Reducing Errors and Increasing Precision over Thousands of Samples per Month

How does a medical instrument company fully automate the lab processing of medical samples and do it in a benchtop device?

From start to finish, a lab technician can process a single specimen faster than a machine. But Hologic, a global healthcare and diagnostics company, knew that its customers weren't interested in processing a single specimen – they were interested in processing dozens per hour, hundreds per day and thousands per month with full accuracy and consistency.

Building and managing a staff of human technicians that could sustain that throughput efficiently would be too costly over time. Besides, the technicians' expertise would be better applied to high-value tasks, so Hologic (and its instrument systems group, the former Gen-Probe) saw the opportunity to automate the entire workflow of specimen processing in the lab.

Hologic looked at the landscape of sample handling instruments and decided to go one better by starting from scratch.

Finding the Right Design Partner for Tomcat

In search of a design partner that could take a fresh look at this engineering problem, Hologic approached D&K Engineering. Hologic engaged D&K for an initial feasibility project that involved the automated handling of medical sample tubes. D&K was able to apply a level of expertise in robotics and motion control far beyond client expectations.

Convinced that D&K's engineering and program management were strong enough to design solutions to complex problems, Hologic engaged the firm for the main project, to include both design and manufacture of Tomcat.

The client's goal was to raise the productivity bar by developing Tomcat, a benchtop instrument that processed as many as 300 samples in an eight-hour shift. Hologic specified a machine capable of all the steps that a human would follow while processing samples:

- Picking up the customer sample via a gantry robot from the input rack and transporting it into the processing station
- Reading the barcode of the patient sample and mixing (vortexing) the customer sample tube to ensure proper aliquoting in the processing station
- Removing the cap from the patient sample tube and aliquoting from the sample with the pipettor robot arm
- Checking fluid levels in the bottle before and after dispensing to ensure the appropriate amount was aspirated
- Recapping the patient sample while picking and placing an output tube into the processing station
- Ensuring that the patient sample barcode matches that of the tube being prepared for analysis
- Uncapping the output tube
- Dispensing the patient sample into the output tube with the pipettor robot
- Checking pre- and post-dispense fluid levels in the bottle to make sure the appropriate amount was dispensed into the output tube
- Adding appropriate amount from the reagent bottle into the output tube with the pipettor arm

- Replacing the cap on the output tube
- Placing the output tube into the incubating module or into the output rack, indicating it is ready for analysis
- In case of a problem, returning the output tube to its original position next to the patient sample in the input rack .
- Returning the patient sample tube to its original location in the input rack
- Racking completed samples for molecular testing
- Disposing of waste after each aspiration-and-dispense step
- Maintaining inventory of the remaining consumables and waste spaces
- Updating status of samples successfully processed

Of course, Tomcat would need to follow all of those steps at sustained, high rates of throughput across a variety of workflows, ensuring that all steps were properly taken.

It is easy for a lab technician to see whether there is fluid in the tube and whether a sample was properly mixed, but more difficult to repeat the steps precisely over thousands of samples. Tomcat needed to verify that the same amount of patient sample is collected each time, saving the remainder for further testing. It was also necessary for Tomcat to ensure use of the correct reagent in the appropriate amount, without loss.

It was up to D&K to design and prototype the most efficient version of Tomcat possible.

Applying 4 Phases of Product Development

The project underwent the four phases governing all of D&K's electromechanical design work.

Phase 1: Program Planning, Functional Decomposition and Architecture

Hologic presented D&K with a system architecture and a product requirements document for Tomcat that described the most important characteristics of the instrument. The system architecture described the types of modules needed and the workflow to be used for aliquoting from the patient's sample:

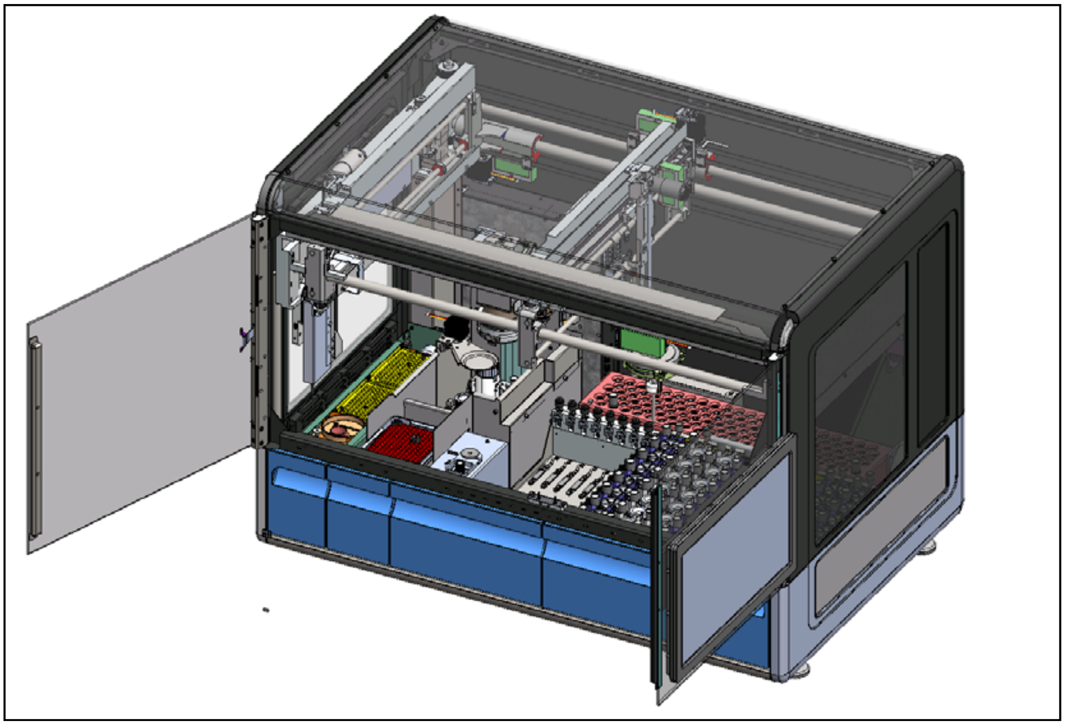
- Which subsystems it would include
- Which workflows it would execute with different tubes and analysis methods
- How lab technicians would operate and, when necessary, pause it
- How it would match input and output tubes
- How it would recover from errors and maintain a log
- How many samples it could handle in given scenarios and workflows
- How it would manage inventory

D&K began by breaking down the product requirements into subsystem specifications and by evaluating architectural elements:

- Electrical topology – How would Tomcat control 12 different types of motors? What type of communication would it use to operate them all in concert and at appropriate speeds? What would the external interface look like? What type of data should the instrument collect?
- Mechanical architecture – Which paths would the robot arm follow while carrying tubes around inside the instrument? Which paths would the other robot arm follow to transfer fluid without risking contamination? Which technologies were best for motion in each of the three axes? Which would occupy the least space?

- Software architecture – What type of communication was best at the level of the motors? How much control should Tomcat exercise at the master level and at each of the motor nodes? Which software tool sets were best for the real-time operating system (RTOS), OS, database and Component Object Models (COM)?
- Mechanical handling – What was the most reliable way of gripping, transporting, vortexing and capping/uncapping the tubes?

Phase 1 lasted six months, by which time D&K had developed a complete CAD model of the instrument with all modules, defined the complete electrical topology and developed high-level master controller software and low-level firmware infrastructure in an RTOS environment. The phase gate presentation to the client demonstrated that all components were sufficiently developed for detail design to begin.



Tomcat (CAD rendering)

Phase 2: Development – Design and Engineering Prototypes

In phase 2, D&K detailed and procured all the subsystems for initial engineering prototypes. They calculated tolerances, analyzed risks, conducted paper studies on worst case scenarios and estimated the cost of components sourced off the shelf or custom-built.

D&K spent six months arriving at a design that balanced all of the electrical and mechanical systems in Tomcat – robots, fluid transfer, motors, controls, touchscreen PC, airflow and hot plate for incubation. The resulting instrument had to fit Hologic's requirements for size, throughput and capacity. In the many iterations of proposed layout, Tomcat's size increased slightly.

The need for rigorous program management was acute during this phase as some modules in Tomcat were ready for sign-off and release before others. For example, while the plastic enclosure was relatively simple in design, the X-Y-Z-axis robotic system had to move at 150mm per second to ±.5mm accuracy over 600mm, which required much more engineering and testing time.

During this phase, a number of design and architecture problems arose that D&K had to overcome:

- The original 10mm shafts did not afford the desired motion control, performance and reliability, so D&K increased their diameter to 14mm.
- There was very little clearance for replacing tubes into their predefined racks, requiring special algorithms.
- Tubes needed to remain firmly in the vortexor in spite of more than 30g acceleration during mixing.
- The racks needed to hold multiple tubes in tight geometry, yet the gripper needed to be able to access every tube in every rack precisely.

Phase 3: Design Verification

D&K built another round of machines based on lessons learned in phase 2, redesigning the system to achieve reliability of 1 million tubes processed.

Having created customer demand for Tomcat by now, Hologic asked for ways to shorten the schedule, so D&K eliminated one of several design-build-fix iterations. That saved time, but it resulted in the need to build pre-production instruments during phase 4 based on the verification and validation (V&V) of phase 3 instruments.

Phase 4: Product and Manufacturing Process Validation

In phase 4, D&K built preproduction instruments under change management and production controls, revising manufacturing processes to get production started.

During testing, they discovered problems in handling a tube type that was not designed for automation, which required that they implement major design improvements to make Tomcat more reliable.

Finally, the pre-production instruments went to Hologic and its customers to execute validation protocols and collect feedback on machine performance.

Lean Product Realization Process (L-PRP)

All phases of the Tomcat project included L-PRP's highly structured set of milestones and deliverables across three areas:

- Program management – managing the people, processes, tools and infrastructure of the overall project
- Product design – creating a design that conforms to product requirements
- Manufacturing process development – putting everything in place for the eventual handoff to manufacturing

Tomcat moved from one phase to the next only after passing a strict phase gate review, in which program management, quality, R&D and manufacturing development assessed project status and demonstrated that design and performance were stable enough to meet requirements.

> *"We had customers ready for Tomcat, so we didn't want last-minute design changes to keep us from going to market. D&K was very strict in its phased approach to designing Tomcat. Most design houses have a product development process with a few phases, but D&K's phases, evaluations and gate reviews really have teeth. That rigor, combined with their ability to solve tough problems and their in-house manufacturing capacity, convinced us that we could entrust both the design and build of Tomcat to them."*
>
> Rolf Silbert, Systems Engineer, Hologic Inc.

The result: Tomcat

By the end of phase 4, Tomcat was ready for manufacture. It successfully combined several electromechanical systems, each of which represented months of design and engineering work:

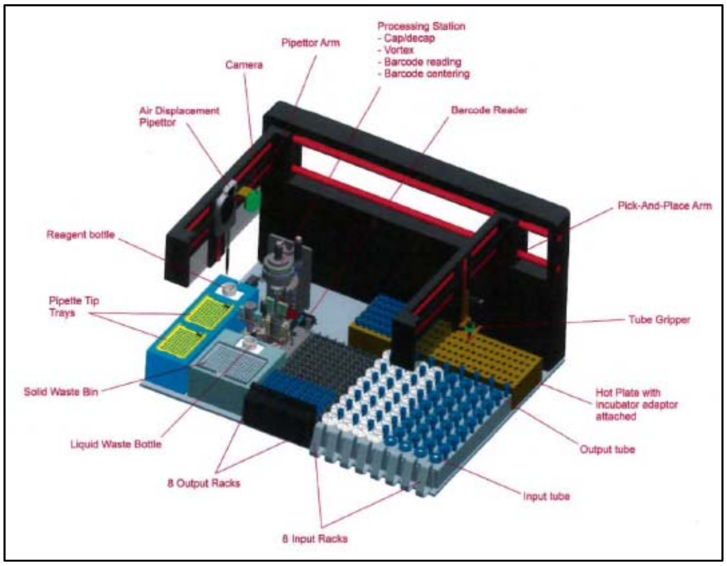
- Robotics – Two gantry-style robots with four degrees of freedom perform pick-and-place, pipetting and removal of consumables and waste. A three-point, field-replaceable gripper holds tubes during pick-and-place.
- Vortexing – A planetary gear system mixes samples and reagents in a cradle that accommodates different workflows and tube sizes.
- Manipulation – A robot removes and replaces caps on input and output tubes.
- Fluid amount verification – The pipettor arm withdraws the sample or reagent. Corresponding controls verify that the pipettor has withdrawn the prescribed amount of fluid from input and deposited the same amount to output.
- Process controls – Sensors verify fluid levels and control incubation temperatures. Firmware algorithms verify the presence or absence of caps and tubes.
- Flexible workflow – Operators have easy, continuous access to samples, consumables and waste. When the waste tray is full, Tomcat ejects it for emptying.
- Touchscreen interface – A mini-ITX computer running an embedded operating system drives a touchscreen UI. The computer is connected over a CAM bus and Ethernet to real-time controllers on all motors.
- Compact footprint – D&K integrated multiple subsystems into a small workspace with two robots working in concert. Most instruments in the category of Tomcat are considerably larger.

Tomcat spends approximately one minute processing each sample. This is on par with a human lab technician's processing time, but Tomcat can sustain the pace over an entire workday, week or month of operation.

Benefits of Tomcat

Hologic touts several important benefits of Tomcat:

- Error-free operation of sample handling process, every time
- Standardization of the aliquoting process, such that each amount aspirated and dispensed is consistent
- Greater confidence in chain of custody of samples
- Control measures to lower the risk of cross-contamination
- Reliability in handling samples over a long service lifetime



"Our customers are enjoying improved lab throughput with Tomcat," says Rolf Silbert, systems engineer with Hologic. "Automated sample processing frees up lab technicians for tasks that can generate more revenue. D&K has helped us both design and manufacture high functionality like robotics and fluid amount verification into a small but astonishingly capable medical instrument."