Nanowires.” *MDPI*, Multidisciplinary Digital Publishing Institute, 16 Sep. 2021, www.mdpi.com/2079-6374/11/9/342.

“Acute Kidney Injury.” NHS Choices, NHS, www.nhs.uk/conditions/acute-kidney-injury/. Accessed 24 May 2024.

“Acute Kidney Injury (AKI).” *National Kidney Foundation*, www.kidney.org/atoz/content/acute-kidney-injury-aki. Accessed 24 May 2024.