

# A Collection

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ROBERT C. MALENKA & ROBERTO MALINOW

*Nature* Vol.469 (44 – 45) / 6 January 2011



ISTOCKPHOTO

Where did I put those keys? What did I have for dinner last night? Cognition — most notably, the ability to store memories — inevitably declines with age. What's more, for an increasing proportion of individuals, this decline progresses aggressively to the point that they cannot care for themselves. Alzheimer's disease is the leading cause of such dementia in the elderly, affecting almost 50% of people over the age of 85. But despite considerable progress in understanding the biology of this disease, an effective treatment remains elusive. On page 47 of this issue, Cissé *et al.*<sup>1</sup> provide compelling evidence that manipulation of a specific membrane protein — the receptor tyrosine kinase EphB2 — in a mouse model of Alzheimer's disease can reverse the characteristic memory deficits and so may make for a promising therapeutic strategy.

The leading hypothesis for the cause of Alzheimer's disease — based initially on human genetic findings, and supported by many cellbiological, animal-model and human studies — is chronically high brain levels of a peptide fragment termed A $\beta$ . Indeed, mutations in the enzymes that generate

A $\beta$  or in the A $\beta$  precursor protein, which lead to increased A $\beta$  levels, are associated with early-onset Alzheimer's<sup>2,3</sup>.

Mice genetically engineered to express these same mutations develop cognitive deficits as they age<sup>2,3</sup>. In normal mice, meanwhile, raising neuronal A $\beta$  levels causes a loss of synaptic junctions between these cells that correlates well with the degree of dementia in humans. Furthermore, A $\beta$  can now be imaged non-invasively in the human brain, and brain images of patients with Alzheimer's disease show A $\beta$  accumulation, the extent of which correlates with memory decline<sup>4</sup>. Thus, there is great motivation to determine how A $\beta$  accumulation leads to memory impairment.

Learning and memory are thought to require long-term potentiation (LTP) of transmission at synapses — a form of plasticity that occurs prominently in the hippocampus region of the brain. The hippocampus is not only required for memory formation, but is also affected early on during Alzheimer's disease<sup>2,3,5</sup>. It is perhaps not surprising, therefore, that hippocampal LTP is also impaired in mouse models of the disease and after A $\beta$  application<sup>2,3</sup>. But the detailed



molecular mechanisms that underlie the impairments in LTP and memory in models of Alzheimer's disease are unknown. More importantly, reversing these impairments has proved very difficult.

To make headway on these problems, Cissé *et al.*<sup>1</sup> examine the mechanisms behind the loss of a crucial synaptic protein complex, the NMDA receptor (NMDAR). This receptor is required for triggering LTP and for hippocampus-dependent memory formation<sup>5</sup>, so it makes sense that its loss and malfunction would contribute to the symptoms of Alzheimer's disease. Indeed, previous studies have found that A $\beta$  both reduces the synaptic function of NMDARs<sup>6</sup> and triggers their internalization from the cell surface<sup>7</sup>.

Cissé and colleagues focus on EphB2. This protein interacts with NMDARs<sup>8</sup>, and its deficiency reduces LTP<sup>9,10</sup>. The authors find that A $\beta$  binds to EphB2, decreasing its levels. What's more, the effects of reducing EphB2 levels in the dentate gyrus — the input region of the hippocampus — in the normal mouse brain mimic the reduced synaptic NMDARs and LTP that occur in an Alzheimer's disease mouse model.

These findings lay the foundation for the key question: can virus-mediated expression of EphB2 in the dentate gyrus of an Alzheimer's mouse model overcome the associated synaptic and memory deficits? Remarkably, Cissé *et al.* report that this manipulation 'cures' the mice, with both NMDAR-mediated synaptic responses and LTP returning to normal levels. Of greatest clinical relevance, however, is the authors' finding that EphB2 expression allows the Alzheimer's mice to learn and remember normally in three different behavioural tasks that test hippocampus-dependent memory.

Cissé and co-workers' observations provide compelling evidence that EphB2 may be a valuable target for the treatment of Alzheimer's disease. The authors point out several ways by which treatment might be achieved, such as interfering with the binding of A $\beta$  to EphB2, decreasing EphB2 degradation and increasing EphB2 expression. But before researchers in academia and the drug industry vigorously pursue this novel therapeutic mechanism, some cautionary notes are worth mentioning.

Given the complexity of this challenging subject, it is essential that these key findings be replicated. Moreover, which of the Alzheimer's disease models, if any, accurately reflects the human condition is debatable. As a result, whether

EphB2 expression rectifies synaptic and memory deficits in other models of the disease should also be tested.

Alzheimer's disease affects several brain regions. So it is surprising that, in Cissé and colleagues' mice, expression of EphB2 in the dentate gyrus alone could completely overcome the memory deficits. As the authors suggest, improving the function of a subset of neurons may be sufficient to improve the performance of the larger networks in which they function. Nonetheless, it must be determined whether EphB2 can remedy the A $\beta$ -induced deficits in other brain areas.

Finally, a key challenge is determining the time point during the progression of Alzheimer's disease at which administering a certain treatment would still be effective. Cissé *et al.* expressed EphB2 before any of the classic neuropathological features of Alzheimer's disease occurred. It should be determined whether expression of this receptor at later time points is equally effective.

Despite these caveats, this work opens up a new avenue of investigation into the pathogenic mechanisms of Alzheimer's disease, and points to a previously unknown mechanism that can be targeted for therapeutic purposes. It also offers hope to a research field that has recently suffered several highly publicized failed clinical trials. These findings<sup>1</sup> should provide renewed energy and optimism that will hopefully lead to new drugs in time for many of us to take before we develop this devastating disorder.

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# A stroke of X-ray

X-rays were discovered more than 100 years ago. They have since become a staple tool for medicine and science, so researchers are continuing their efforts to find innovative ways to produce them.

STEFAN KNEIP

*Nature* Vol.473 (455 – 456) / 26 May 2011



A few years ago, a discovery<sup>1</sup> was made that flabbergasted scientists and laymen alike: peeling a common adhesive tape produces X-rays bright enough to take an image resolving a human digit. Writing in *Applied Physics Letters*, Hird *et al.*<sup>2</sup> now describe how they have developed a prototype that promises to turn this principle of X-ray production into a simple, low-cost X-ray source.

Since their discovery in 1895, X-rays have affected many aspects of our lives, allowing us to visualize the insides of our bodies, infer the structure of DNA and test the integrity of aircraft wings. The humble tube that first produced X-rays has seen considerable development and is still widely used. But demand for — and development of — complementary sources of X-ray radiation has also abounded. This has educed some of the most sophisticated scientific apparatuses catering for cutting-edge research, and continues to foster the development of innovative X-ray sources for routine applications<sup>1,2</sup>.

The phenomenon that underlies the production of visible light and short bursts of X-ray emission when tape is peeled<sup>1,3</sup> is called triboluminescence. Analogous to sonoluminescence<sup>4</sup>, in which energy from sound waves is converted into flashes of light, triboluminescence<sup>5</sup> concentrates diffuse mechanical energy into light. This can happen as a result of pulling apart, ripping, scratching or stroking material.

Light is emitted when electrons are accelerated or stopped, or when they jump between energy levels. Therefore, to obtain X-ray photons with energies of tens of kiloelectronvolts (keV) — the energies required for medical applications — electrons of at least that energy must be produced. Endowing electrons with kiloelectronvolt energies is thus a common challenge for many commercial and scientific sources of X-ray radiation. This challenge is met by high-voltage equipment, which affects safety requirements, portability, usage range and the minimum size of the sources' X-ray tubes.

The demonstration<sup>1,3</sup> that X-rays could be produced with an object as simple as adhesive tape, and without the

application of an external source of high voltage, encouraged scientists to investigate further. Hird and colleagues' prototype<sup>2</sup> is the outcome of one such investigation. Their device offers the prospect of building a low-technology, economical and compact X-ray apparatus for commercial engineering, and to systematically improve our understanding of the physics of triboelectric charge transfer — the phenomenon that underlies triboluminescence.

The latest prototype fits into the hand and is intriguingly simple (Fig. 1a). It consists of an actuator that repeatedly brings an epoxy surface in and out of contact with a silicone membrane. This stroke motion causes the silicone and epoxy to acquire a charge imbalance. Triboelectrification — that is, charging up due to (frictional) contact between materials — can create high electric fields, in excess of hundreds of kilovolts per centimetre<sup>6,7</sup>. This is high enough to ionize the surrounding air and produce a spark — similar to the static shock that can be generated by touching an object such as a doorknob.

Hird *et al.*<sup>2</sup> find that, when their experimental apparatus is enclosed in a moderate vacuum, X-ray radiation is generated at a rate of more than 100,000 X-ray photons per contact cycle. The radiation is produced by atomic transitions and by decelerating electrons. This results in narrow spectral lines on top of a broad spectrum. According to their calculations, the silicone–epoxy system generates up to  $10^{10}$  charges (electrons) per square centimetre across the contact area of the device (65 mm<sup>2</sup>). The discharge physics is not yet fully understood<sup>1,2</sup>, but at such charge densities, as the silicone and epoxy are separated, the ambient gas that surrounds the vacuumenclosed apparatus should be ionized. This gas ionization is confirmed by the characteristic orange–red of neon glow discharge that is seen when the X-ray source is operated in a low-pressure neon environment (Fig. 1b).

The authors chose silicone because of its strong tendency to charge negatively; a list known as the triboelectric series<sup>8</sup> exists that ranks a material according to its propensity to

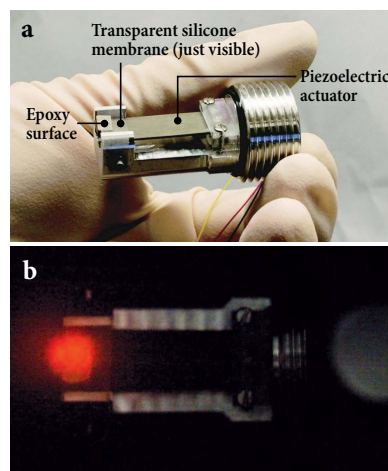


**Figure 1**

**A triboelectric X-ray machine.**

**a**, Hird and colleagues' hand-held device, shown here without its vacuum encapsulation, produces X-rays (not shown) when a piezoelectric actuator repeatedly brings an epoxy surface in and out of contact with a silicone membrane.

**b**, The image shows the vacuum-enclosed apparatus in operation in a low-pressure neon atmosphere, in which the characteristic orange-red of neon glow discharge can be clearly seen. (Images courtesy of UCLA.)



become charged. To test their device, they added silver to the epoxy surface, and observed the characteristic X-ray K-line emissions (around 22–25 keV) of silver. In doing so, Hird *et al.* prove conclusively that electrons from the discharge process are accelerated to tens of kiloelectronvolts of energy and produce X-rays on impact with the epoxy. The capability to load epoxy with materials of different atomic number gives the apparatus flexibility — it can both be tuned to a desired X-ray line emission energy and increase the efficiency with which X-rays are generated.

What's more, Hird and colleagues<sup>2</sup> find that, by reducing the ambient pressure, the X-ray emission can persist for more than a second after the epoxy and silicone have been separated. However, to increase the X-ray yield with contact-cycle frequency, it is more desirable to achieve short bursts of X-ray emission. Although this is at the expense of X-ray energy, the emission time can be reduced to less than 10 milliseconds when the device is operated at a higher ambient pressure of 30 millitorr of nitrogen. At such pressure, the authors were able to demonstrate linear scaling of photon number with the frequency of contact cycles. This scaling suggests that the limiting factor to achieving a photon yield of  $10^8$  per second is finding a linear actuator capable of millimetre displacement and a contact-cycle frequency of 0.1–1 kHz. Their 'mark 1' device was based on a solenoid-magnet actuator capable of 20-Hz contact-cycle frequency. Their 'mark 2' model (Fig. 1), which works with a 'piezoelectric' actuator, can achieve a frequency of 300 Hz.

But contact-cycle frequency may not be the only way to increase the X-ray yield of Hird and colleagues' apparatus. The triboelectric series and literature suggest that material pairs exist for which contact or frictional electrification leads to charge densities of  $10^{13}$  electrons per square centimetre<sup>8,9</sup>. If fully discharged, such densities would lead to a 1,000-fold increase in X-ray yield to  $10^8$  photons per stroke or  $10^{11}$  per second at a stroke rate of 1 kHz (for the same contact area of  $65 \text{ mm}^2$ ).

Triboluminescence has been shown<sup>10</sup> to work on microscopic scales, which suggests that, in principle, the device<sup>2</sup> could be scaled down to submillimetre sizes. The challenge will be to manufacture miniature actuators capable of two-dimensional stroke motion for optimal frictional contact. It is possible to imagine a matrix of tiny, individually addressable X-ray sources coupled and synchronized to a fast-readout camera, which would harness the emission from many sources and build up X-ray images in short exposures. If manufacturing techniques for micrometre-sized electromechanical systems can be used, such a triboelectric X-ray source could be realized economically and scaled to large areas ( $\text{cm}^2$ ). Together with their industrial partners, Hird and colleagues have started pursuing this idea. Their work paves the way to a mechanically driven X-ray source for imaging applications in medicine, industry and the life sciences, without the need for a high-voltage power supply.

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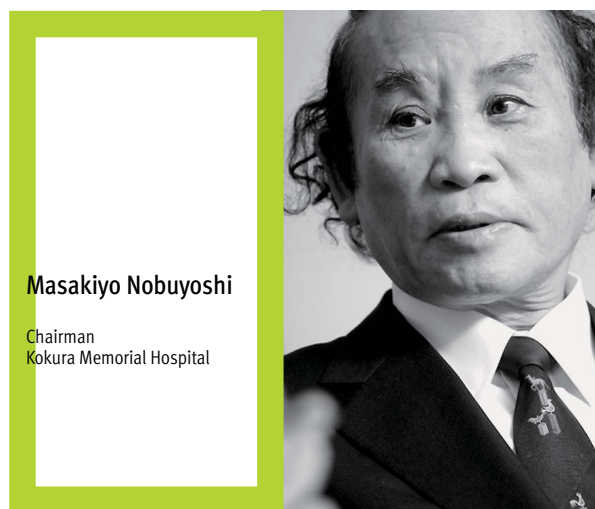
# Kokura Memorial Hospital

for the advancement  
of percutaneous coronary intervention (PCI)



## Masakiyo Nobuyoshi, chairman of Kokura Memorial Hospital — the first Japanese clinician involved in PCI

Heart disease is the second leading cause of death in Japan. In fiscal 2010, 43,209 people died from acute myocardial infarction and 32,272 people died of other ischemic heart diseases according to figures from the



**Masakiyo Nobuyoshi**

Chairman  
Kokura Memorial Hospital

Ministry of Health, Labour and Welfare. A patient survey release by the ministry also estimates that 808,000 people were undergoing continuous treatment for ischemic heart diseases in 2008. Without a doubt, ischemic heart disease is one of the most important illnesses when considering health and healthcare costs.

In the treatment of ischemic heart disease, it is important to eliminate any constriction of the coronary artery, which can lead to myocardial infarction. The primary surgeries employed for treatment are aortocoronary artery bypass graft surgery, which involves connecting the stenosed coronary artery to a different artery, and percutaneous coronary intervention (PCI), sometimes called percutaneous transluminal coronary angioplasty, which expands the constricted artery directly.

In PCI, a thin guide wire is inserted through an artery in the groin or arm and threaded into the constricted portion of the coronary artery. A narrow catheter tube with a small balloon tip is then threaded along the guide wire into the artery, where the balloon is inflated to expand the vessel, a procedure called 'balloon angioplasty'. At the same time, the surgeon performs endovascular treatment by inserting a stent in the coronary artery, which involves positioning a metal mesh stent and expanding it in the artery to maintain the vascular lumen. If the stenosed portion of the artery is severely calcified, and no guide wire can be inserted, a specialized drill called a 'rotorbrator' is used to cut away the calcified portion in a procedure called 'atherectomy'.



Kokura Memorial Hospital

Kokura Memorial Hospital, located in the city of Kitakyushu in Fukuoka Prefecture, prides itself on having the world's top therapeutic techniques and facilities, with 45 medical doctors in the cardiovascular department. The hospital has more cardiovascular specialists and surgeons than major university hospitals in Japan. It also has the largest number of PCI cases in Japan, already in excess of 50,000 patients.

Masakiyo Nobuyoshi is a pioneer in PCI and founding chairman of the Japanese Association of Cardiovascular Intervention and Therapeutics. Before the introduction of PCI, Nobuyoshi started using coronary angiography in 1979 when the technique was first introduced. In 1981, he became the first physician to apply balloon angioplasty in Japan. The first case was a 74 year-old man with effort angina — tightness of the chest with body movement. That patient presented with 90% coronary artery stenosis. “Although the treatment was successful in that case, there were cases where the treatment lost its effect during the course of treatment. In such instances, we switched to coronary artery bypass surgery, and received a lot of surgical support. Things began to pick up some time in 1982,” recalls Nobuyoshi.

From the very beginning, Nobuyoshi thought that less invasive PCI would be used more widely than the open-chest aortocoronary bypass graft surgery. “At that time, aortocoronary bypass surgery required 30 days of hospitalization. With PCI, patients are discharged in three to five days with no scars on the body,” says Nobuyoshi. At a

time when the number of PCI cases was still limited in the world, Nobuyoshi improved the track record for treatment by using stents in 1990 for the first time in Japan. “The doctors around me told me that they dreaded the thought of inserting a piece of metal into coronary arteries, but they soon started referring patients to me, pleading for the stent procedure,” chuckles Nobuyoshi. An increasing number of healthcare professionals visited his hospital, and he began conducting live demonstrations of PCI in 1984 to spread its use. Since then, he has given 28 demonstration sessions. With the recent advent of the drug-eluting stent, which is coated with a drug to prevent restenosis, the track record for treatment is still improving.

Indispensable to PCI is the angiography system — an X-ray-based diagnostic imaging instrument. Kokura Memorial Hospital has been using Shimadzu products since 1993 and is a long-term partner in product development. Nobuyoshi expresses his deep trust in Shimadzu: “Their products are easy-to-use and their after-sales service is excellent.” All six units of the angiography system installed in the cardiac catheter room of the new hospital, which was completed in late 2010, are manufactured by Shimadzu.

After tackling the introduction of coronary angiography and PCI as well as the construction of a new hospital, Nobuyoshi now hopes to collaborate with hospitals in China to meet the challenges of patient referral and training in PCI and other medical technologies of Kokura Memorial Hospital.

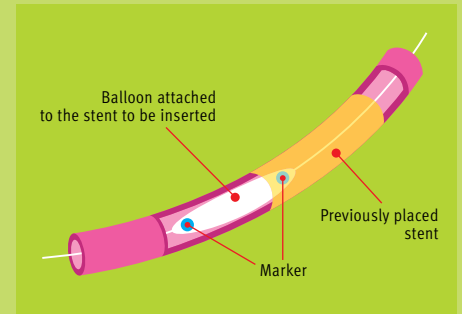
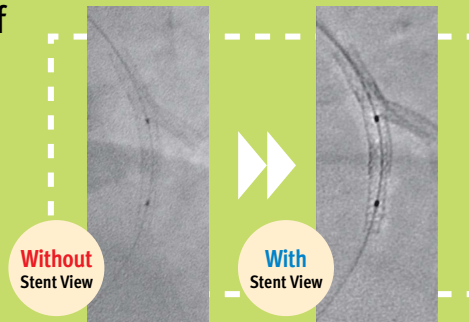
# Clear visibility available only from Dynamic Stent View!

Dynamic Stent View is software designed specifically to support PCI procedures based on Shimadzu's extensive expertise in real-time image processing technology. This software is especially useful for positioning overlapping stents or balloons to re-expand stents.

1

## Real-time display of dynamic images

High-speed image processing offers real-time display of enhanced stent images for smoother PCI without interruptions to the procedure workflow.



2

## Static display of stent compensating for cardiac motion

In Dynamic Stent View, the screen is split into Stent View, Dynamic View, and Detecting View areas.

### • Stent View Area

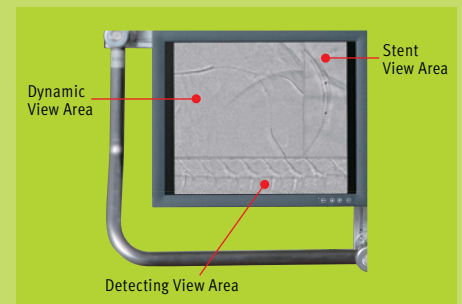
Stent movement due to cardiac motion is arithmetically processed around a fixed marker. This offers static images that are ideal for observations of the stent.

### • Dynamic View Area

Displays the same view field as normal live images to offer a clear overview.

### • Detecting View Area

Always displays the marker.



# Joint development of software for real-time viewing of stent status

**As people live longer, an increasing number of patients who have had PCI and similar treatments are developing restenosis of the coronary artery, necessitating follow-up treatment**

According to Masashi Iwabuchi, who leads the clinical team as director of the Department of Cardiovascular Medicine at Kokura Memorial Hospital, the hospital now performs PCI procedures in nearly 2,500 cases annually, using drug-eluting stents in a little less than 90% of elective PCI procedure patients and bare metal stents in the rest of

the patients. Around 30% of patients with bare metal stents require a second treatment, while only a few per cent of patients with drug-eluting stents need re-treatment. "Now that intravascular ultrasound is covered by national health insurance and the drug-eluting stent is available, the incidence of restenosis is further decreasing. We use intravascular ultrasound to check the calcification associated with the progression of arteriosclerosis, the branching portion of the coronary artery and the crimping condition of the stent to the vascular wall," explains Iwabuchi.

Even a physician like Iwabuchi who is skilled in PCI experiences difficulties when a second stent needs to be inserted to treat restenosis. "When a second DES is placed on top of the previously placed DES, the substantial stent overlap can cause excessive release of the anti-restenosis drug, which could result in side effects. However, it is difficult to see the position of the two stents during insertion.

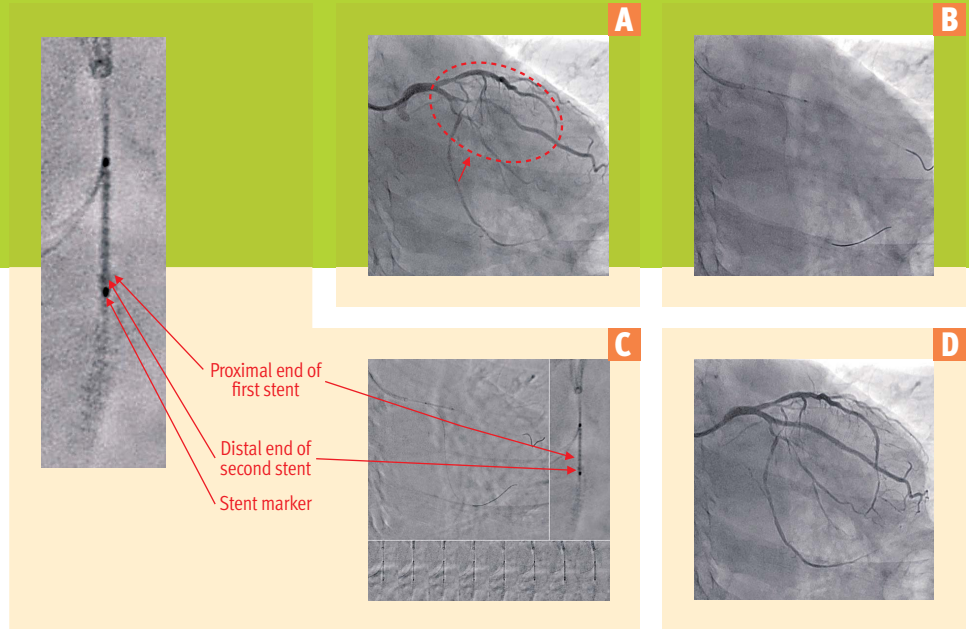


[ 75-year-old man with effort angina ] Coronary angiography reveals diffuse severe stenosis in circumflex seg. 12.

- A** Pre-treatment coronary angiography (diffuse severe stenosis in circumflex seg. 12)
- B** A NOBORI 2.5 x 24 mm stent is inserted into the distal part of lesion.  
A second NOBORI 2.5 x 14 mm stent is inserted into the proximal part with only the stent ends overlapping.  
“Conventional Cinematogram” for positioning of second NOBORI stent while the second stent marker is recognizable, the position of the first marker is unclear.
- C** “Stent View Image” for positioning of second NOBORI stent  
The first stent is clearly visualized. It is also shown that the proximal end of the first stent is not fully expanded.
- D** Post-treatment coronary angiography



FPD angiography system BRANSIST safire installed at Kokura Memorial Hospital



We have no choice but to minimize stent overlap by avoiding inserting the stent too far.”

With the help of Iwabuchi and his colleagues, Shimadzu developed new a software package called Dynamic Stent View that improves the visibility of the old and new stents during the procedure. The new software was launched in June 2011.

With refinement of the software in collaboration with clinicians at Kokura Memorial Hospital, the software now provides reliable images of the stents with views available from multiple angles in real time.

Among the software applications available for this task, only Dynamic Stent View can give real-time imaging of the stents during the procedure. Iwabuchi gives his seal of approval to the software. “It is a very convenient and effective tool as I can adjust the positions of the balloon and stent to within millimeters. I can see all of the stents without any problem, regardless of the material, structure or thickness of the stent or the type of coated drug.” Although the procedure now takes a little longer than before as the physician makes fine adjustments to the positions of the stents, the procedure now proceeds much more smoothly and the outcome is much better for patients. The new software also carries the advantage of improved visibility of stents in patients with a thicker body trunk and extensive calcification, which make

observation difficult in conventional angiography.

Iwabuchi is now hoping that Shimadzu will develop products with lower X-ray dose characteristics. He also wants to see a new imaging technology that can determine whether the obstructed segment of the artery is soft or hard in cases of chronic total obstruction of guide-wire access.

A growing number of patients are expected to undergo PCI in the future as more patients opt for this low-invasion procedure as an alternative to aortocoronary bypass graft surgery. “As a scientist, I will emphasise evidence. As a clinician, I will listen closely to what each patient has to say, and treat each patient based on experience and sensitivity,” says Iwabuchi. His interaction with Shimadzu products will continue to save the lives of many patients.

**Masashi Iwabuchi**

Director  
Department of  
Cardiovascular Medicine  
Cardiovascular Center  
Kokura Memorial Hospital





# Serving more countries than any other Shimadzu overseas affiliates

Shimadzu is expanding sales and services for reliable products in the Middle East and Africa where populations and economies are growing



Yoshiyuki Fujino  
General Manager

Shimadzu Middle East & Africa FZE (SMEA) has its roots in Shimadzu's Cairo Office in Egypt. The Cairo Office was launched in 1977 and relocated to Istanbul in Turkey in 1995. In 2007, Shimadzu established SMEA as an overseas affiliate in Dubai in the United Arab Emirates to serve those oil-producing countries in the Middle East that had taken off in the early 2000s when crude oil prices started rising. At the same time, the Istanbul Office was reorganized into one of SMEA's branch offices. Now, SMEA is serving more countries than any other Shimadzu overseas affiliates: 13 countries in the Middle East with a total population of 270 million and 53 countries in Africa with a total population of 950 million.

In these regions of population growth and economic development, SMEA is steadily increasing sales with good results especially in Turkey, Egypt, Saudi Arabia and South Africa. There are also growing expectations for increased demands due to reconstruction needs in Iraq.

Competition is fierce but a flexible approach is called for in these regions, which feature a diversity of religions, cultures and histories, as well as currencies and economic situations. The economic disparities both within each country and among regions are notable. Local customs, religions and business cultures each place specific requirements on business. In the Islamic world, for example, Fridays are holidays, and business activities including liaison and corporate performance management are decelerated during Ramadan — the holy month of fasting. In Africa, confirmation of payments often takes several months, requiring long-term approaches.

Recent political instabilities in the Middle East and North Africa, too, have delayed the revenue and expenditure accounting and the passage and implementation of budgets in each country. "Our business performance was adversely affected," says Yoshiyuki Fujino, general manager of SMEA.

Fujino points out that the keys to successful business in the Middle East and Africa are the "establishment of sales channels, development and improvement of the customer support system, and the ability to offer products that fit the buying power of customers in the region."

## SMEA expects increased business opportunities with new research and educational institutions and introduction of telediagnostic systems

SMEA's flagship analytical instrument is the high-performance liquid chromatograph (HPLC), which is actively sold to the research and development and quality management departments of pharmaceutical companies as well as universities, national research institutions and analytical service providers.

SMEA's initiatives, including regular visits to customers and the hosting of seminars, with the objective of achieving the largest share in the pharmaceutical market in each country, are paying off. In 2009, SMEA earned the lead position in the Turkish market, the largest market in the region. In the service training facilities located in the Dubai headquarters and the branch office in Turkey, service training sessions are held regularly for technicians at local distributors, contributing to customer support in each region.

Many countries in the regions are embracing the policy of industrial

development and educational enhancement to address the challenges of increasing population and unemployment, and many more universities and research institutes are expected to be constructed in the coming years. "There will be waves of major business opportunities for the wide-ranging line-up of Shimadzu products," says Hideya Nishi, area manager of the Scientific Division.

SMEA's major lines of medical equipment include general X-ray, mobile X-ray, fluoroscopy and Cath Lab, which are delivered to public and private hospitals. Their principal markets are Turkey, the United Arab Emirates, Saudi Arabia, Iraq, Algeria, Nigeria and South Africa.

Shuhei Hasegawa, area manager of the Medical Division, explains: "There are substantial needs for a one-stop solution in a digital X-ray diagnostic system." For those countries in the Middle East with a limited number of radiologists, SMEA is getting ready to supply a telediagnostic system that links large city hospitals with small rural hospitals. "This system has big potential in the future," Hasegawa emphasizes.

Nishi and Hasegawa agree that "SMEA's strength is the customer perception that Shimadzu products are high quality and reliable, and that they are backed by consistent after-sales support by us and by our local distributors."

For 2011, SMEA has a lofty sales target of \$54 million, topping the \$50 million target in 2008 when the medical Cath Lab became a major success. "Our philosophy is to focus on the accumulation of know-how in risk management and the establishment of trusting relationships through personal connections," says Fujino. "It is important that we show our business partners our commitment to achieving our goals, and make them feel comfortable going ahead with mutual investment."



Staff of the Dubai headquarters



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# News & Topics from Shimadzu

## Mobile X-ray System MobileDaRt Evolution now available with Wireless FPD

With no cables connecting the digital X-ray detector (FPD) to the main MobileDaRt unit, this model allows rapid positioning to reduce the burden on the patient. The simple hygiene management makes this model ideal for use in pediatric and orthopedic wards, as well as in intensive care units. These systems are becoming increasingly popular for emergency medicine, earthquake and other disaster relief, and for applications in infectious disease wards.



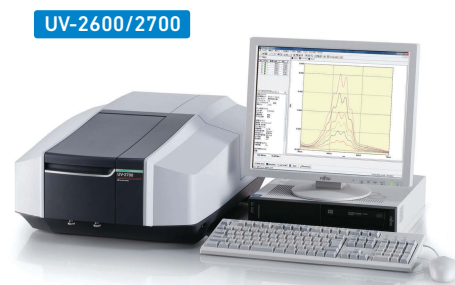
## Nexera MP Ultra High Performance Liquid Chromatograph Boosts Throughput for Pharmaceutical R&D

The Nexera MP is an ultra high performance liquid chromatograph unit designed for use as an LC/MS front end. It increases the LC/MS analysis throughput for R&D in pharmacokinetics and synthesis departments during the drug discovery process. This product combines ultra fast sample injection with the ultimate in low carryover and high repeatability. It can be combined with a Shimadzu mass spectrometer to configure a system for faster, more accurate analysis of multiple samples.



## Compact Spectrophotometer Offering More Extensive Materials Properties Evaluation and Simpler Instrument Inspection

UV-2600/2700 UV-VIS spectrophotometers are ideal for R&D and quality control in the fields of pharmaceuticals, foods, chemicals, environment, and life science. But they also offer highly accurate evaluation of the characteristics of materials used in the electrical and optical fields, including the anti-reflection films and polycrystalline silicon wafers for solar cells and the polarizing film for LCD panels. These models offer instrument validation software as standard to enhance the functionality and operability.




## National Cancer Center and Shimadzu Corporation Sign Comprehensive Collaborative Research Agreement

Shimadzu signed a comprehensive collaborative research agreement with the National Cancer Center, Tokyo on June 15 for the development of world-leading, pioneering advanced medical technologies for the treatment of cancer. The goal of the collaborative research is to develop medical technologies and systems that contribute to suppressing cancer and improving human health, such as the ultra-early diagnosis of cancers, pharmacokinetic analysis for innovation in drug discovery processes, and the development of medical treatment technologies.

## Dynamic Stent View Software Supports Smooth Cardiovascular Intervention Procedures

This software can be installed in Shimadzu cardiac angiography systems to enhance the visibility of micro stents implanted in cardiac blood vessels and to fix the stent position in realtime video images. The simultaneous display on the same monitor screen of a cardiac blood vessel overview image and fixed-position stent image as real-time dynamic images provides effective support for smooth medical procedures.



A Collection  
from nature and SHIMADZU  
Vol. 08

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