PCChM Chip - Continuous Post-Chemotherapy Patient Care System

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Problem Statement: As the leading cause of death worldwide, cancer care and treatment options, particularly chemotherapy and radiation therapy, are responsible for a substantial increase in survival rates. However, while chemotherapy is effective, it has countless drawbacks from its cytotoxic effects and its cost to healthcare providers. The average chemotherapy episode lasts 6.6 months, and in developing nations where leukemia and breast cancers have 800-1000% greater mortality rates[1], access to a hospital is heavily restricted by distance. 3.16 billion people cannot access healthcare in less than 1 hour, while 618 million Africans (>50%) have to make week-long trips to receive care[2]. Administering the chemotherapy drugs only makes up a small part of this episode. More than 80% of these chemotherapy visits and encounters are part of outpatient or "ambulatory" care which involves following up with patients to monitor their symptoms. Thus, the majority of hospital resources and costs go into outpatient care which is 53% greater than normal physician visits[3]. However, the latter are readily inaccessible across the globe. This greatly exacerbates this decrease in cancer survival rates given the poor quality and access to reliable chemotherapy outpatient care. Early detection, timely treatment, access to innovative therapies, and supportive care services play a crucial role in improving survival rates and the overall quality of life for cancer patients.

Background: Chemotherapy is dangerous as it uses toxicity to kill circulating cancer cells, but in doing so harms blood cells and bone marrow. Low blood cell counts pose various risks: low white blood cells and neutrophils increase infection risk, especially in poorer countries; mild infections can severely impact cancer patients. Anemia, indicated by low red blood cells, leads to fatigue, and breathlessness, and may disrupt cancer treatment. Platelet deficiencies cause bleeding susceptibility, affecting treatment and necessitating transfusions to mitigate risks, particularly from small cuts in areas like the nose or gums. The prevalent acute toxicities in chemotherapy encompass myelosuppression, neutropenia, hyperbilirubinemia, and alopecia, accompanied by physiological effects such as nausea, vomiting, fatigue, and heightened vulnerability to minor infections. Up to 87% of patients who undergo chemotherapy experience at least one significant adverse effect during or after their treatment, either due to dose regulation or a general weakening in the immune system[4]. Induced blood toxicities were found in up to 38.9% of patients with grade 1 cancers in their first round of chemotherapy, indicating the importance of continuous patient monitoring to manage potential treatments and side effects. Monitoring patients is essential for managing potentially fatal side effects during chemotherapy, preventing delays in administering these life-saving drugs, and reducing downstream costs for healthcare providers. According to a pilot program run at Memorial Sloan Kettering, pro-active outpatient care had up to a 30% enhancement in quality of life for patients with chemotherapy[5]. Delays in receiving chemotherapy treatment hinder the achievement of ideal health results and pose risks to patients, including missed medication schedules, inadequate disease management, and, in severe cases, mortality. Due to improper dosing regimens and a lack of patient monitoring tools, some patients with depleted blood cell counts may undergo rounds of chemotherapy that can be fatal. Conversely, increased chemotherapy episode lengths can increase the risk of patient mortality. A study of 7190 leukemia patients found that over 1800 of those patients experienced neutropenia, of which patients had a 7.52x greater chance of mortality after the first month of infection. It found that patients have a significantly elevated risk of mortality up to 6 months following a neutropenia-related infection, indicating that patients have to be monitored longer than previously expected, leading the total chemotherapy patient care episode to be around 12 months[6].

Standard of Care: Physicians monitor chemotherapy-related cytotoxicities through a complete blood count (CBC) test. This test quantifies the total red blood cell and platelet count in a sample and performs a 5-way white blood cell (WBC) differential test to get lymphocyte, granulocyte (neutrophil, eosinophil, basophil), and monocyte counts[7]. This involves taking a blood sample from a patient intravenously, performing a blood smear, and running the sample through a flow cytometry system or imaging the sample after prepping a stain to get a cell count[8]. These traditional systems are not only time-consuming, but the instruments required are large and expensive ($USD 100k) and are not scalable. Furthermore, having to visit a clinic to perform a CBC in almost all cases at a frequency that can accurately track blood composition changes is simply not an option for many people – tests that can take weeks to produce results that can produce unreliable results due to low neutrophil half-lives. Upon test results, physicians can provide improved dosing schedules and prescribe different drugs to alleviate any chemotherapy-related symptoms. While there are a handful of treatments available, genetic variation across cancer patients leads to different responses to post-chemotherapy drugs. Currently, this valuable chemotherapy-induced patient toxicity data and the frequency of CBCs relative to the ailments are collected only from clinical trials concerned with approving new treatments[9]. Existing cytotoxic drugs have limited efficacy, reducing potential market opportunities for drug manufacturers. Preclinical studies rely on self-reported toxicity data, which differs significantly from real-world patient experiences. Trial participants often differ from real-world cancer patients in health status and outcomes due to diverse complications, cancer types, care standards, and socioeconomic disparities. Observational studies on chemotherapy-induced toxicity, particularly in breast cancer patients, are lacking. Better methods to monitor and share critical patient data can help provide novel therapies and identify new markets to distribute optimized, efficacious therapies for dealing with chemotherapy-related issues, thereby significantly improving and unburdening healthcare infrastructure at scale.

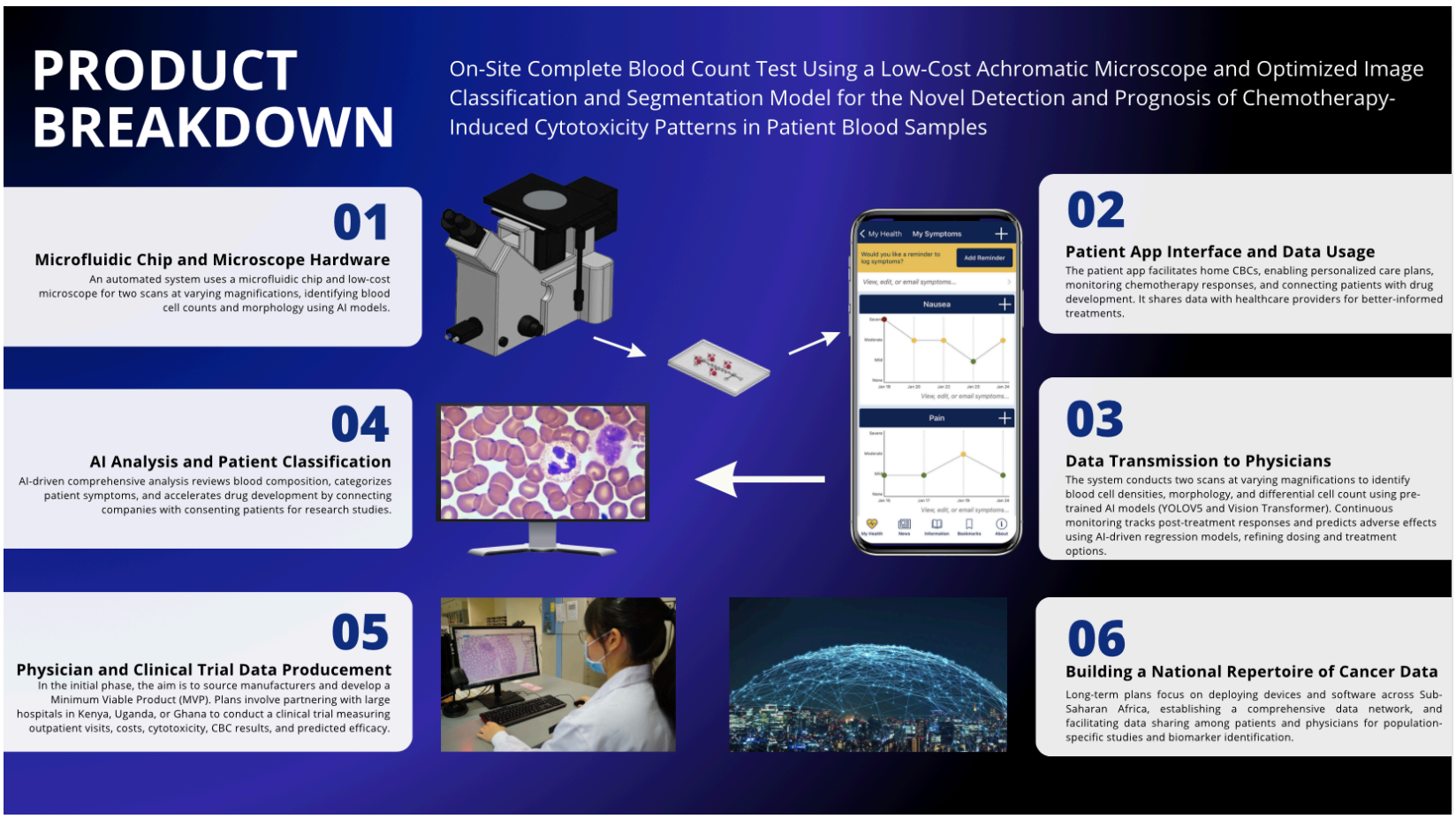
Solution: Thus, there is a significant demand for a low-cost, at-home routine remote monitoring device capable of producing an accurate CBC count that is affordable on a per-test basis and integrating with physician workflows in developing regions where cancer mortality rates are increasing dramatically. Our proposal is a continuous CBC count monitoring device that consists of a

microfluidic chip that collects and automatically prepares a patient blood sample and a cheap microscopic device that captures blood smears. Using a ViT (Vision Transformer) and other machine learning models, physicians and patients receive high-quality WBC 3-differential (lymphocytes, granulocytes and monocytes), RBC, and platelet counts and greater-detail morphological data on specific cells that can offer unique insights on the progression of potential infections, the efficacy of chemotherapy treatments, and other cytotoxic-related complications at a greater resolution.

Landscape Analysis: Remote Patient Monitoring (RPM) in cancer care is multifaceted and complex. The protocols vary significantly based on cancer type and stage, leading to different technologies, workflows, and patient experiences. However, remote Patient Monitoring protocols have demonstrated success in managing various chronic diseases such as diabetes, heart failure, chronic wounds, and pulmonary diseases. The applicability and effectiveness of RPM in these areas have laid the groundwork for its integration into cancer care. Despite the proven effectiveness of RPM, its widespread adoption is hindered by challenges. Clinicians often lack real-time access to crucial patient health data. This lag in information impedes the ability to provide timely interventions and optimize patient care[10]. Effective solutions to the creation of remote patient monitoring would be able to comprehensively monitor risk factors across blood samples and create centralized data solutions for the development of proactive care systems.

In the evolving landscape of healthcare technology, the focus on Remote Patient Monitoring (RPM) for post-chemotherapy and post-radiation therapy care remains a niche area with limited attention from companies. One notable player in this space is Athelas, a company established in 2016, which has introduced the "Athelas Home" device. This device, designed to monitor chronic conditions and post-chemotherapy care, provides a comprehensive view through total White Blood Cell count and Neutrophil percentage metrics[11]. While Athelas's product is noteworthy for its relevance to patient care, it primarily concentrates on these specific metrics, lacking a broader scope that covers multiple cell counts. In addition to this, Athelas' can be very costly, up to 20 dollars/month to use, and has lackluster insurance coverage across their target market, which simply is not pragmatic for under resourced individuals.

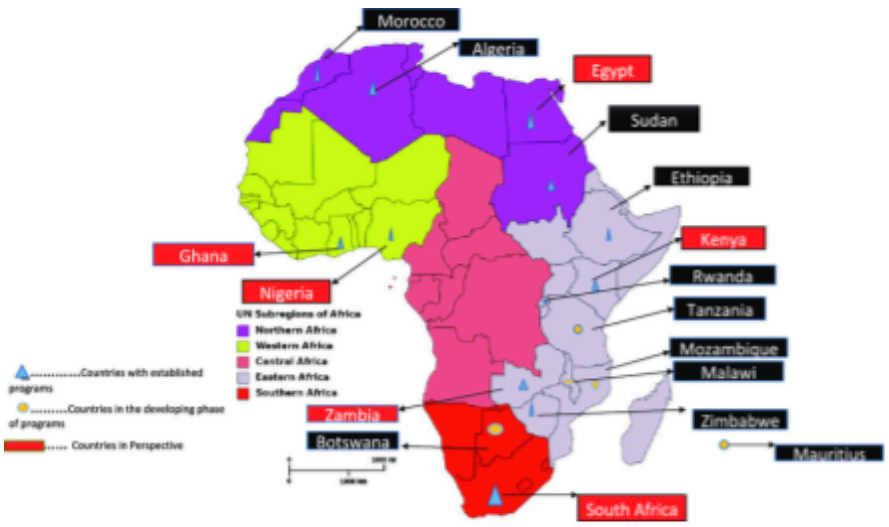
Another noteworthy player is CareVive, headquartered in Boston, Massachusetts, with a distinct focus on oncology. However, the company's remote monitoring system relies heavily on patient-reported data. This heavy reliance on subjective information raises concerns about confidence in treatment plans, given potential variations in patient perceptions, the risk of incomplete reporting, and the absence of medical expertise in self-reporting. The prevalent use of self-reporting as the standard for monitoring post-therapy symptoms underscores the urgent need for more quantitative, clinical solutions in the realm of remote monitoring for post-chemotherapy care[12]. The current industry landscape reveals an absence of comprehensive aggregation of post-chemotherapy patient data, impeding a holistic understanding of long-term outcomes. The establishment of a centralized repository is imperative to facilitate analyses, identify patterns, and inform evidence-based interventions. Companies, such as Chicago-based Tempus and IBM Watson Health use computational solutions, but there is a lack of data aggregation for widespread use in research and patient care development.



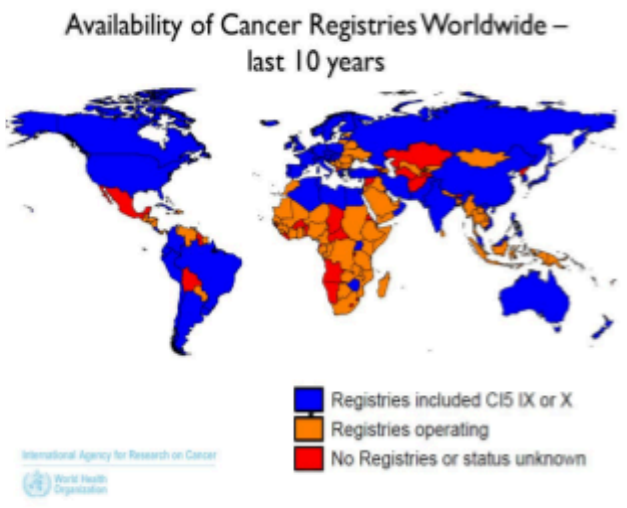
Product Breakdown:
The proposed device is an automated, portable system for performing a CBC at a patient's home, reducing the burden on hospitals and patients. Centered around a microfluidic chip, it disperses blood to create a monolayer scanned by a low-cost microscopic device. The initial scan at 10x - 20x magnification identifies red and white blood cell densities, erythrocyte counts, color, and rough morphology using a pre-trained YOLOV5 model. A Vision Transformer model is then trained for classification and differentiation. The second scan at 60x - 100x magnification analyzes differential cell count, morphology, and the presence of parasites. This comprehensive data analysis allows for a review of the patient's blood composition, guiding adjustments to their care. The proposed data use has three aspects: powering pre-treatment analyses for personalized care plans, understanding patient response to chemo doses to predict adverse effects, and matching patients with drug development companies for accelerated clinical trials. Performing home CBCs facilitates continuous monitoring before and after treatment. Monitoring before dosing establishes baseline blood composition and identifies morphological areas of interest. This data informs personalized dose recommendations and is shared with healthcare providers.

Post-treatment monitoring tracks patient response and identifies potential adverse effects. Predicting these effects allows for preemptive treatment options. Predicting these effects using linear regression models allows for preemptive treatment options. Ideally, training a model to recognize patterns in patient responses given baseline conditions would further refine dosing and treatment options. Categorizing patients based on symptoms is crucial, especially in developing countries with limited tracking of patient responses to treatment. The device provides a method for data collection and analysis, building a repertoire of patients and their responses. The data also facilitates matching companies to consent patients with specific conditions for research studies, addressing the disconnect between self-reported and clinically assessed toxicity readings in clinical trials. This approach accelerates the drug development process, allowing companies to efficiently connect with patients, providing them with a voice in pharmaceutical design phases.

Implementation Roadmap: In the 1st year, we hope to first source potential manufacturers for lenses, custom silicon chip and microfluidic fabrication, and lancets to develop a usable MVP. Under CPT Code 85025, the medical device itself can be insured by the hospital, and through our technical innovations in AI-powered image diagnostics and predictive modeling, we hope to eliminate 70% of the cost so patients have to pay just $0.31/test while reaching an estimated 1% CV (from current benchmark models in hematology classification and segmentation models beat existing 5% CV standard) and reduce the total number of parts in the microscope from 110 to just over 50. After developing an MVP, we hope to partner with one of the large public hospitals in Kenya, Uganda, or Ghana (size should fit Mulago International Hospital) given their large patient influx and poor-quality outpatient standards to launch a clinical trial (blind, 50 participants). In the trial, we hope to measure total outpatient visits, costs per patient, mean deviation from baseline cytotoxicity, normalized CBC results, and efficacy of predicted results. After a 2-month trial, we can submit our 510(k) clearance to demonstrate efficacy. The primary challenges we will face in this process will involve building on-ground partners that can help us navigate the African hospital network and the legalities surrounding patient clearance, trial monitoring, and recruitment.



De Villiers et al: Map of African Countries with Established Oncology Practices and Training for Potential Clinical Trial and MVP Deployment Scouting



WHO: Availability and Quality of Cancer Registries Worldwide in 10 Years 2019

The costs associated with trial management, paying nurses, and collecting/aggregating data will be $13k (non-invasive, software solution)[13] which we hope to subsidize with funding from local NGOs or institutional support (Mercatus Ventures, Berkeley Public Health Department, etc). We hope to identify well-trained nurses, support staff, and representative trial patients by partnering with department heads and physicians who can provide referrals and their patient and nurse recommendations.

Our long-term plan is to use our medical device and software platform that allows physicians to monitor their patients to build a national repertoire of cancer data. The quality of care in rural developing countries and the advent of population-dependent

interventions is limited due to the lack of data surrounding demographic factors for potential drug trial recruitment, direct patient care, and educational systems. Across all of Sub-Saharan Africa (SSA), registries that should contain epidemiological or clinical data are non-existent. Our team will spend the latter half of the year building this data network framework after consulting with DS-I, the Fogarty Institute, and local healthcare providers and insurance companies to build the software system for reporting patient data. We can then deploy our solution directly in one large hospital network, and by the end of the year, we hope to deploy in the 3 largest public health hospitals in SSA to allow more than 500k cancer patients and physicians to share their chemotherapy outpatient data. Over the year, we hope to build the relevant infrastructure and high-quality patient data repertoire required to attract greater interest and substantive evidence to design life-saving population-specific studies that will focus on identifying subregion-specific biomarkers that may be relevant clinically. We're aiming to have 500k data entries in our repertoire which would be more than enough to help run a single population study through our service.

Team Bios and Background

Sanjay Amirthraj is a first-year student majoring in Bioengineering and Electrical Engineering/Computer Science. With experience as a Research Lead of the Sathasivan Lab at the University of Texas, he has comprehensive experience in team management and bioengineered product development. As a member of the Huffman lab at Texas State University and the Hollenbeck lab at Indiana University, Sanjay has worked on novel drug discovery and bioinformatics research.

Shaun Liechty is a first-year student studying the joint Bioengineering and Material Science Major at the University of California, Berkeley. Shaun has extensive experience working in the field of Molecular and Protein Dynamics, where his research has led him to compete at multiple national and international competitions such as ISEF. Shaun is also actively conducting leading research in the field of microfluidics fabrication for various biological applications under UC Berkeley's Bioengineering Department.

Dev Patel is a first-year student in the College of Engineering studying Bioengineering and Electrical Engineering/Computer Science. As a Machine Learning engineer for the University of Toronto's DNA Diagnostics Lab, Dev has experience with designing and deploying disease diagnostic and monitoring solutions that leverage AI that are internationally recognized by iGEM. He has also spent time working at various startups in the world of clinical trial design, automation, and recruitment. As a member of UC Berkeley's Health Engine, Dev works with early-stage startups to help plug them into a community of mentors, investors, and students to grow their businesses.

References:

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2) Global maps of travel time to healthcare facilities

3) Total Cost of Cancer Care by Site of Service: Physician Office vs Outpatient Hospital

4) Incidence and severity of self-reported chemotherapy side effects in routine care: A prospective cohort study

5) Using Remote Monitoring to Reduce Hospital Visits for Cancer Patients

6) Risk of mortality in patients with cancer who experience febrile neutropenia

7) Complete Blood Count (CBC)

8) White blood cell detection, classification and analysis using phase imaging with computational specificity (PICS)

9) Chemotherapy-Induced Toxicities and Their Associations with Clinical and Non-Clinical Factors among Breast Cancer Patients in Vietnam
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12) Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial
13) Medical Device Academy - How much does a 510k cost