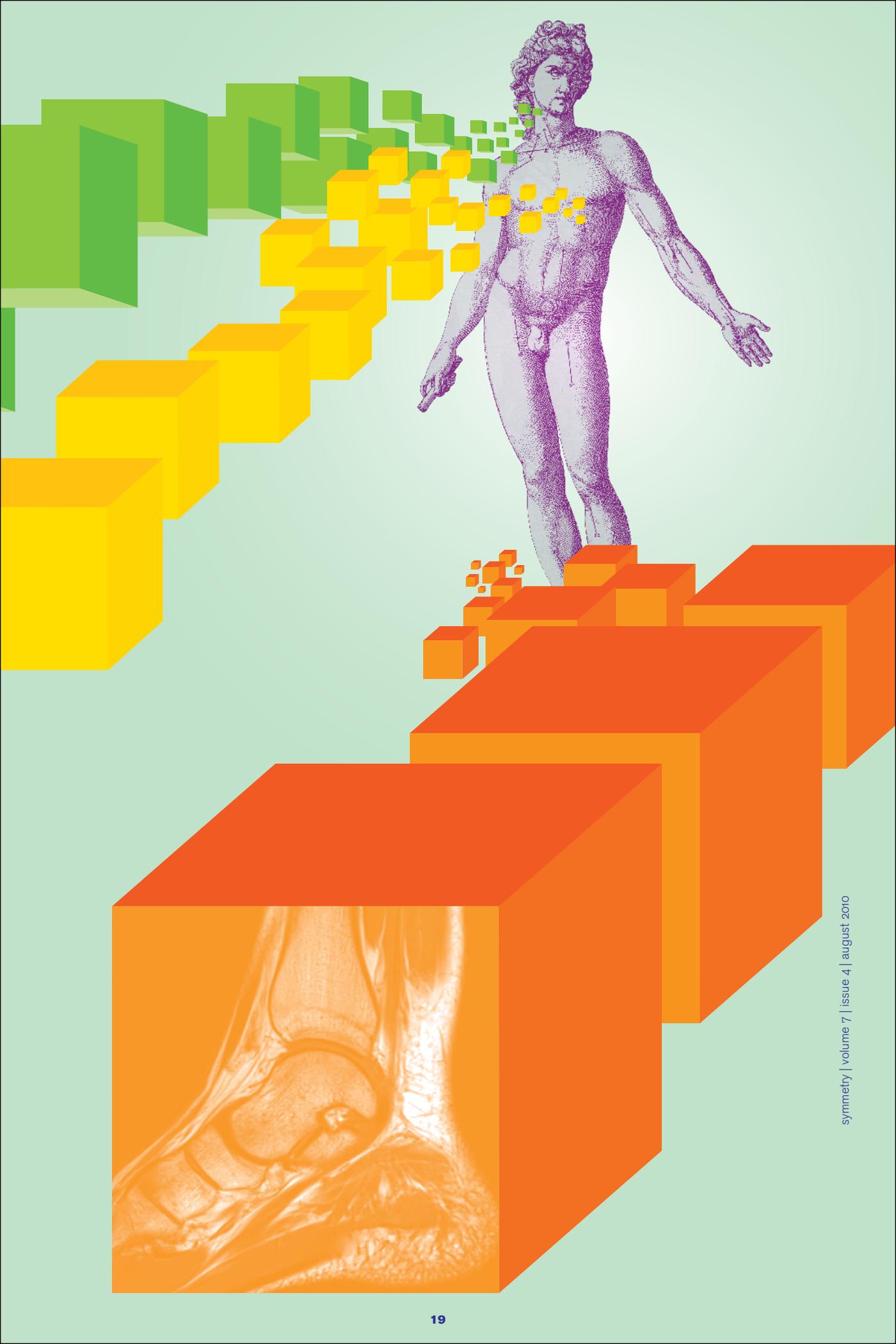


NEW IMAGING TOOLS FROM THE LHC

Technology developed for the Large Hadron Collider is changing the way we see our bodies.

By Daisy Yuhas



About four years ago, radiologist Anthony Butler was visiting CERN, the European particle physics laboratory, when he saw something that left him, as he put it, “flabbergasted.”

Michael Campbell, a CERN engineer, showed Butler a 14-square-millimeter electronic chip, the product of a decade’s research. It was derived from other chips that precisely record the charges and locations of individual particles coming into detectors at the Large Hadron Collider.

What Butler was astounded by, however, was not the physics. What surprised Butler was the chip’s potential in a *medical* context.

“I was flabbergasted to see this on a physics bench and not in a medical school,” Butler says.

This little X-ray imaging chip could find a home in biomedical imaging for more accurate and efficient diagnoses. It could transform the treatment and study of disease. It could be part of the first line of response for seriously injured patients in the emergency room or intensive care unit. And it’s just one example of how high-energy physics at the LHC has contributed to a growing revolution in our knowledge of the body.

POTENTIAL-PACKED PIXELS

Every second, the LHC brings billions of particles into high-energy collisions. The collider’s four detectors are like super-microscopes that illuminate the infinitesimally small, fleeting particles coming out of those collisions, looking for events that have never been seen before.

At the heart of the ATLAS detector sit 1744 silicon pixel sensors containing a total of 80 million pixels. A pixel is the smallest individual element of a digital image. Just as the millions of pixels in a digital camera capture photons, or particles of light, the ATLAS pixels record information about individual subatomic particles flying out from collisions. But they can just as well record X-rays, which are a form of light more energetic and penetrating than the light we see. That’s why scientists are so excited about their potential for medical imaging.

Researchers from the University of Bonn, led by Professor Norbert Wermes, slightly modified the ATLAS pixel sensor to create the Multi Picture Element Counter, or MPEC, in the early 2000s.

They found that MPEC and the follow-up CiX chips created clearer, cleaner X-ray images than conventional technology, while eliminating over- or under-exposure. Doctors get a sharper picture of what’s going on inside the body and the patient undergoes fewer examinations.

“The application is virtually a one-to-one transition of ATLAS to X-ray technology,” Wermes says. “I’ve never before in my scientific life seen such a straight spin-off application from fundamental research.”

WANDERING SOLUTIONS

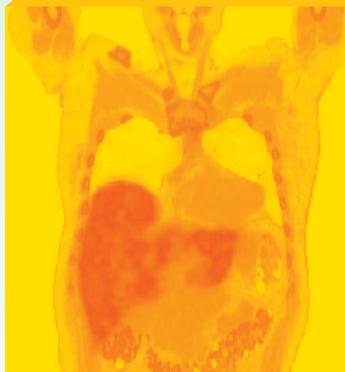
The chip that Campbell showed Butler four years ago at CERN was, like MPEC, a pixel detector. In the early 1990s, researchers creating detectors for multiple LHC technologies began testing the quality of their chips by recording X-rays emitted by a radioactive source. They realized in the process that their chip could also be a tool for medical imaging. They dubbed their project Medipix.

What makes Medipix special is its system of embedded electronics, which convert information about the locations and charges of individual particles into a digital format for more robust, efficient imaging. Campbell and his collaborators have created three generations of chips for a variety of non-physics projects, from dentistry to education.

“It’s like a solution walking around looking for a problem,” physicist Lawrence Pinsky of the University of Houston says of the chip’s protean abilities. Pinsky, who works on the LHC’s ALICE experiment, is using second-generation Medipix chips in dosimeters that keep track of astronauts’ space radiation exposure.

Campbell has been involved with the research since its beginning and is amazed by the diversity of applications.

“What we learned over the years is that bringing people in from other areas of science is not a simple one-plus-one-equals-two sum,” Campbell says. “They bring in other ideas and directions. It’s been quite an adventure.”



In a positron emission tomography (PET) scan, the patient swallows, inhales, or is injected with a radioactive tracer that accumulates in a particular part of the body. A scanner records gamma rays from the tracer and a computer processes the data, revealing oxygen consumption, blood flow, the metabolism of sugar, and other important body functions.

Image courtesy of Radiological Society of North America

PROBLEM FOUND!

Butler, affiliated with New Zealand's University of Canterbury and University of Otago, Christchurch, has a special fluency for translating technologies into the medical field. His research led to MARS, the Medipix All Resolution System CT Scanner.

Doctors use CT (computed tomography) scans to map the body's anatomy and condition. These scans X-ray the body from a number of angles and combine the digital images to get a comprehensive picture. In some cases the patient is given a "contrast agent," such as a solution containing barium or iodine, by injection or mouth to sharpen the view of a particular organ or system.

The MARS scanner is unique in that it can be used with several contrast agents at once. The resulting color images show multiple body systems at the same time, with greater clarity and less total radiation exposure from X-rays. For instance, an iodine contrast agent might light up the vascular system in red, while a barium agent paints a blue image of the liver. Since becoming commercially available in December 2009, the MARS scanner has been used to study cancer, heart disease, and the breakdown of blood vessels.

Someday, doctors could use these scanners in hospitals to monitor, in unprecedented detail, how a patient's body is responding to complicated internal injuries.

IF AT FIRST...

Transferring a technology like Medipix to the commercial sector requires strong support from the group of scientists that developed it. It can be an uphill battle to find funding for research and production.

Sherwood Parker of the University of Hawaii is familiar with these challenges. He was involved in the research and development of pixel detectors for the Superconducting Super Collider, then under construction in Texas, when the mother of one of his graduate students was diagnosed with breast cancer. He became intrigued by the possibility of applying his research to mammography for breast-cancer detection.

Parker's group set about developing an X-ray system for detecting breast cancer. This was 1993, however, and what Parker didn't know was that the ill-fated SSC would soon have its funding cut, and with it the funding for his group's project.

Parker and his group published their research, demonstrating that their X-ray system doubled the resolution of then-conventional technology with 10 times less radiation. However, their study came to a halt when the National Institutes of Health rejected their applications for funding.

THE MOLECULES OF LIFE

The experience could have dissuaded Parker from further attempts to transfer technologies to other fields. However, a few years later Parker found himself on the same committee that had once rejected his proposal. It was there that he met physician and biophysicist Edwin Westbrook, now director of the Molecular Biology Consortium.

At the time, Parker was working on advanced detectors for a future upgrade of the LHC, and he realized that one of these detectors could greatly improve data collection for Westbrook, who was using X-rays to probe the structures of proteins.

"I realized that I was talking to somebody who was writing the raw material for the textbooks of the future," Parker says. "Spin-offs don't only have to be for industry; they can be for basic research, and basic research can be used in the medicine of the future."

The system Parker and Westbrook are developing with Al Thompson of Lawrence Berkeley National Laboratory and Christopher Kenney of SLAC National Accelerator Laboratory is called 3DX. It's designed to aid biologists studying the structures of macromolecules such as proteins and DNA—studies that promise greater insight into the building blocks of life.

SIMPLY SCINTILLATING

At another LHC detector called CMS, physicists measure the energies of particles flying out of collisions with an electromagnetic calorimeter. The calorimeter contains 78,000 crystals that have been grown to very specific parameters so they produce light, or scintillate, when a particle passes. Physicists measure this scintillation to determine the particle's energy.

Developing these crystals for CMS began two decades before the LHC saw its first collisions. In 1990, physicist Paul Lecoq established a research group at CERN, called Crystal Clear, to study scintillating crystals.

"The collaboration was established to answer the requirements of the detector, which are continuously changing, and it continues to respond to new challenges," Lecoq says. "This requires that we maintain the front edge of this science."

While studying different kinds of crystals, the group became increasingly aware of how their research could benefit other projects. Since Crystal Clear began, they have researched scintillating crystals for use in industry, security applications such as luggage and cargo scanning, biology, and medicine, as well as in high-energy physics.

CLEAR AS CRYSTAL

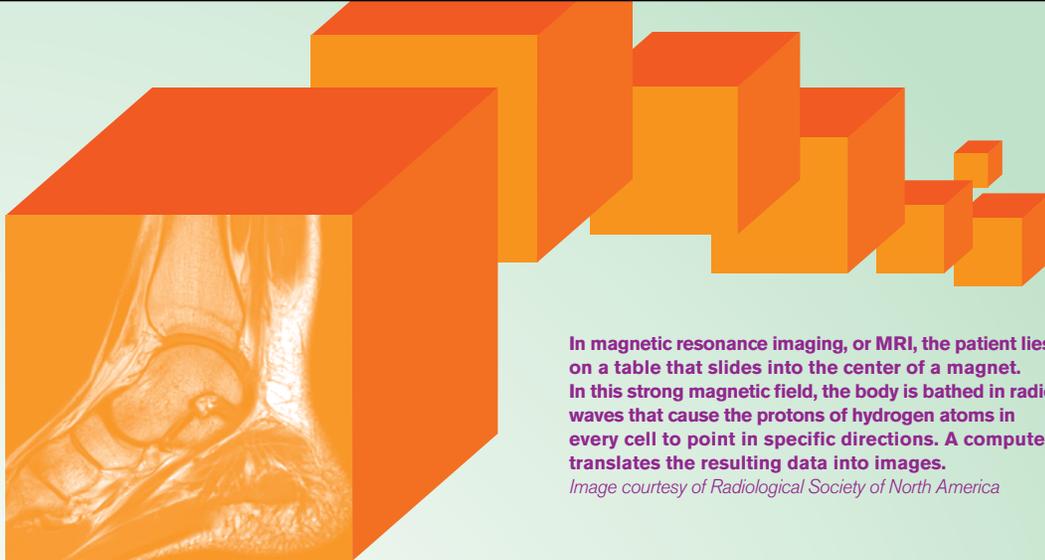
One of these cross-disciplinary projects was ClearPET, a positron emission tomographic or PET scanner that incorporates scintillating crystals. PET scans reveal the metabolic activity of organs and tissues, providing a window on the body's responses to disease and treatment. ClearPET does the same, but images small test subjects and small areas of the body in higher resolution than a conventional PET scan.

It was this feature that led to the development of a new target for scintillating-crystal research: mammography. Crystal Clear scientists in Portugal are developing what they call ClearPEM, using lessons learned from ClearPET for better breast cancer detection.

Computed tomography (CT) scanners X-ray the body from a number of angles and combine the data to get a comprehensive, 3D picture. In some cases the patient is given a "contrast agent" by mouth or injection to make the image crisper. These contrast agents—solutions of barium or iodide, for example—each light up a particular body organ or system.

Image courtesy of Radiological Society of North America





In magnetic resonance imaging, or MRI, the patient lies on a table that slides into the center of a magnet. In this strong magnetic field, the body is bathed in radio waves that cause the protons of hydrogen atoms in every cell to point in specific directions. A computer translates the resulting data into images.

Image courtesy of Radiological Society of North America

Today, researchers estimate that up to 60 percent of mammograms that show evidence for cancer are false positives. The Crystal Clear research suggests that ClearPEM is more than five times as sensitive and efficient as conventional X-ray mammography and could reduce the number of false positives, eliminating unnecessary biopsies and operations. ClearPET is now commercially available for a range of biological and biomedical studies.

WHAT COMES NEXT?

This successful interplay among fields inspired Lecoq's latest project, the European Center for Research in Medical Imaging (CERIMED), a multi-disciplinary training campus to research and develop new imaging technologies.

Already, participants have designed a ClearPEM with an ultrasound probe and will install the machine at Marseilles Hôpital Nord this autumn.

Dr. John O. Prior, professor and head of nuclear medicine at the Centre Hospitalier Universitaire Vaudois Lausanne, is one of the medical professionals involved with CERIMED. The rapid transfer of detector technologies to a medical setting—what he calls “bench to bedside”—is the focus of his research.

Looking ahead, Prior says, research into endoscopic probes could put radiation detectors inside the human body. Physicians could image tumors from within the body's natural openings or through minute holes in the skin. Recently developed hybrid PET/magnetic resonance scanners give unprecedented information about the brain. These could unlock medical mysteries and help find new drugs for treating neurological diseases, such as Alzheimer's, that are difficult to recognize and treat.

When doctors began using the CT scan in the late 1970s, the new information provided by the scan led physicians to change the course of treatment for their patients in 14 percent of cases. Already, new hybrid PET/CT scan technologies alter treatment in 30 percent of cases by revealing how the body is responding to a given therapy or drug. Advances in medical imaging allow doctors to tailor treatment to a particular tumor, based on its response to therapy.

Prior believes these advances will enable physicians to offer personalized medicine that is better adapted to their patients. Sensitive, low-radiation imaging makes it possible to understand the nuances of each individual.

SEEING THE FUTURE

No one knows what the next great advance or discovery will be. If the present pace of research is any indication, breakthrough techniques will exponentially increase through mutually supportive, cross-disciplinary research.

The progress made using LHC technology is an exciting reminder that in the quest to learn more about the universe, we also learn more about ourselves. When scientists and engineers apply complementary technology to medicine, they can improve medical diagnoses, treatment, and care. Technology and research in high-energy physics at the LHC can have a concrete impact on all of us.

We cannot actually see the future, but the future's imaging is getting clearer by the minute.