# POCT-compatible Glucose Analyzer Antsense ROSÉ
## Introduction and Application in Our Hospital

Osamu YAMADA

Our hospital introduced POCT-compatible devices for blood glucose testing in our wards and other locations for point of care testing. Additionally, we utilized a data management system to handle both device management and data management. As the use of electronic chart systems increases in medical institutions, improving the quality of blood glucose testing with points of care and applying measurement data have become important issues. By combining sophisticated measurement devices with a data management system, we succeeded in pointing the way toward one integrated solution.

## Introduction

Scientific progress in recent years has made it possible to realize amazing advances in various fields of study. From manual to automatic transmission technology in automobiles to the discovery of hitherto unknown pathogens causing disease and the future prevention based on genetic analysis. This technical progress has also extended to the field of clinical lab testing. Increased test accuracy and micro-volume quantification are obvious examples, and new testing parameters and testing methods are being developed in rapid succession. These advances are also having an effect on treatment methods and diagnosis methods, as well as point of care testing and even organizational structure. (Figure 1)

The subject of this article, "blood glucose", is one of the test parameters that has been affected. The principles of measurement for blood glucose have shifted from methods that were based on chemical properties of glucose such as the reduction method and the condensation method, to the enzyme method and the electrode method. As these methods were developed, efforts were made to improve testing precision, processing speed, and stability, and this has played a contributing role in clinical testing technology. Blood glucose measuring devices, like other lab devices, have evolved from manual operation to automated operation and have increased in general use.

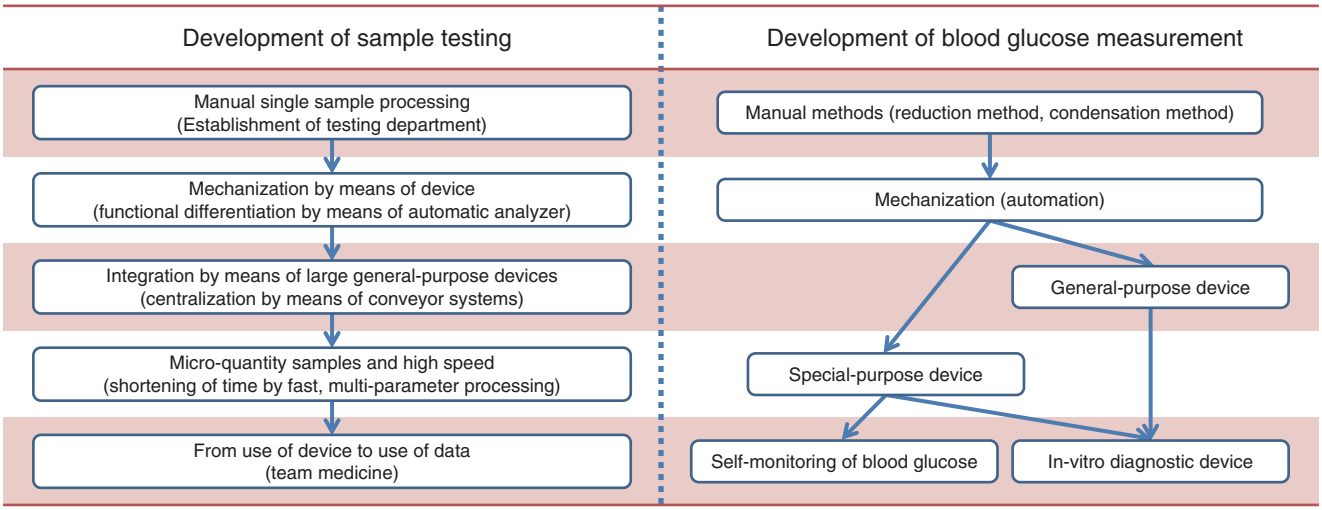


Figure 1 Development of sample testing and blood glucose measurement

Glucose is a unique assay, whether from the perspective of the properties of glucose or from the perspective of the history of diabetic disease, and glucose testing is seeing sustained and active development with specialized devices. (Figure 1)

## Blood Glucose Measurement in Routine Medical Care

Measurement of blood glucose is routinely performed in all clinical institutions, and is possible using almost any multiple assay biochemical analyzer. This assay is measured not only during routine clinic visits, but also in emergency situations and hospital outpatient visits, and it is not an exaggeration to say that it is the most commonly recognized assay of biochemical analysis. As is well known, blood glucose values are highly affected by food intake. In some cases, blood glucose is measured repeatedly throughout the day, and the observed changes in the values are used in the diagnosis of diabetes. At the same time, blood glucose is susceptible to interfering substances, and there is a need for special collection in a sample tube with NaF added. In addition the testing must be performed quickly after collecting the sample. Until recently, blood glucose was generally measured for the purpose of ascertaining the patient's nutritional status and diabetic pathology. Of course, accurately assessing the patient's condition also enabled adjustment of fluid replacement and insulin dosages, and thus was not unrelated to improved care. However, in recent years it has been reported that active management of blood glucose in ICU (Intensive Care Unit) patients and perioperative patients following cardiac or other surgery has a significant effect on patient prognosis.[1-4] (Table 1) To accomplish risk avoidance and blood glucose control in diabetic patients, the doctor must quickly and accurately ascertain the patient's blood glucose level and decide what action to take. This in turn requires that the medical staff build a testing system that enables rapid reporting of results. Analysis techniques that reduce the labor required for the sequence of tasks from sample collection to preprocessing are gaining attention and being adopted by many institutions, and this is one reason for the wide variety of devices that have appeared on the market recently.

Table 1 Risks of high blood glucose during perioperative period

- Occurrence of immunocompromised state (supportive of bacteria growth) due to high-glucose concentration in urine and sputum during immunodeficiency caused by surgical stress
- Reduction of circulating plasma volume accompanied by osmotic diuresis caused by high blood glucose (occurrence of cardiac events and encephalopathy)
- Nonketotic hyperosmolar coma (extreme dehydration)

## POCT and Self-Monitoring

In previous medical environments, it was natural for the medical staff to perform testing. The collected (drawn) sample was preprocessed and analyzed by specialists in the testing department, and the results reported to the clinician. However, in modern diabetic treatment, the administration of insulin based on self-management of blood glucose (intensive insulin therapy) has been established as an option, and patients are monitoring their own blood glucose levels on a routine basis. In addition, the Ministry of Health, Labor, and Welfare in Japan issued "Guidelines for Sample Testing Laboratories" in April 2014, and a new form of treatment appeared whereby individuals collect blood and perform measurement outside of a medical institution. This means that when we consider future clinical testing, we must distinguish who will be conducting the testing.

At the current time, clinical tests that can be performed by individuals are pregnancy testing, urine testing, and blood glucose testing. Test kits used for pregnancy testing and urine testing are classified as OTC (Over The Counter), and can be obtained at any pharmacy. Blood glucose testing is referred to as SMBG (Self-Monitoring of Blood Glucose), and guidance and management of SMBG that accompanies self-administration of insulin is covered by health insurance.

Along with the advent of self-testing, changes have also been occurring in the clinical testing performed by medical staff. These changes can be characterized as "large-scale intensive" > "satellite laboratories (distribution)" > "downsizing of test devices and function integration" > "new services (team medicine) and external expansion". Clinicians are working to improve cost performance and lifesaving rates by rapid treatment, and their testing needs are also changing. In the midst of these developments, the concept of performing immediate bedside testing and applying the results to treatment was initiated in the U.S.A. in the 1990's. This is referred to as POCT (Point of Care Testing). A feature of POCT is that all testing is managed and performed by medical staff. This testing setup can be thought of as taking advantage of the downsizing of devices and simplification of testing techniques, which have been enabled by the advance of technology, to apply clinical testing knowhow at the point of care.

Differences between the two types of testing lie in whether or not the results are immediately used for treatment. Having the advantages of rapid reporting of results and easy of use, POCT is frequently employed for

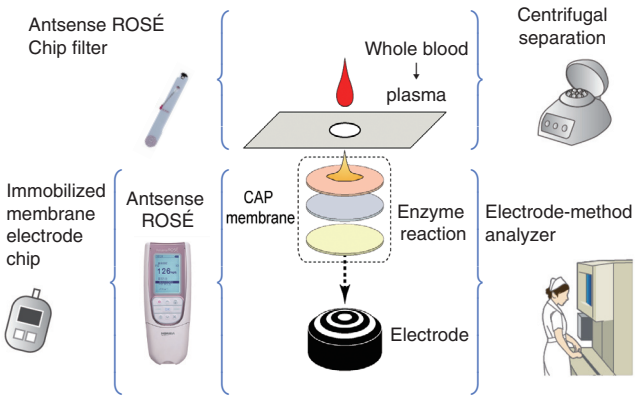


Figure 2 Differences by analyzer

Table 2 POC Coordinator Certification Units

| Division | Description |
|---|---|
| General | Definition of POCT, functions, POCT Management Committee (establishment and management), education, economy, etc. |
| Measurement technology theory | Understanding principles of measurement, reproducibility, linearity, and technical theory of interfering substances, how to read operation manuals, etc. |
| Operation technology theory | Sampling, data assurance, quality control, technical theory, standard values / abnormal values, maintenance and inspection, inventory control |
| Records/ commun ication | Deployment, system building, data recording A Coordinator Completion of Training Certificate is issued when a total of 12 units, with at least one unit in each of the above divisions, are obtained. |

diagnosis in medical settings such as emergency rooms and ICUs, where the condition of a patient can change abruptly.[5] By contrast, testing performed by the patient allows the patient to check his condition and be aware of the state of the disease, but the results are almost never directly applied to treatment. Another difference is the quality of the testing that is enabled by the involvement of medical staff. To obtain accurate results, proper testing techniques and management of devices and reagents are necessary, and specialized knowledge is indispensible. (Figure 2) Even more important is correct sample collection and evaluation of results. As pointed out by Yamazaki, the composition of blood varies depending on how and where it is taken, and the effect of this on the result is not negligible.[6] In addition, many researchers point out that glucose levels vary depending on the location from which the blood is taken. When testing using a micro volume of sample is a requirement as in POCT and SMBG, these effects cannot be overlooked. As such, it is only when the condition of the sample and devices are known that the result truly has value. In other words, the difference in the two types of testing may be regarded as the difference between having or not having a clear foundation that underlies the results.

## POC Coordinator

The next question is, what type of talent is needed for the medical staff that handles POCT related work? Ideally, these people have a thorough knowledge of medicine, they are familiar with testing techniques and measurement, and they are able to appropriately evaluate the test results. However, in modern medicine with its high level of specialization, few practitioners other than clinical testing technicians are well versed in testing, and few technicians have a wide knowledge of medicine. This being the case, the POC Technology Committee of the Japan Society for Clinical Laboratory Automation is fostering talent that has received suitable guidance and education, and is certifying those who have completed the required training as "POC Coordinators". (218 people certified as of August, 2014) (Table 2)[7]

## Global Trends

The U.S. and Europe are moving aggressively to implement POCT. In the U.S. in particular, stipulations related to POCT have been incorporated in the requirements of certification organizations such as CAP (College of American Pathologists) and JCI (Joint Commission International), and action on the part of the entire organization, such as mandatory audits of the organization and operational system, is now required. (Table 3) The role of the coordinator is slightly different than in Japan. Not only is an active role demanded of the coordinator as a POCT practitioner, but the coordinator has duties as a member of the POCT steering committee. The coordinator also has duties as the clinical testing expert, including maintenance of the devices, quality assurance, quality control data, training/education of other operators, and thus the scope of work is extensive.[8] As the range of application for POCT widens, it is likely that this work will expand and the demands made of the coordinator will increase even more.

As explained above, I was comparing POCT with self-

Table 3 JCI Requirements for POCT

- Definition of objectives of use (diagnosis, treatment, screening, etc.), criteria for necessity of confirmation testing
- Identification of supervisor of testing staff and testing work
- Record of appropriate training of testing staff, and of maintenance of skills
- Maintenance of procedure manuals specifying collection and storage of data, measurement divice performance, quality control, etc.
- Definition of quality control checklist corresponding to minimum cases of manufacturer
- Appropriate quality control and maintenance of testing records

From "The Transformation of Medicine and Clinical Testing by POCT", Chapter 4

Table 4 Install location of SMBG, ABG and ROSÉ

| Department | SMBG | ABG | ROSÉ |
|---|---|---|---|
| General wards | 67 | | 32 |
| Intensive care center | 2 | 2 | 2 |
| Surgery room | 2 | 1 | |
| NICU, Perinatal Center | 4 | 1 | 1 |
| Emergency room | 3 | 1 | 1 |
| Outpatient | 5 | | |
| Clinical laboratory | 10 | 1 | 4 |
| Total | 93 | 6 | 40 |

SMBG and ABG numbers are as of January 2006, ROSÉ numbers are as of January 2013

monitoring of blood glucose in order to deepen the reader's understanding. In the following, I report on our hospital's experience with the introduction of the "Antsense ROSÉ" POCT-compatible Glucose Analyzer.

## Our Hospital's Initiative

The hospital laboratory first began collaborating with our medical treatment department in 2004 when we started building a network for our blood gas analyzers ("ABG analyzers" below). At that time, ABG analyzers were deployed in multiple hospital locations, and we were unable to perform data management with the analyzers, let alone centralize analyzer management. Quality control and maintenance for these scattered ABG analyzers required time and effort. This was a heavy burden on the responsible personnel, and the frequency of maintenance necessarily declined. (Table 4) We therefore introduced a Data Management System (DMS) to facilitate data collection and understanding of operational conditions in the facility, with the goal of enhancing our medical resources by alleviating the work load and storing data. As a result, we demonstrated that the analyzers in our ward can be managed centrally by DMS, and by ascertaining the state of our devices in advance, we demonstrated that the workload of personnel responsible for maintenance could be reduced. However, non-standard operations existed, about 20% of the data was omitted, and manual billing work remained. Having gained this experience, it was decided that we should actively take part in point-of-care blood glucose measurement, for which a strong desire had been voiced prior to this, and we, the clinical laboratory, began working with the Diabetes Treatment Support Committee to improve the quality of blood glucose measurement.[4]

### Step 1 Ascertaining current conditions and enhancing the laboratory system

We began by organizing the operational rules for blood glucose measurement. Despite the fact that blood glucose levels were used throughout the hospital, there was little attention paid to how the levels were obtained. Having also received the aforementioned notice from the Food Hygiene Office of the Ministry of Health, Labour, and Welfare, we began replacing our SMBG devices with POCT-compatible devices. (Table 4) Based on 1) data reliability, 2) operability, 3) ability for the technician to intervene, and 4) visual appearance as criteria for the new device, we selected the "Antsense III". The Antsense III was the only small glucose analyzer that had the measurement mechanism inside the device unit, and it used the same measurement principle as regular specialized blood glucose analyzers. (Figure 2) The measurable range was wider than conventional SMBG devices, quality control was supported, and the test technician could intervene in data management. At the same time, there were some negative points in terms of usability, such as a larger size than the SMBG devices, a measurement time of about 20 seconds, and a required sample volume of 10 μL. The laboratory held multiple study meetings related to device management, as well as study meetings for the ward, and obtaining the understanding of the nurses and other staff, in particular the Diabetes Treatment Support Committee, we were able to complete the introduction of the new devices in about half a year from the time the device replacement proposal was first considered. At that time, use of the Antsense III was limited to the endocrine internal medicine patient ward, but with the support of the laboratory and the encouragement of the Diabetes Treatment Support Committee, we gradually gained a greater understanding of the problems that occurred in the use of blood glucose levels, and created an environment conducive to introduction of the Antsense III in all wards.

### Step 2 Install location of the devices

It was pointed out that the next issues were 1) simplification of data entry work, 2) reduction of errors arising from data entry errors, 3) speed of data referencing and maintenance of chronological order, and 4) expansion of install locations. The Antsense III had external output ports, but no proven results in linking with systems, and was not suitable for hospital management based on HIS (Hospital Information Systems).

Facing these issues, an announcement arrived from HORIBA, Ltd. regarding development of the next generation of Antsense III and DMS. In blood glucose Point of Care Testing "POCT", the following information; "when", "who performed the test", and "who was the patient " must be obtained together with the test result in order to link with the system. For this purpose, source input is necessary, and a device function that allows

acquisition or input of information is desirable. The "Antsense ROSÉ" ("ROSÉ" below) has this type of function, and we thought that it might be the solution to our problem.

### Step 3 Data integration

In terms of both expense and labor, directly connecting multiple devices to HIS and LIS (Laboratory Information System) was difficult. Based on our experience with ABG devices, it was thought that DMS would be most suitable for solving this problem. DMS was essential for both management and data collection, and it was our hope that the introduction of DMS would improve the convenience of laboratory operations.

## Role of DMS

In parallel with the development of analysis devices, recent years have seen active development of DMS, which is used for result and device management. While there are no major differences in the relation between DMS and devices, there are a variety of differences in the communication protocol used and in the functions provided. In addition, the demands made of DMS often vary by facility. In some cases, tight linkage with HIS is needed, with patient and user management functions in addition to analysis data management. When we introduced the ROSÉ, our requirements for DMS were good operability, transparency of connection specifications, and low cost. We wanted a convenient system that was tailored for data management and system connectivity, with system connectivity implemented based on standard specifications. The DMS for ROSÉ (ROSÉ LINK) satisfied these requirements. Distribution by CD was possible and system connections complied with IHE (Integrating the HealthCare Enterprise). System installation was possible in one hour, and thanks to IHE, discussions regarding LIS connection were short and consisted mainly with exchanging specifications sheets. ROSÉ LINK satisfied our requirements for DMS, such as monitoring device operation and reagent usage, and enabled centralized management of devices and data at reduced cost and labor burden.

## Analysis Device Connections

When we used SMBG devices, we had more than 80 devices installed in the hospital. (Table 4) However, budget constraints made it difficult to procure the same number of ROSÉ units, so we reduced the number of units to be installed. (Table 4) Even so, we installed almost 40 units throughout the hospital, and settings for LIS connection required an entire day. The devices have been in operation for almost two years, and more than 300 tests are performed using the ROSÉ devices every day. The data from these tests is sent to the host system, but this does not create a heavy load. Although we have observed that the processing speed of DMS itself slows as the quantity of data grows very large, operation continues to be satisfactory, smooth data transmission is maintained, and the system promptly provides data for treatment locations.

## Current Issues

The connection to DMS allowed us to reduce manual entry of test results, and this lightened the workload of nurses and other staff. However, through analysis of DMS data, we discovered that 4% of test results were not being sent to LIS due to communication errors. The error data indicated that the patient ID was not acquired in about 90% of the cases. When we made inquiries at "POCT" locations, the possibility of mis-operation due to differences from other authentication operations, such as those for blood transfusions and intravenous medications, was suggested. In addition, because the device does not allow distinction of the patient ID and the operator ID, we determined that incorrect values were being read in some cases. We again recognized the need to improve confusing operations that originated in differences of operational rules, and devised ways to provide an environment where the operator could operate the device with confidence.

With the introduction of ROSÉ and ROSÉ LINK, it became easier to acquire test results. However in the ward, the device is carried while rounds are made, and the device is almost never returned to the docking station until the blood glucose from multiple patients has been measured and care is given. In some cases, almost two hours elapsed before the initial measurement result was sent to the host system, and thus in terms of immediacy, we did not see the results we were hoping for. Compared to SMBG devices, speed and accuracy have improved, but we have not fully satisfied the desires of our medical team. In other words, we have achieved measurement accuracy, but not operational precision, and further improvements are necessary.

## Conclusions

Blood glucose measurement is commonly performed in medicine, however, there is both blood glucose measurement with thorough quality control, and blood glucose measurement with less than thorough quality control. Although the background of each is very different, there was often a tendency to treat the two as

the same thing. Just as the relation between patient condition and blood glucose level is being reconsidered, the act of measurement is also being reconsidered, and along with high accuracy, devices with good operability are desired. It was in these circumstances that the "Antsense ROSÉ" POCT-compatible Glucose Analyzer and the "ROSÉ LINK" data management system appeared, and by aligning these with the networking of our business system at the time of introduction, we were able to effect a significant change in our blood glucose measurement system. Regarding the device itself, we have received complaints from the nursing staff about its weight and size. In terms of functionality, desires have been voiced for a smaller required sample volume and a shorter measurement time. Based on our experience using the device we have noticed a number of problem areas that require resolution, such as variations of cap membrane consumption depending on frequency of use, and a decrease in linearity in the high-concentration region of the measurable range. However, thanks to this sophisticated device have achieved a new business model that allows the active participation of the laboratory in "POCT" testing for blood glucose, which was previously the sole domain of doctors and nurses. We believe that this forms a possible way forward for the much talked-about "team medicine approach".

## References


[1] Van den Berghe G., et al., "Intensive insulin therapy in the critically ill patients", The *N Engl J Med*, **345**, 1359 (2001)

[2] Funary AP., et al., "Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting", *J Thorac Cardiovasc Surg*, **125**, 1007 (2003)

[3] Van den Berghe G., et al., " Intensive insulin Therapy in the Medical ICU", *The N Engl J Med*, **354**, 449 (2006)

[4] Osamu Yamada, Miwa Ishii, Kumiko Natsume. Feature article (2), "Blood glucose risk management – realization and POCT as a tool, 3. Risk management in hospital glucose monitoring reported by the laboratory", *The Journal of Clinical Laboratory devices and Reagents*, **33(4)**, 491 (2010)

[5] Atsuhisa Fukuda, Meri Kubota, et al., "Positioning of POCT as emergency testing", *Journal of Clinical Laboratory Medicine*, **47**, 57 (2010)

[6] Ieharu Yamazaki, "Problems and correct blood drawing in self-monitoring of blood glucose (SMBG): effect of technique and location on measurement when blood is collected by self-puncture", *Rinsho Byori*, **59(3)**, 281 (2011)

[7] POCT Guidelines 3rd Edition: The Japan Society for Clinical Laboratory Automation, 38, Suppl. 1

[8] The Japan Society for Clinical Laboratory Automation: POC Technology Committee Edition, The transformation of medicine and clinical testing by POCT, Review 2014



Osamu YAMADA

Chief Manager, Clinical Laboratory
Paramedical Affairs Bureau
Okazaki City Hospital