Multi-function Automatic Analyzer for Better Local Healthcare amid Changing Environment for Clinical Testing

At the same time as the changing environment for clinical testing over recent years is bringing greater diversity to the working practices of laboratory technicians and a rapid expansion in the scope of the testing they are called upon to perform, they are also being asked to further improve the quality of medical testing. To meet this challenge, Hitachi High-Tech Corporation supplies the Hitachi Automatic Analyzer 3500. The 3500 combines the features needed to conduct a range of different types of testing on the same analyzer, augmenting the functions of a conventional automatic clinical analyzer with a scattered-light photometer for immunoassay and a coagulation unit for blood coagulation analysis. Along with boosting testing efficiency in the constrained space of a laboratory, these features are intended to facilitate integrated community healthcare that includes specialist clinics offering advanced therapies as well as other small and medium-sized medical facilities.

Hiroshi Oga
Sakuichiro Adachi
Chie Sugiyama
Megumi Takizawa

1. Introduction

Clinical testing is vital for determining people's state of health and for diagnosing illness, selecting therapies, and assessing their effectiveness. It can be broadly divided into the laboratory testing (blood, urine, stool, cells, or other material taken from the patient) and physiological function testing such as electrocardiograms or electroencephalograms (EEGs) that are conducted on the patient's body.

Laboratory testing in particular is being increasingly automated and laboratory technicians find themselves operating instruments for testing a wide variety of areas.

Meanwhile, demand for improvements to the quality of medical testing have been steadily rising over recent years, with a growing number of clinical testing laboratories having obtained certification of their quality and capabilities under the ISO 15189 international standard. New rules for ensuring the quality and accuracy of laboratory testing were also included in the 2018 revisions to Japan's Medical Care Act. Rising expectations include compliance with these international standards and laws while also managing the calibration and maintenance of a range of different testing instruments. This is imposing an increasingly heavy workload on laboratory technicians.

In terms of the overall healthcare system, a 2015 decision by the Japanese cabinet switched focus away from hospital-based and toward community-based healthcare.

The Ministry of Health, Labour and Welfare's Regional Medical Care Visions up to 2025 identifies a need to establish systems and practices that encourage the effective and efficient allocation of resources commensurate with healthcare functions and that enable patients to receive higher quality healthcare services that are suited to their circumstances and are provided at care facilities that are appropriate to their condition through the acute, recuperative, and chronic stages of their illness. There is an urgent

need to create an environment in which medical resources currently concentrated in large cities are more widely dispersed so that high-quality healthcare can be delivered close to where people live.

Recognizing these changing circumstances, Hitachi High-Tech Corporation developed the Hitachi Automatic Analyzer 3500 (hereinafter "3500") to help reduce laboratory technician workloads, facilitate the coordination of community healthcare, and enhance the quality of life (QoL) of patients and their families.

2. Multi-function Automatic Analyzer

Small and medium-sized hospitals (100 beds or less) operate a large number of different instruments in limited laboratory space staffed by only a small number of technicians. These laboratories divide up patient blood samples to perform tests on a number of different analyzers and then collate the results into a single report. A lot of time and effort is involved in conducting these many and varied tests using different testing techniques. This work also calls for stringent procedural and management practices to ensure safety, including the prevention of human error in the testing process and avoiding contact with patient samples.

If different laboratory tests were able to be processed on the same analyzer, on the other hand, it would improve the operation of clinical testing and be very helpful to medical services.

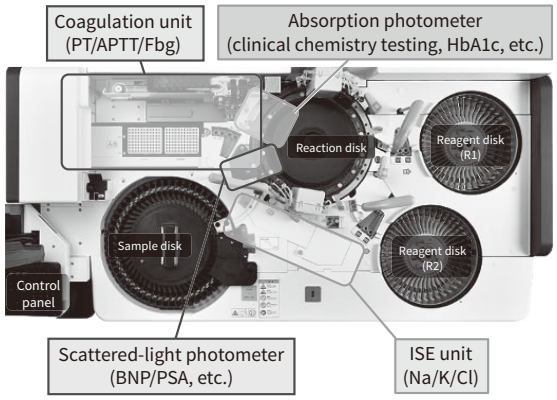
Hitachi High-Tech has led the market for large-sized automatic analyzers, in 2002 becoming the first in the industry to develop an integrated clinical chemistry and immunoassay analyzer based on a module assembly design able to combine a number of different types of instruments.

Figure 1 — Hitachi Automatic Analyzer 3500

Despite being the same size as previous models, the 3500 combines five different analysis functions, offering immunoassay and blood coagulation analysis as well clinical chemistry, ion selective electrode (ISE), and HbA1c testing. Capable of up to 1,200 tests/hour (when using the ISE), the 3500 analyzer is helping to improve workflows and the efficiency of clinical testing at small and medium-sized medical facilities.

Figure 2 — Interior View of Analysis Units

The figure shows the arrangement of analysis units. The 3500 achieves its compact size by using the main mechanisms across different types of analysis.



BNP: brain natriuretic peptide PSA: prostate-specific antigen
PT: prothrombin time APTT: activated partial thromboplastin time
Fbg: fibrinogen HbA1c: hemoglobin A1c Na: natrium K: kalium Cl: chlorine

Likewise in the market for mid-range automatic analyzers, Hitachi High-Tech expanded the range of available tests with the addition of an ion selective electrode (ISE) analysis unit in 1992 and the incorporation of a hemoglobin A1c (HbA1c) analysis function by means of an automatic hemolysis option in 2010 to meet the demand for health checks specifically targeted at metabolic syndrome.

The 3500 is a multi-function automatic analyzer that, in addition to clinical chemistry, ISE, and HbA1c testing, can also perform brain natriuretic peptide (BNP) and other immunoassays using a scattered-light photometer and blood coagulation analysis using a coagulation unit (see **Figure 1**).

By utilizing the main mechanical and electronic mechanisms for different types of analysis and only adding those additional units that are really needed, the 3500 is no larger than previous automated clinical analyzer models.

Combining a number of different testing functions in a single compact analyzer not only frees up considerable space in the laboratory, but it also enables laboratory testing to be consolidated to reduce the time and motion and data handling workloads imposed on clinical laboratory technicians (see **Figure 2**).

3. New Photometry Technique

3. 1
High-sensitivity Measurement Using Scattered-light Photometer

Hitachi High-Tech developed a scattered-light photometer for the 3500 that is capable of high-sensitivity measurement for immunoassay using a latex reagent. This immunoassay

involves an antigen-antibody reaction between the target compounds in the blood sample and antibodies coated on latex particles which are served as a reagent, thereby allowing the concentration of these compounds from the resulting change in the turbidity due to aggregate formation in the reaction mixture. Conventionally, this change in the turbidity has been measured by latex turbidimetric immunoassay, which uses an absorption photometer to measure transmitted light. To improve the sensitivity of the conventional latex turbidimetric immunoassay, however, the company instead adopted scattered-light photometry in which the background can be reduced to highlight the aggregation caused by the reaction. The optical conditions needed to achieve high measurement sensitivity were determined using techniques that included observation of the aggregates and an optical simulation that modeled the reaction mixture. This provided the basis for designing a scattered-light photometer that detects forward-scattered light from a light-emitting diode (LED) light source with a wavelength of 700 nm. The photometer is equipped with multiple optical detectors to allow its use with a wide range of reagents, thereby expanding the measurement range into lower concentrations. The measurement range was also expanded by designing the analyzer to use two different photometers to obtain measurements from the same reaction cell, using data from a scattered-light photometer for the low-concentration range and from an absorption photometer for the high-concentration range (see **Figure 3**).

3. 2
Blood Coagulation Analysis Using Coagulation Unit

Hitachi High-Tech developed a coagulation unit for the 3500 to enable blood coagulation analysis. This blood coagulation analysis involves mixing the sample with a reagent and using the change in turbidity that results from the coagulation reaction (the conversion of fibrinogen into fibrin) to measure this coagulation time. The sequence of steps is as follows.

(1) The analyzer's sample dispensing mechanism injects the sample into the reaction cuvette, and the reaction cuvette is transferred to the coagulation detector.

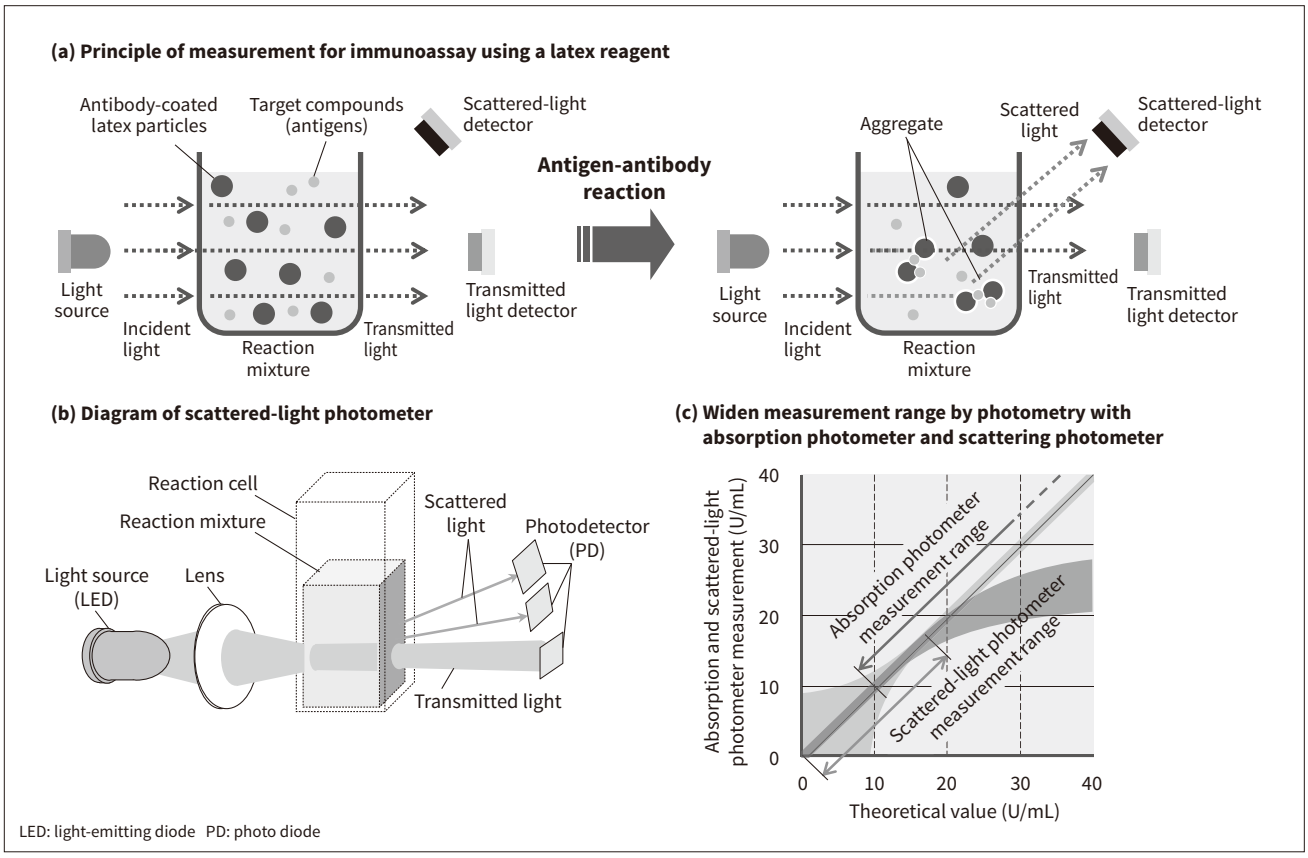
(2) The reagent pipetting mechanism dispenses the coagulation reagent with enough force to cause it to mix with the sample (dispensing stirring).

(3) The reaction mixture is heated to 37°C in the coagulation detector, and the scattered-light intensity that changes with the change in turbidity is measured at 0.1-s intervals to calculate the coagulation time. The reaction cuvette is disposed of after the measurement is complete.

The 3500 works by transferring the coagulation reagent from the reagent disk to the coagulation unit by means of a reaction cell in the reaction disk used for clinical analysis.

Figure 3 — Diagram of Benefits and Measurement Principle for Scattered-light Photometer in 3500 Analyzer

The figure shows: (a) The principle of measurement for immunoassay using a latex reagent, (b) A diagram of the scattered-light photometer, and (c) How abscatter (combination of both absorbance and scattering) expands the measurement range.



LED: light-emitting diode PD: photo diode

The coagulation unit outputs reliable coagulation time by directing 700-nm light from the LED light source from the side of the reaction cuvette and detecting the scattered light at a 90° angle (see **Figure 4**).

By incorporating these features, the 3500 has been equipped with a blood coagulation analysis function without compromising its compact size.

4. Clinical Testing Required for Community Healthcare

The preceding sections have described the technical features of the 3500. This section presents examples of how these features are helping to overcome the challenges facing customers.

4. 1
Minamino Cardiovascular Hospital (Hachioji City, Tokyo)

Minamino Cardiovascular Hospital specializes in providing advanced therapies for cardiovascular disease. Equipped with the same level of medical equipment as a general hospital, the facility delivers patient-focused care that extends from precision testing through to the provision of pharmacological treatment, catheter-based procedures, and support for preventing relapse. The hospital installed a Hitachi Automatic Analyzer 3500 in April 2018 to satisfy the need for rapid and precise patient test data.

Prior to installation of the 3500, clinical chemistry and coagulation tests were performed on separate analyzers. As the number of tests increased, this put an increasing burden on the laboratory technicians. Moreover, these simpler analyzers were unable to handle all of the hospital's testing requirements. With the installation of the 3500, however, they were able to handle both testing for lifestyle diseases and highly urgent pathology testing. In addition, the consolidation of equipment contributed to the reduction of the laboratory technician's workload.

The medical staff members are also putting their faith in the further potential of the 3500, such as providing a wider variety of tests in the future. Hitachi High-Tech will continue to work toward further operational improvements.

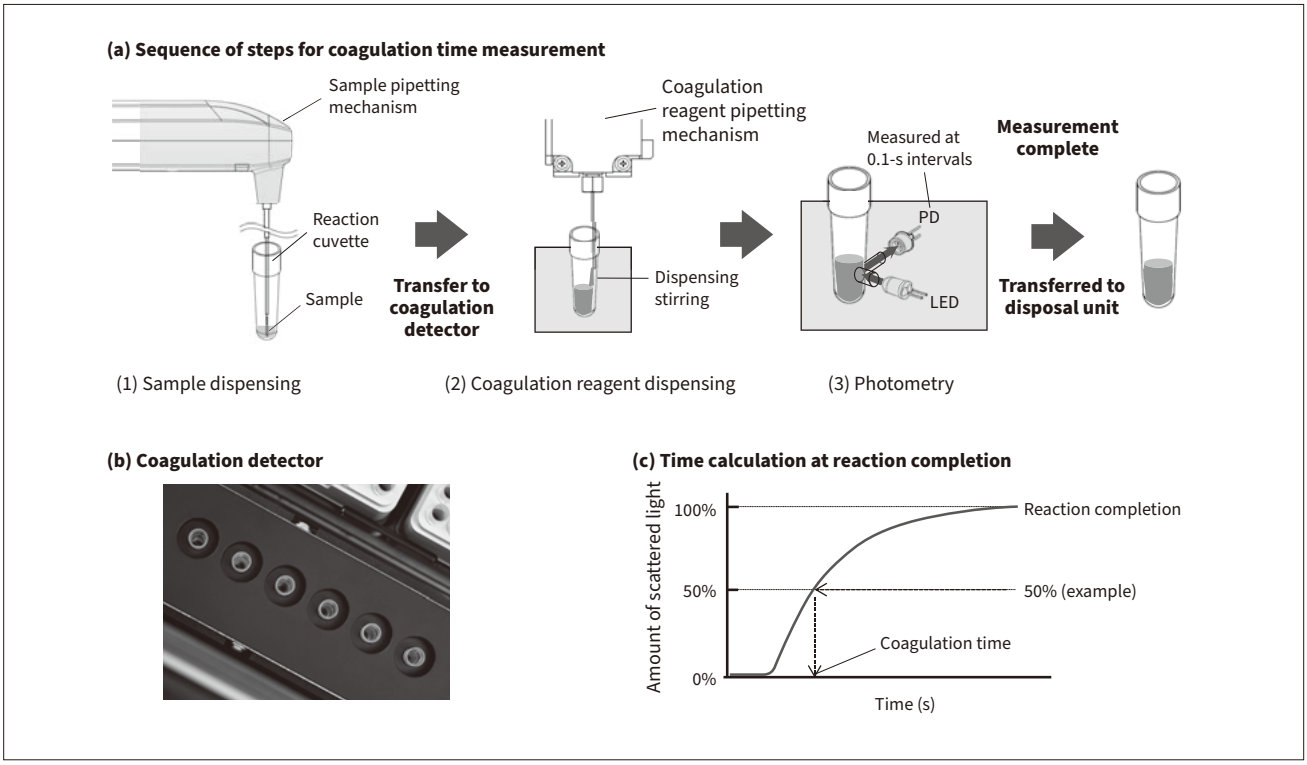
4. 2
Hematology Ohta Clinic, Shinsaibashi (Osaka)

The Hematology Ohta Clinic, Shinsaibashi specializes in blood disorders. A Hitachi Automatic Analyzer 3500 was among the original complement of equipment when the clinic opened in 2018. The flexibility to provide patients with the best possible care quickly is a key strength of the clinic, which consolidates all of the functions needed to deliver their specialist services on the same floor of the building.

Given that hematology includes chemotherapy, the availability of same-day testing is a significant benefit. The 3500

Figure 4 — Measurement Using Coagulation Unit in 3500 Analyzer

As shown in (a), the test uses a disposable reaction cuvette, with the reagent pipetting mechanism and coagulation detector raising the solution to a constant temperature of 37°C. As shown in (b), the 3500 has six measurement ports in the coagulation detector where it can place reaction cuvette for measurement. Similarly, (c) shows how the coagulation time is determined from the time it takes the scattered-light intensity to reach a certain proportion of its value at reaction completion (50% in the example shown here).



is able to perform clinical chemistry and coagulation testing at the same time, perform measurements rapidly (on the order of 10 minutes), and work through the various testing steps (including sample collection, pre-processing, testing, and data confirmation) to quickly deliver data for clinical use. These features help reduce the burden on both clinicians and patients.

Shortening the time taken for medical treatment is important for providing a healthcare environment that places a high value on patients' work and personal time. It is not uncommon for patients with blood disorders to be accompanied to the clinic by family or other support persons. This means that the prompt delivery of care acts directly to improve the QoL of both patients and those who support them.

The Hematology Ohta Clinic, Shinsaibashi has established collaborative healthcare arrangements whereby it undertakes specialist testing and treatment for blood disorders as local family doctors. As well as referring patients with special requirements such as hematopoietic stem cell transplantation or the need to be cared for in an aseptic environment to the hematology departments of major hospitals, with the clinic then handling the subsequent outpatient chemotherapy, transfusions, and so on, the clinic also contributes to community healthcare by acting as a hub for a number of medical facilities that offer different services.

5. Conclusions

While improving the QoL of patients and their families has long been an objective of the healthcare industry, how they have gone about doing this has changed to require more precise diagnosis and rapid choice of treatment. Amid intensifying competition to develop new tests and testing equipment to meet the need, the question of how new technology can help do a better job toward overcoming the challenges facing patients and medical professionals is an important one.

To create an environment in which medical resources currently concentrated in large cities are more widely dispersed, thereby allowing high-quality healthcare to be delivered close to where people live, patients need to feel confident about receiving both forms of medical services as a precondition. Along with providing access to similar levels of testing infrastructure for both large general hospitals and family doctors, Hitachi High-Tech also believes that maintaining the integrity of testing data will bolster patients' confidence in their family doctor.

If the reliability of testing data is to be further improved, there is a need to strengthen the mechanisms whereby not only patients and medical professionals but also other stakeholders such as suppliers of medical equipment and reagents are able to share testing information in real time.

Along with incorporating new technologies into medical testing equipment and establishing infrastructure for the real-time sharing and use of large quantities of testing data, Hitachi High-Tech intends to persevere with its development of systems for acquiring and identifying highly useful and reliable data for the next generation of medical practice as it strives to highlight and overcome the challenges facing integrated community healthcare.

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Authors

Hiroshi Oga
Medical Systems Design 3rd Department, Life & Medical Systems Product Division, Analytical & Medical Solution Business Group, Hitachi High-Tech Corporation. *Current work and research:* Design and development of medical systems.

Sakuichiro Adachi
Medical Systems Design 3rd Department, Life & Medical Systems Product Division, Analytical & Medical Solution Business Group, Hitachi High-Tech Corporation. *Current work and research:* Design and development of medical systems.

Chie Sugiyama
Medical Systems Design 3rd Department, Life & Medical Systems Product Division, Analytical & Medical Solution Business Group, Hitachi High-Tech Corporation. *Current work and research:* Design and development of medical systems.

Megumi Takizawa
Marketing Department, Life & Medical Systems Business Division, Analytical & Medical Solution Business Group, Hitachi High-Tech Corporation. *Current work and research:* Marketing of medical systems.