Interview with Shinya Murai, Project Team Manager for Promotion of QKD Business, Katsuro Ejima, Project Team Sub-Manager for Promotion of QKD Business, New Business Development Office, and Minoru Yonezawa, Director of New Business Development Office, Cyber-Physical SystemsxDesign Division, Toshiba Corporation

Japan Developing a New Frontier for the Global Economy by New Technologies

By Japan SPOTLIGHT

In the midst of the pandemic crisis, with global growth significantly declining, innovation is expected to be vital in dealing with these difficulties, with high tech companies playing a key role. One such Japanese company is Toshiba Corporation, which has two new technologies introduced below. Both of them could be expansively used and trigger robust growth.

Japan SPOTLIGHT held interviews with the key players in developing these technologies. (Interviewed on Dec. 18 & 23, 2020)

I. Quantum Key Distribution (QKD) System

(Interview with Shinya Murai, project team manager for promotion of QKD business, and Katsuro Ejima, project team sub-manager for promotion of QKD business of the New Business Development Office, on Dec. 18, 2020)

Background to QKD

JS: What is the background in which QKD is now needed?

Murai: One of the main reasons for QKD drawing much attention in business is that a quantum computer is now within reach of being put into practice. This computer can deal with massive data in a short time, and so there would be a risk that the existing codes widely used now for computers could be immediately broken. We will need more secure codes than those in use now before this computer can be introduced in earnest. Also, even now there is a kind of cyber-attack called data harvesting that has been breaking through codes for a long time after having intercepted data. To cope with this as well, we need more effective encryption.

Key Description of the Technology

JS: How would you describe the key points of QKD?

Murai: The key must be a cryptographic key. In the existing key distribution system, a cryptographic key is sent through the Internet, concealed by a cryptographic algorithm. It would take an overwhelming amount of calculations to decode it. However, such calculations could be done in short time in the case of a quantum







Shinya Murai

Katsuro Ejima

Minoru Yonezawa

computer. There would be a possibility of the cryptographic key being intercepted shortly. QKD is a solution to countervail it. In QKD, a cryptographic key is transmitted on photons. A photon has two characteristics: "inseparable" and "impossible to copy anything on a photon". So it will definitely be possible to find any interception, if it is intercepted. Taking advantage of these characteristics, if intercepted, we can create a cryptographic key and share it only based on the information on the cryptographic key not intercepted, disposing of the intercepted one. In such a way, in theory, interception would be impossible. Though this technology has technical limits such as the need for an optical fiber facility transporting photons and the transmission distance among the sending and receiving equipment being restricted to a little more than 100 kilometers, it will become a crucial technology to be gradually introduced hereafter in business areas like public services, banking and medical services where tremendous damage could be done with the leakage of information.

To be more specific about its introduction in practice, we can think about communication among the offices of a specific user or direct communication between a data center and back-up base points. The limit of distance to little more than 100 km could be loosened by linking together plural base points of quantum cryptography and extended. Further, we believe that a service platform providing a safe cryptographic key for any arbitrary point can be completed by building up a multi-based ring network.

Global Trend

JS: What is the global trend of QKD?

Murai: China is overwhelmingly leading its social implementation. According to public information, there is a QKD network built up as far as 2,000 km from Beijing to Shanghai and to Wuhan, used by financial telecommunication companies. South Korea and Germany follow. In South Korea, social implementation of QKD is promoted with the involvement of the principal telecommunication business operators as a national policy. Trials of QKD implementation are also being attempted in other sectors such as public services, healthcare and industries. In Europe as well, the OPENQKD project in which any European country can take part has been initiated and Germany is predicted to start building up a QKD network within a year or two from now.

History of R&D

JS: How long has this technology been studied?

Murai: There is a nearly 30-year history of its R&D since the Cambridge Research Institute was founded in the United Kingdom in 1991.Toshiba's key distribution speed is higher than those of other companies and its transmission distance is long and thus our technology, I believe, is at the top level in the world. In addition, we have done a number of trials both internationally as well as domestically. With the high speed of transmission, it would be easier to provide a cryptographic key for many users and application programs. With long-distance transmission, the number of relay points could be reduced. We have also succeeded in "signal multiplexing", a distinguished technology directly leading to reduction of introduction costs, enabling QKD with the use of the existing optical fiber network.

As our example of trial operations, in 2019 in the network of the US firm Quantum Xchange, aimed at financial institutions (32 km distance between New York's Manhattan area and New Jersey back offices), we achieved distribution of encryption data and quantum keys. In the UK as well, we did a trial for our company's QKD between the National Composites Centre (NCC) and the Centre for Modelling and Simulation (CFMS) in collaboration with BT, the large British telecommunications company, by using the existing infrastructure. Until then between the two, highly sensitive data had been stored in a portable storage and transported by a human being, but QKD enabled online transmission.

In Japan, we achieved a trial of real-time transmission of genome

analysis data, the most critical personal data, for the first time in the world in collaboration with Tohoku Medical Megabank Organization of Tohoku University. We have also been participating in a joint trial for QKD in the financial sector since December 2012, which is the first joint trial in Japan. Nomura Holdings, Nomura Securities Co. Ltd., the National Institute of Information and Communication Technology (NICT), Toshiba and NEC joined this trial. This was done with a facility necessary for QKD set up in real-time system operation.

Size of Future Market

JS: How big do you estimate the size of the future market of QKD to be?

Ejima: The global market of QKD will be around US\$20 billion in 2035, in our estimate. The market is defined to include equipment necessary for sending and receiving cryptographic keys, optical fiber facilities and distribution services of cryptographic keys for end-users. By region, around one-third of the global market would be the Chinese one and this would be monopolized by Chinese companies. Therefore, at Toshiba we are aiming to catch about \$3 billion in business operations corresponding to a quarter of the rest of the global market, that is two-thirds of the global market.

International Cooperation

JS: How do you plan to proceed with international operations?

Ejima: We plan to build up QKD networks on the existing optical fiber networks in collaboration with service providers in other nations and provide QKD services that any user can use any time when necessary. We are now in business discussions with Quantum Xchange, a start-up QKD company in North America, and with one of the large companies in this area, Verizon Communications, as possible partners to realize this plan. In the UK, we continue to collaborate with BT. In the Asian region, we are also in business talks with local telecommunication operators in South Korea and Singapore, and in South Korea we have done several trial experiments as well.

Future Business Plans

JS: What do you think you should promote as part of your future business plans?

Murai: It will be important to extend the telecommunication distance to build up global QKD networks. To achieve this, there will be two ways forward: one is a new way for telecommunications by using satellites, and the other is to extend the existing distance limit. We are now working on R&D for doubling the distance limit, 100 km now, while engaging in development of QKD by using a satellite for telecommunications across continents.

JS: At this moment, you assume the introduction of highly confidential information by telecommunication. However, for market expansion you would need to lower the cost of introducing this technology. How do you think the market will grow?

Ejima: The cost of QKD services will vary depending upon future technological progress and the size of the networks. For example, having calculated in the US the cost of introducing the network, for an area like the Tokyo Metropolitan Area we estimate several million yen per month as the cost at this moment. We believe that this will reduce to less than one-tenth of this figure as the market expands in the future. We are at this moment preparing development of new technology that could enable this cost reduction in our R&D roadmap. We also believe that market expansion will be ultimately determined by our users' views on the value of data. In terms of feasibility studies, in the case of government agencies with lots of highly sensitive information such as defense-related data, early introduction of QKD would be necessary to be well prepared for the introduction of quantum computing, even if they see a rise in costs to some extent.

On the other hand, in the case of financial institutions such as investment banks where large numbers of transactions are done, we assume the utilization of QKD at market would prevail as the critical nature of their transacted data will increase in proportion to total transactions.

We are starting R&D, infrastructure building and planning to provide the service framework for the QKD market, while exploring costs and prices that could be accepted by our customers in our discussions with them in a variety of business areas.

II. Cancer Detection Technology by Use of MicroRNA

(Interview with Minoru Yonezawa, director of the New Business Development Office, Cyber-Physical SystemsxDesign Divison, on Dec. 23, 2020)

Introduction

JS: Could you please briefly introduce the Cancer Detection Technology developed by Toshiba and officially announced at a press conference in

November 2020? This technology is said to detect 13 kinds of cancer with 99% accuracy. Could you also tell us the background of its development?

Yonezawa: This technology is a simple cancer detection technology but with high accuracy by using microRNA in blood. When we introduced it with a catchy phrase in a press release saying the technology detecting 13 kinds of cancer with 99% accuracy from a drop of blood, some medical doctors said that it would be too much to say "a drop of blood". It is certainly true that we take several tens of millilitres of blood at blood sampling, but only a drop of blood as the specimen necessary to be measured by chip after preprocessing is good enough and within about only two hours we could identify whether a patient has any of those 13 kinds of cancers or not.

Cancer has been top of the list of the causes of death of the Japanese for a long time and there is an estimate that around one in three persons dies of cancer. Meanwhile, looking at the survival percentage of the lung cancer patients per stage of progression, if they start a treatment at the earliest stage (stage 0), 97% of the patients can survive for more than five years. Thus, even in the case of lung cancer with the fastest speed of progression, early finding and early treatment could work effectively (*Chart 1*).

There are several ways to find a cancer, but there is much room for improvement in them in terms of accuracy or cost. A well-known tumor marker can be examined by a simple blood test at cheap cost and thus it is an option in health checks. However, the Area Under the Curve (AUC), an indicator of its accuracy, is only 0.6 to 0.7. There are some cases that wrongly show positive. On the other hand, diagnostic imaging such as Computed Tomography (CT) or Position

Background of development of technology

Enhancing survival rate of the patients with cancer by early finding of cancer is a key challenge for society

 \cdot Cancer is top on the list of mortal diseases in Japan

CHART 1

• Finding cancer at its stage 0 would raise the survival proportion (97% of the lung cancer patients at stage 0 can survive for more than 5 years).



Source: Ministry of Health, Labour and Welfare in Japan https://www.mhlw.go.jp/toukei/saikin/hw/jinkou/geppo/ nengai18/dl/gaikyou30.pdf Source: Okami et al., Journal of Thoracic Oncology 14, 212-222 (2019) Emission Tomography (PET) is expensive and pregnant women are not permitted to take this test. Metabolite analysis, another test for analyzing amino acid in blood, cannot ensure stable accuracy in reality. In the light of such circumstances, we have been studying methods using microRNA to check the risk of diseases such as cancer.

Inspection Method & Outcome

JS: What is microRNA?

Yonezawa: It is short nucleic acid molecule with about 20 base controlling genes or proteins in a body and it is transcribed and created from DNA. Though it is not theoretically clarified yet, since 2010 it has been reported that there is a high possibility of specific microRNA emerging as a sign of cancer. There are about 2,500 kinds of microRNA and if we can specify a microRNA emerging when a human body gets affected by cancer, we can use it as a diagnostic marker for cancer. With this thought, our company has been promoting R&D and finally achieved this technology.

JS: This diagnosis takes only two hours. Could you please tell us how it works?

Yonezawa: Yes. Diagnostic flow consists of four steps. First, you make blood serum out of the sample blood. Second, extract microRNA from blood serum. Third, prolong microRNA with an artificial array to make it easy to amplify. As the length of microRNA's base is around 20 and it is very short, with this prolongation we could measure the concentration of microRNA, which is our original interest. And lastly, we can measure concentrations of microRNA by dropping one drop of this processed blood into a chip and putting it on an inspection machine *(Chart 2)*.

Chart 3 shows the research outcome of a joint study among Toshiba, Tokyo Medical University and the National Cancer Center Research Institute. We discovered a clear difference of concentration of microRNA between patients with cancer and people without it by plotting concentrations of microRNA for the 13 kinds of cancer after the inspection of around 400 samples.

Assuming the red line in *Chart 3* as the threshold between the people without and those with cancer in the chart, we found the outcome would be available with 0.99 accuracy, extremely high, in terms of AUC inspection accuracy. With this accuracy, errors would only be one per 100. At this moment, we can only prove that a person inspected suffers from any of those 13 cancers. However, we think that we can specify an organ suffering from cancer by the same platform. We will continue our research in pursuit of this outcome. Comparing this with the other firms' benchmarking outcomes of

CHART 2

Toshiba's unique cancer detection technology by use of microRNA

Inspection with microRNA chip within 2 hours to be achieved



Source: Toshiba Corporation

CHART 3

Thorough screening of cancer

Making a distinction with high accuracy between the patients of any cancer of the 13 kinds and the normal



Source: Toshiba Corporation

their existing microRNA inspection technology, we found that ours could be available in a short time and with high accuracy and also at a cheaper cost in principle. Thus, we are now getting into a phase to put this into practice.

Putting Technology into Practice

JS: In what context do you assume this technology will be used?

Yonezawa: We can assume its application in two stages. The first is in medical checkups. We can find out if a person is suffering from any cancer from his or her blood sample. At this moment, we do not know yet exactly what cancer the person suffers from, but there would still be merit in this inspection as we could identify whether the person has cancer or not. If the person has any cancer, he or she can proceed to more detailed test to specify the cancer. The second is a checkup for recurrence or spread of the cancer after the treatment. I think there would be merit in this test as only a blood test can show it simply.

We are planning to have another trial experiment on this technology within FY 2020 in pursuing these two applications. In the previous trial, it was done mainly for samples of cancer patients and fewer normal samples. But in the coming trial, the test is to be done mainly for normal samples and thus we would like to confirm our correct judgement in identifying normal samples. That would lead to the next step of its being put into practice.

JS: Toshiba is now putting particular efforts into medical technology. Will this be another effort in line with your medical business development?

Yonezawa: Yes. As is well known, our company has a very long history of medical R&D and medical equipment R&D. On diagnostic imaging equipment, we transferred the business to another company in 2016 and since then we have had fewer relations with the medical business community. However, we now see clear signs of business with this cancer detection technology, seven years after we started research on it even before the transfer of the diagnostic imaging equipment business. We believe that "early finding of the disease" and "customized treatment" have important social implications. In this regard, this technology will be one of the most that we will put our energy and efforts into.

International Reputation of the Technology

JS: How do you think the world views this technology? We think it is more advanced than any other, as we can have the result of the detection test simply and immediately.

Yonezawa: After the press release of the technology, we received a number of inquiries from medical institutions around the world, from Asia, Europe and North America. In the United States and other countries, early detection of cancer is truly a hot topic and we understand a variety of R&D and trials are under progress. But the mainstream of such R&D is pursuing analysis of DNA fragments in the blood. We think this analysis will take longer and be more expensive. Our method is simple and speedy and has high accuracy. and thus we can make distinctions among the needs for inspection.

Market Size

JS: Besides those merits, it is cheap. So can you expect a large-scale market?

Yonezawa: To accelerate its practical application, we are now calculating the size of the market as an ultimate contribution to society. We are now in a situation where Covid-19 is spreading and cancer consultation rates are declining in Japan, and cancer patients cannot have appropriate treatment. In this light as well, I think the need for a simple detection test is rising.

Impact on Medical Services

JS: Will this technology be useful for reducing the burden on healthcare workers as well?

Yonezawa: Yes, that is also what we are pursuing. How inspection results are provided to the doctors in charge or how they will be shown to the inspected people will be very important for us. We would like to discuss the best way with the doctors in charge of treatment.

Future Plans

JS: Could you please tell us your future plans, if possible? Is there any plan for international R&D collaboration?

Yonezawa: The next step would be, first of all, to confirm the technology's effectiveness and safety and also explore the right way to show the outcome of inspections to doctors and patients. We are also working on identification of specific organs affected by cancer using the same platform as we have now and as soon as the research on it is completed, we plan to put this into practice. For our global business development, international collaboration with medical institutions overseas will be indispensable. Hereafter, I JS believe joint study with global researchers will begin soon.

Written with the cooperation of Naoko Sakai who is a freelance writer.