

Medical

OUR PRODUCT DEVELOPMENT SERVICES:



Brainstorming and
Concept Generation



Feasibility Studies and
System Architecture



Detailed Product Design



Prototyping



Design for Manufacturing (DFM)



Verification Testing



Manufacturing Assembly
and Test Equipment



Sustaining Engineering

CYTOMETRIC SEPSIS DIAGNOSTIC SYSTEM

CLIENT

Medical device startup

OBJECTIVES

- Develop a cytometry system and disposable cartridge for clinical data gathering
- Achieve a rapid sepsis diagnostic score rate—from sample to score in five minutes
- Complete design of the disposable cartridge assembly and transfer to manufacturer

APPROACH

- Performed story mapping with client stakeholders to determine key requirements and workflow
- Created a multidisciplinary team to allow for close communications with client and subcontractors
- Produced integrated prototypes

RESULTS

- Delivered cytometry system and associated disposables that were ready for clinical trials within the client's 18-month timeframe
- Designed a complete product that produces repeatable results for clinical data gathering
- Achieved rapid sepsis diagnostic score rate—from sample to score in five minutes
- Designed precision pressure, dynamic temperature control, and submicron motion system
- Completed regulatory manufacturing documentation
- Facilitated design transfer to manufacturer for production of verification units and the disposable cartridge assembly

LIFE-SAVING POTENTIAL

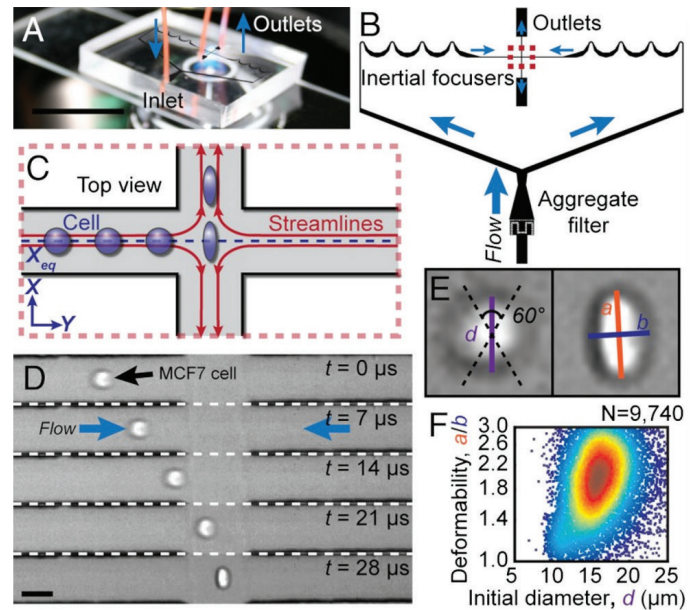
Sepsis, a potentially life-threatening condition that occurs when the body's extreme response to an infection damages its own tissues,¹ is the leading cause of death in US hospitals. More than 1.7 million adults in the US are diagnosed with sepsis each year, and nearly 270,000 Americans die as a result of sepsis annually.²

There is currently no single diagnostic test to confirm sepsis; instead, a diagnosis is based on evidence of an infection and organ dysfunction.³ Unfortunately, sepsis can be difficult to diagnose in its early (and most treatable) stages because many of the symptoms of sepsis are also common with other conditions.⁴ Time is critical in the outcome for patients who are diagnosed with sepsis because every hour that treatment is delayed increases mortality by as much as eight percent. As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment.⁵ A faster method of sepsis detection therefore has the potential to save 216,000 lives each year in the US alone.

COMPLEX PROBLEMS

Our client developed a novel microfluidic assay to diagnose sepsis in patients by observing whether and to what extent single white blood cells deform when subjected to hydrodynamic forces. A healthy white blood cell will stay round under pressure, but a white blood cell from a patient with sepsis will deform and elongate as much as 10 times its original length. The client's technique involves using a high-speed camera running at over 500,000 frames per second to capture images of white blood cells as they are exposed to hydrodynamic forces, then analyzing those images with a proprietary algorithm to determine the likelihood that the cells are from a septic patient.

The client wanted an engineering partner to help them turn their proof-of-concept prototypes into a medical device and associated disposables. The goal was to create a device and disposables that were ready for clinical trials while considering the cost, manufacturability, and usability required for such a medical device. Building their own engineering team was outside of the client's business model, so they chose to



partner with ALTEN Technology to leverage our robust [quality management system \(QMS\)](#), our mature [product development process](#), and our experience developing [medical devices](#).

PROJECT APPROACH

Because this was a complex project, we began with a phase 0 story mapping exercise. Our engineers sat down with our client's project stakeholders to map out features of the system, including functional blocks of the system and workflows, and identify the work required to address the client's needs. This process reduces the client's risk in working with us because there is a clear map of what needs to be done and because the client isn't under any obligation to continue working with ALTEN Technology once the phase 0 is complete. This allows the client to see if ALTEN Technology is the right fit for their project before they commit to working with us on a large and complex project.

After the phase 0, ALTEN Technology quickly expanded the project team from five people to 23 people to meet the client's aggressive timeline. The development team incorporated every discipline at ALTEN Technology, including [mechanical engineers](#), [electrical engineers](#), [software engineers](#), [systems engineers](#), project management, and quality assurance. Systems engineering and quality assurance were heavily involved with this project to manage the more than 1,000 requirements and ensure that the project conformed to

several standards, including:

- ISO 13485:2016 (Requirements for regulated medical devices)
- ISO 14971 (Risk management for medical devices)
- IEC 62304 (Medical device software life cycle processes)
- 21 CFR Part 820 (FDA regulations for medical devices)
- IEC 61010 (Safety and electromagnetic compatibility)
- [EMC] requirements for lab instruments)

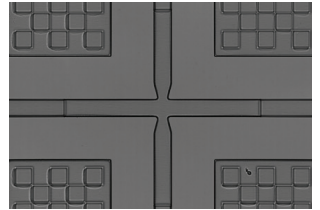
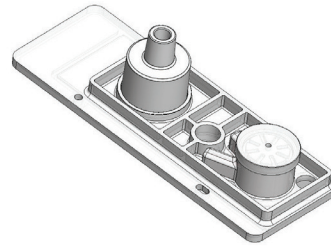
TECHNICAL CHALLENGES

This project presented several technical challenges because it required accurate and precise controls for the temperature system, the pressure controls, and the camera. What's more, the whole diagnostic process—bringing the sample to the correct temperature, focusing the camera, capturing the images of the white blood cells as they are subjected to hydrodynamic forces, processing the images with a computer vision system, and delivering a diagnostic score—needed to happen within five minutes to meet the client's target speed.

Because temperature changes the properties of the lysed blood used in the assay, the device needed precise thermal controls to bring the cartridge containing the lysed blood sample from ambient temperature to the correct temperature within 90 seconds and then hold it at that temperature for the duration of the analysis. To this end, ALTEN Technology designed and programmed a custom circulating fluid system with TEC and Peltier devices on a fluid reservoir. Once the sample is at the correct temperature, a ALTEN-designed pneumatic control system maintains the correct pressure ± 0.1 PSI and moves the sample through the cartridge.

The high-speed camera needed to be able to quickly and accurately focus on the area of the cartridge where the white blood cells would be deformed—no mean feat since white blood cells are only $10\ \mu\text{m}$ in diameter and slight temperature changes could substantially move the focus area. To address this, ALTEN Technology used a sub-micron, 3-axis motion stage to center and focus the cartridge within the high-speed camera's field

of view. ALTEN Technology also designed software to find fiducials on the cartridge to facilitate the focusing process.



RESULTS

Within an aggressive, 18-month timeline, ALTEN Technology met the client's objectives:

- Delivered cytometry system and associated disposables that were ready for clinical trials within the client's 18-month timeframe
- Achieved rapid sepsis diagnostic score—from sample to score in five minutes
- Designed precision pressure, dynamic temperature control, and sub-micron motion system
- Completed regulatory manufacturing documentation
- Facilitated design transfer to manufacturer for production of verification units and the disposable cartridge assembly

ALTEN Technology designed a cytometric sepsis diagnostic device and associated disposable cartridges that implement the client's microfluidic assay in a quick,

easy-to-operate manner. This system has the potential to change the standard of care for patients for several reasons. Its rapid results enable medical professionals to preemptively screen patients for sepsis multiple times a day. It shows a highly correlated diagnosis even before a patient displays symptoms, which could allow doctors to treat patients in the early stages of sepsis when there is a higher likelihood of positive outcomes. Furthermore, early sepsis detection could mean a reduction in the use of preventative antibiotics and immune-boosting medications. Ultimately, this device may contribute to the rapid diagnosis and treatment required to save as many as 216,000 lives annually in the US alone.

ABOUT ALTEN TECHNOLOGY

ALTEN Technology is an engineering consulting company that provides innovative solutions for engineering, technology, and product development projects across the product life cycle. For decades, ALTEN Technology has been helping clients develop products that are changing the world, whether by shaping the future of space exploration, saving lives with medical devices that set new standards of care, or creating the fully autonomous electric taxi of tomorrow. We provide support across industries including aerospace, defense, medtech and life sciences, unmanned systems and robotics, automotive OEM and tier 1 suppliers, commercial vehicles, electric vehicles, energy and environment, rail and more.

SOURCES

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