Oyo-Buturi International

Interview

A conversation with Mr Toshio Nakatsubo about his contributions to the research and development of the gastroendoscope.

The pace of technical development of medicine and surgery since World War ii has been tremendous. One major research field in Japan is that related to stomach cancer. The gastroendoscope has become an indispensable diagnostic tool of stomach cancer and many other problems of the gastrointestinal tract.

The development of this technology over the last 40 years has depended upon collaborations between researchers from a wide range of backgrounds.

A central figure who contributed to the engineering aspects of the gastroendoscope from the very beginning was Mr Toshio Nakatsubo.

This interview gives a rare glimpse behind the scenes of the development of a technology. Gastroendoscopy is now an integral part of modern health care. It has undoubtedly saved countless lives, not only in Japan but around the globe.

OBI: Can you tell us why you started research related to the endoscope?

Mr Nakatsubo: It was quite a long time ago! I joined Olympus in 1949 and at that time Professor Uji of the Tokyo University Medical School was researching methods to observe the inside of the stomach. He was trying to diagnose stomach cancer in its very early stages; actually there were many research groups investigating stomach cancer. It was at a time when stomach cancer was widespread in Japan so it was urgent to develop a new technology to diagnose the cancer at an early stage.

OBI: What was the main method used for diagnosis at the time?

Mr Nakatsubo: There was X-ray diagnosis, but the use of X-rays had its problems. The method was only indirect at best and in the early stages, when a cancerous region was still very small, there was the possibility that it might not be visible in a radiograph. So the group wanted a way of looking directly into the stomach optically for signs of cancer. The original idea of looking directly into the stomach is more than 100 years old: apparently a metal pipe was used for looking inside the stomach. The method was never commercialised, though, because of some fundamental limitations.

The initial approach was not so much to observe the inside of the stomach directly, as to try to photograph the lining of the stomach. So the Tokyo University group approached Olympus in order to develop a camera that could take photographs of the inside of the stomach; that was just the beginning.

I had only recently joined the company when my manager, Mr Sugiura, told me about the proposal. We set up a small group to develop the "gastrocamera" as we called it.

OBI: Quite a problem to resolve.

Mr Nakatsubo: Yes. How to make an ultra-small camera that could be inserted into the stomach and still take clear photographs. That was the challenge. Being 1949, there was very little useful technology available, nor basic materials for construction for us use. We needed a lens, film and light. Thankfully, my company already had the technology to make an ultra-small lens. So the first major problem to overcome was how to light the stomach, the inside of the stomach being totally dark! We resolved that problem by developing a tiny lamp that could be inserted into the stomach. The next issue was the film. No colour film was available, we had no choice but to use monochrome. Conventional 35 mm type was far too big so we developed a 5mm wide film with about 20 exposures per roll. The film was rolled on to a magazine. Then we had the lens, film and light. The next step was to integrate them and build a body to house them. The final version of the first ever "gastrocamera" was only about the size of a little finger. The camera was then small enough to be inserted into the stomach and the photograph was ready to be taken. But there was yet another problem to overcome: how to take a "flash" photograph. At that time, magnesium bulbs were used for conventional flash photography- there were no xenon gas flash tubes then. Also, we needed to take about 20 flash photographs without having to remove the bulb every time. So I designed a very small flash bulb with a tungsten filament where a very short pulse of high voltage was applied, resulting in sudden illumination, a flash of light. At first, most of the bulbs would only work for one or two flashes, but in due course, the capacitance and time were adjusted until 20 photographs could be taken with only one flash bulb.

The camera was like a classical "pinhole" camera. It had no shutter - the flash exposed the film. The lens had an aperture of about f=11-12, which was extremely small. A film speed of asa 20 was used in order to get high contrast images.

The camera was now ready, but the "pipe" for actually transferring it into the stomach was yet another problem. The choice of material was a crucial factor; the pipe had to be flexible yet rigid – a slight contradiction in requirements! It took some time, but a practical pipe was eventually developed with a diameter of about 12 mm. It took about 3 or 4 years to get to this stage but it was still not possible to use the camera in practice and many experiments had to be performed first using flasks and beakers in order to test it out. Other problems included how to position the camera at a suitable distance from the wall of the stomach; a distance of about 5-6 cm was necessary. This was achieved by introducing air into the stomach. There were many issues to be resolved before the camera could be used.

OBI: Did you write a patent to cover this technology?

Mr Nakatsubo: Yes. I don't remember the exact wording, but it was something like "an ultra-small camera that can be remotely controlled...". That patent was perhaps the reason why Olympus has managed to win an 80% share of the endoscope market. It's quite a simple patent and is difficult to break.

OBI: Were there any other groups elsewhere in world doing similar work at the time?

Mr Nakatsubo: There might have been, but none of them got as far as we did. But there was still a problem. It was almost impossible to use the monochrome photographs taken by this camera for diagnosis; there simply wasn't enough detail. So colour film was required. But in those days, the so-called "positive colour film" was not available in Japan. Companies like Eastman-Kodak in the USA and Ilford in the UK did make it, though, so we eventually bought some colour film from the USA and prepared especially narrow 5 mm strips for the camera; the process of developing the film also had to be modified. But once we started using colour film we were able to get really good photographs that could be used for diagnosis. The first "gastrocamera" hit the market in 1955.

OBI: What was the response of the doctors using the new cameras?

Mr Nakatsubo: There was yet another problem; there was no way of knowing what particular part of the stomach was being photographed since there was no viewfinder – it was "blind photography". Some doctors tried to overcome the problem by taking the photographs in a darkened room where they could take a photograph and see the light flash from inside the stomach and have a rough idea of the angle of the camera.

There was also the problem of the time taken before the final photograph could be viewed. It was not a real time process: the photograph was taken, the film developed and the photograph viewed using a slide projector. In those days it took a week before any diagnosis could be made.

OBI: Were there any meetings or conferences where researchers could gather and exchange information related to the use of your camera?

Mr Nakatsubo: Yes, there were. In 1955 the first "ikamera" Research Meeting [obi: *ikamera* literally translated means "stomach camera"] was organised by a group from Tokyo University; this was the predecessor of the present day *Naishikyokai* (Japan Gastroenterological Endoscopy Society). The key member of the group was Professor Tasaka along with his students such as Professor Shinroku Ashizawa who later on went to Tokyo Medical College in Shinjuku. They gathered many researchers from all over Japan to take advantage of this new technology. We provided industrial support in the form of practical demonstrations of how to use the technology.

OBI: What was the reaction of doctors in other countries to the gastroendoscope?

Mr Nakatsubo: In Japan, the use of gastroendoscopy spread quickly, but there was hardly any interest on the part of American and European doctors. I think that the lack of interest overseas was due in part to a lack of confidence in interpreting the photographs and also perhaps, to a certain uneasiness in actually using the technology. So, from 1950 to 1960 hardly any doctors outside of Japan used this method of diagnosis.

OBI: What was the next major advance in the field?

Mr Nakatsubo: That happened with the idea of the "fibrescope" in 1960. The first hint about this technology was given to us by Professor Ashizawa of Tokyo Medical College who, while on a trip to America, learnt that "fibre optics" was being used to make a "fibrescope". He wanted to be able to both observe the inside of the stomach and take photographs of it in real time. The technology required for the purpose became my main research theme from that time on...

OBI: What aspects of the development of the fibrescope were the most difficult to overcome?

Mr Nakatsubo: The first problem was how to make thin, cladded fibres of glass that would guide light without loss for a distance of more than two metres. There was no such technology available at the time, so I decided to use a special type of plastic to make "fibre bundles". The problem, though, was that light would only travel about 10-15 cm along the plastic fibres. So it was decided to develop glass that was absolutely not coloured in any way whatsoever for the glass fibre bundles; each fibre was only a few microns in diameter. The development of practical "monofilaments" and an "image guide" actually took 4 or 5 years. They became commercially available for the first time in 1965.

OBI: Again what was the reaction of doctors to the development of your "fibrescope"?

Mr Nakatsubo: Extremely favourable; it was extremely popular both in Japan and overseas. It became possible to carry out real time diagnosis. The first international conference related to this technology was held in Tokyo in 1966. There has been a lot of progress since and many variations of the "fibrescope" have been developed

OBI: What problems of diagnosis were yet to be resolved?

Mr Nakatsubo: By 1966, the problems of "blind photography" and the inability to take real-time photographs had been overcome by the "fibrescope". But there was still another problem, namely, that it was not possible to carry out an objective diagnosis. I could look through a fibrescope and see a particular image and another person could look through it but not necessarily see the same image; we couldn't both look at the same image simultaneously. We needed a colour video monitor for a number of people to look at the image at the same time. The development of the video monitor system was the next challenge.

OBI: What technology was required for the video monitor?

Mr Nakatsubo: We needed to develop a video camera to replace the still camera. Advances in the semiconductor industry gave us a good range of video cameras to choose from, but in this case we needed an extremely small video camera of only about 3-4 mm square. The development of an ultra high-resolution CCD camera for this application took more than 10 years! The result was the "videoscope"; it was first introduced in 1985.

OBI: What other advantages did this technology offer?

Mr Nakatsubo: Some videoscopes included the ability to carry out an objective diagnosis; minor surgery could be performed by using special attachments at the end of the fibrescope tip so that life-threatening cancerous areas can be removed without having to resort to major open surgery. This reduced the time spent in hospital, which I think is a major contribution of technology to society.

I myself have had an abnormal region removed from by colon by endoscopic surgery. It has saved many people time and in many cases their lives. It has changed from being a "passive" tool to an "active" one – not just for looking, but for performing surgery as well. This is the third generation of instruments, starting with the original "gastrocamera" in 1950.

OBI: What about the future? What will be the fourth generation?

Mr Nakatsubo: The next target is very clear: micro-machining. There are still many demands from doctors; they are still not satisfied! The top two priorities are firstly, to produce an endoscope that can be used without the need for a mild anaesthetic and without discomforting the patient. The second demand is for an endoscope that can be used for even more surgical procedures.

OBI: How will micromachining be used to fulfil these demands?

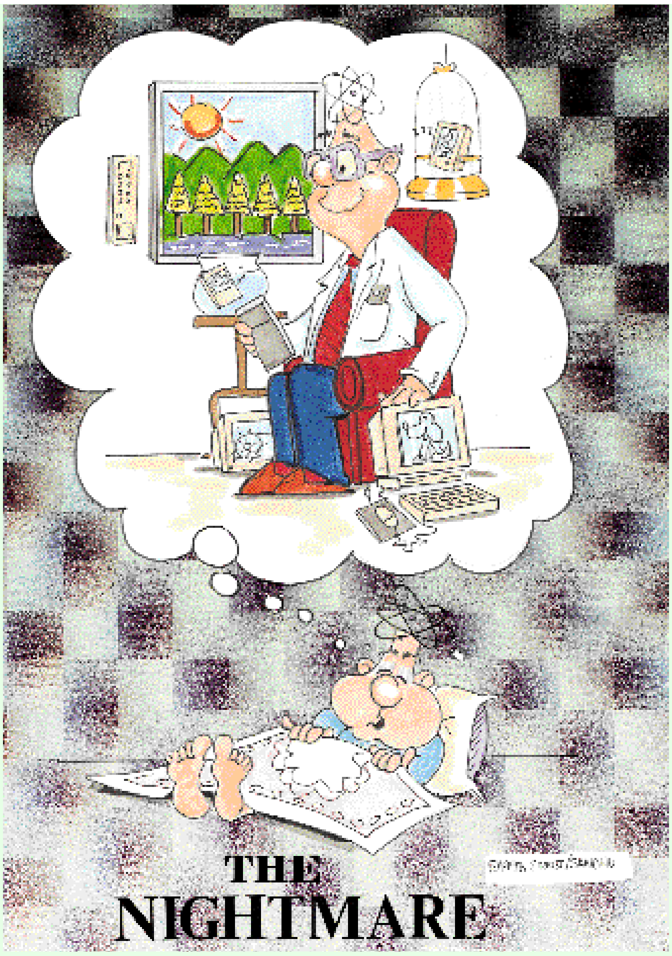
Mr Nakatsubo: The first issue to resolve is how to develop a pipe that can move like a snake, moving smoothly without bumping into corners. Special sensors and materials are being developed for the purpose. The other avenue being explored is how to manufacture "micro-robots" that can be inserted into the body to carry out surgery. The major problem to overcome with micro-robots inside the body is supplying enough energy for them to carry out mechanical tasks. There are still many aspects of this technology to look forward to!

OBI: Finally, how do you feel when you go for an endoscopic check-up and use the technology that you have developed yourself?

Mr Nakatsubo: To be honest, I was a little scared the first time. But after a few times, and especially after the development of the videoscope, I wanted to have a closer look at my own stomach and I was amazed to see how beautiful the human digestive system really is; I will never forget that first experience.

These days I have two check-ups every year and, for myself, I consider the gastroendoscope to be a vital part of health care.

For further information on Olympus endoscope products, see `http://www.olympus.co.jp/LineUp/Endoscope/indexE.html`



Resume

Mr Toshio Nakatsubo graduated from Yamanashi Technical College (now Yamanashi University) in 1949 and joined Olympus Optical Co., Ltd., in the same year. He is now an advisor to Olympus.

Interview by Adarsh Sandhu

Essay

This is the third and final essay based on a keynote lecture by Dr Eiichi Maruyama at the Japan-Sweden Science Club (jssc) annual meeting, Tokyo, 31 October, 1997. jssc is a society for Swedish scientists in Japan and Japanese researchers who have stayed in Sweden. It is open to anyone interested in all aspects of science in these countries. See `http://www02.u-page.so-net.or.jp/fa2/crane/` for details.

Dr Maruyama studied science history, scientific philosophy, and physics at the Tokyo University. After graduating from the university in 1959, he joined Hitachi, Ltd., and became the director of the company's advanced research laboratory in 1985. He is currently executive director of the Angstrom Technology Partnership.

The Meiji Restoration

The Meiji Ishin or Meiji Restoration was a *coup d'etat* initiated and carried through by a group of young samurai from *Choshu* (now Yamaguchi Prefecture) and *Satsuma* (now Kagoshima Prefecture). Choshu is located at the extreme west of Honshu Island, and Satsuma lies at the extreme southern end of Kyushu Island. Both places, being remote, were amongst those least affected by and least attracted to the cultures of Edo and Kyoto.

Science and Education in The Early Meiji Period

Quite a number of Japanese scientists achieved worldwide fame in the Meiji Period. For instance, *Shibazaburo Kitazato* developed the first serum therapy for tetanus under *Dr. Robert Koch* of Germany; *Jokichi Takamine* discovered that adrenaline (or epinephrine), a hormone produced in the adrenal gland causes the body to respond to emergencies; *Kikunae Ikeda* discovered the seasoning effect of kelp extract and, having identified its main ingredient (sodium glutamate) commercialised it as ajinomoto; *Hantaro Nagaoka* proposed an atomic model based on the rings of Saturn; *Kumagusu Minakata* pioneered the study of slime moulds and plants in evergreen, broad-leaved tree forests; *Kiyoshi Shiga* identified the dysentery pathogen, *Bacillus Dysenteriæ*, which was later called *Shigella Dysenteriæ*, the name being based on his surname; *Umetaro Suzuki* discovered that the vitamin B1 (or thiamine) prevented beriberi; and *Hideyo Noguchi* succeeded in culturing the syphilis pathogen, *Treponema* (formerly known as *Spirochaeta*) and was nominated for Nobel Prize (in physiology or medicine) several times.

Alas! No more scholars of renown in Japan until *Hideki Yukawa* was awarded with the Nobel Prize in physics in 1949.

It seems that, during the isolationism of the Edo Period, the intellectual potential of the Japanese became fully charged up, so that after the after the Restoration, many ambitious young men wanted to go abroad to boost their scientific capabilities. I myself think that the education system established in the Meiji Period was actually responsible for the subsequent reduction in vigour of Japanese scientist in the early part of the 20th century

In 1872, the Government established a new schooling system that combined the elementary schools operated by feudal lords with the privately owned *terakoya*, thus providing equal opportunities for children of all the classes under a centrally-controlled education system.The "Law of Education" was enacted in 1879 to reform the primary school system by transferring educational control to local communities. In that way the Government, which was suffering a financial crisis sought to reduce its financial burden. However, in 1886, the "Education Ordinance" was issued, thereby centralising education once again. Separate rules were introduced for primary schools, middle schools and the Imperial universities.

It is particularly noteworthy that the pioneering scientists mentioned above were all unaffected by the new education system of the early Meiji period: in 1886, S.Kitazato was 34 years old, J.Takamine was 32, K. Ikeda was 22, H. Nagaoka was 21, K. Minakata was 19, K. Shiga was 16, U. Suzuki was 12 and H. Noguchi was only 10 years of age. Furthermore, numerous other scholars had finished their early education by 1889, such as *Yukichi Fukuzawa*, the educator; *Kitaro Nishida*, the philosopher; *Daisetu Suzuki*, the Oriental philosopher; *Tomitaro Makino*, the botanist; *Inazo Nitobe*, the religious teacher and agronomist;

Kanzo Uchimura, the religious teacher; *Tenshin Okaura*, the philosopher in fine arts; *Soseki Natsume*, the writer; and *Ogai Mori*, the surgeon and writer.

Most of these people had received their primary education and training at private schools. The creation of the new Imperial Universities as a result of the "Education Ordinance" planted in the mind of the Japanese a belief that great importance should be attached to national universities.

It is my belief, though, that the enaction of the Ordinance of Education in 1886 introduced serious defects into many aspects of the Japanese educational system, including science and technology. It seems that the prevailing opinion among leading educationists today is that special education should be made available to brilliant children, and that should even be a grade-skipping system for precocious students. I find myself totally opposed to such a change. The future of Japan should not be entrusted to those who have a high iq and a high deviation value.

Conclusion and Message for the 21st Century

Issues that we Japanese should address as we approach the 21st century include how to resolve environmental issues, secure adequate supplies of energy, contain the population explosion and maintain peace in the world. Peace in one country or a clean environment in one country is not enough these days. Already, acid rain is crossing national boundaries and geographical barriers. We must work together to find global solutions to global problems. Let us hope fervently that the cop3 Protocol signed in Kyoto in December 1997 will usher in a new era of international technological cooperation.

Science and Technology Collaboration

The *King Mongkut's Institute of Technology Ladkrabang* (kmitl) in Thailand, was established as a result of an extremely successful collaboration between Japan and Thailand involving government, industry and academe.

kmitl is located 30 km east of Bangkok and is the leading science and technology university of Thailand offering a broad curriculum ranging from computer science to agricultural technology. The current student population is 14,400.

kmitl was originally founded as The Nondhaburi Telecommunications Centre in 1960 with technical cooperation from the Government of Japan. The 23 students at the Centre were offered two courses; a 6 month technician course and a one year vocational course. The Centre was reorganised in 1971 and three technical colleges (*Nondhaburi*, *Institute of Telecommunications*, *North Bangkok Technical College* and *Thonburi Technical College*) were combined to form the King Mongkut's Institute of Technology. The following year the Nondhaburi Campus was relocated to a 250 acre plot of land donated by the heiress of *Chao Khun Taharn*, at Ladkrabang Campus. The newly located campus initially consisted of the Faculties of Engineering and Architecture. In 1977, the Faculty of Industrial Education and Science was established. Then, in 1981, the Computer Research and Services Centre was added and a School of Graduate Studies initiated in 1986. The year 1986 was a important year for kmitl, because it was given status as a full autonomous national university.

The tremendous growth of kmitl is a result of the positive and continuous collaboration of government, industry and academe between Japan and Thailand. Many agreements of technical cooperation and grant aids from the Government of Japan have been reached in terms of experts, fellowships, equipment and buildings.

Japanese industry has provided equipment, sent experts (for between 6 months and 2 year) to teach at kmitl, and has accepted students for training in Japan.

Academe in Japan have been fully supportive of the various projects to-date. One of the most active and longest academic collaborations with kmitl has been with Tokai University.

Professor *Tatsuro Matsumae*, an engineer who studied material science at Tohoku University for his Doctorate, is the President of Tokai University Education System, `http://www.u-tokai.ac.jp/English/index.htm`.

Professor Matsumae sums up the successful government, industry and academic collaboration as follows:

"Education in Japan domestically requires collaboration at many levels. I think that the roles of industry and government are such that industry should collaborate for educating young people, not just for training potential employees but with a much wider social view. In terms of developing future technology, industry should support university research; which is becoming more common as industry restructures. The government on the other hand, should strive to devise laws to create a better environment for carrying out collaborative research.

If we consider international projects funded by Japan, then the funding for these projects is often used for building roads, hospitals, dams and installing vast amounts of sophisticated equipment into such facilities. The problem is that in some cases there is nobody locally who can actually operate the equipment installed; there are not enough people who have mastered how to use the technology. Also, if you make a road, it will need repair within ten years, for which the funding is not given.

So I think that more international funding should be used for educating the people to develop their country; equipment and roads may disappear but people will not at the same rate.

One excellent example of where government, industry, and academe collaborated is the project that Tokai University was involved in for establishing The King Mongkut's Institute of Technology Ladkrabang, in Thailand; this may be the first successful example of such a collaboration in Japan. The project was started more than 30 years ago and it has yielded a real foundation for the development of science and technology in Thailand and neighbouring countries".

The future for this collaboration is bright with the announcement of the 4th phase of the project between 1997 and 2002. The emphasis during this phase is on establishing a communications and information research centre. The governmental, industrial and academic exchanges between the two countries will continue and enhance the collaboration.

Further information about kmitl can be found at `http://www.kmitl.ac.th/`

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`http://www.bekkoame.or.jp/~fire/`
Fireworks without the smoke. A wide range of firework simulations; including the sound effects!

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