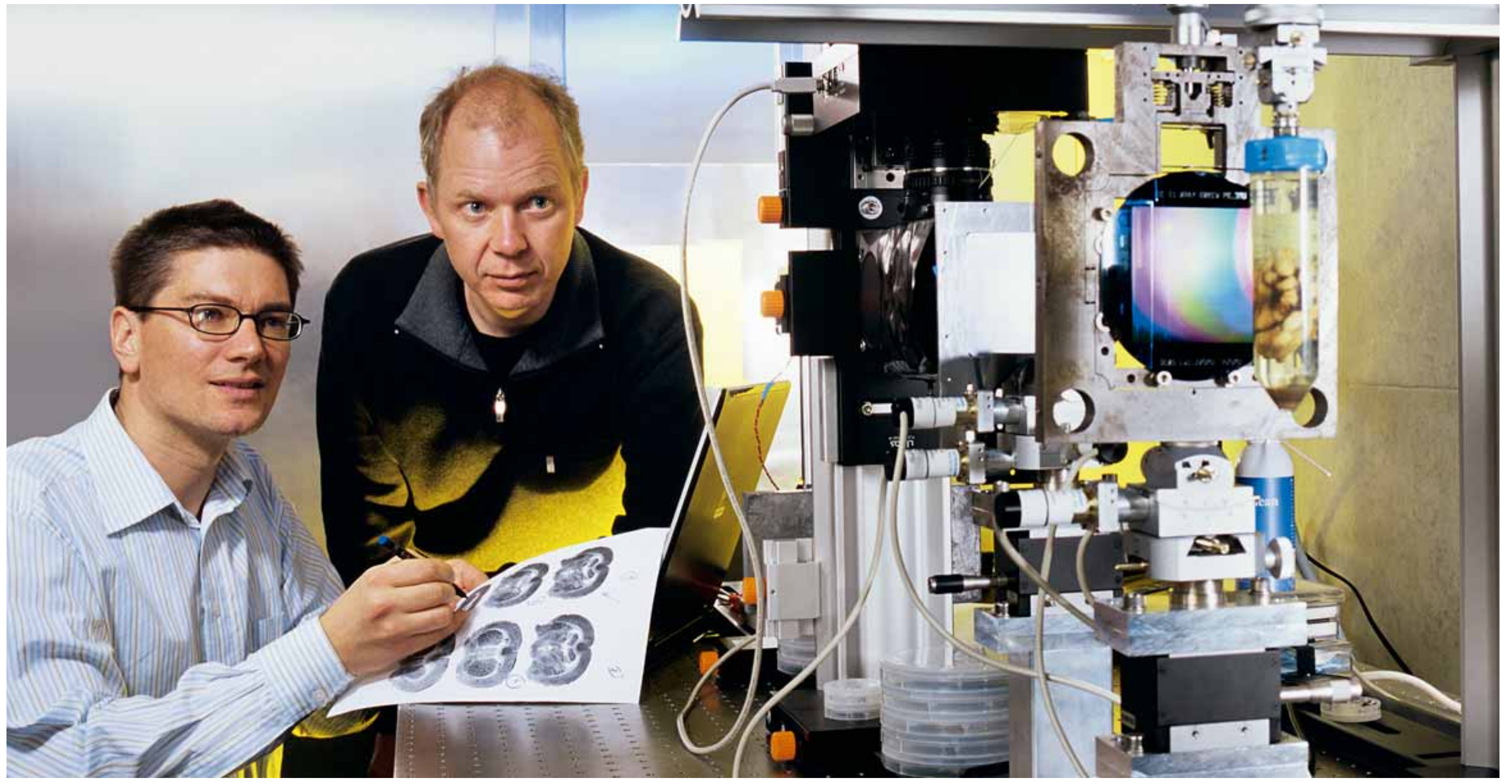


Franz Pfeiffer (left, above) uses a new radiography technique to create images with greater detail than conventional X-ray systems allow — as the photos of a fish and a Kinder surprise egg show (right).

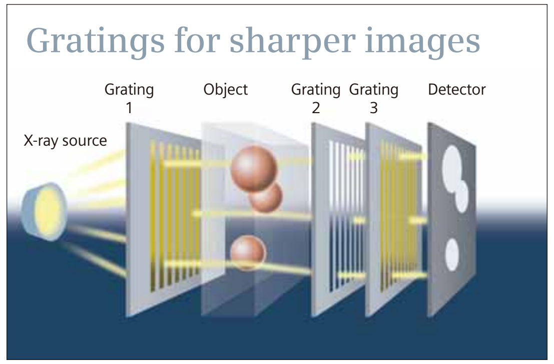
Soft Tissues Revealed

They're used every day in hospitals, but X-ray images don't really offer the kind of detail needed to determine the size and structure of a tumor. With a new technique called "phase-contrast X-ray imaging," however, this may be about to change.

An experienced radiographer can read much more from the gray tones of an X-ray image than can a lay person. But it can be difficult for even a trained eye to determine the exact size and structure of a tumor. This information, however, is vital for selecting the right treatment. In a joint project established in 2008 with the support of Germany's Federal Ministry of Education and Research (BMBF), researchers from Siemens, the University of Erlangen-Nürnberg, the Institute of Technology in Karlsruhe, and the Technical University of Munich (TUM) are now investigating a promising new imaging method known as "phase-contrast X-ray imaging."

Unlike conventional radiography, which is based on the absorption of X-rays, this technique could reveal various types of soft tissue such as muscles and tendons, all in high contrast. Conventional radiography exploits the fact that bone and tissue absorb X-rays to differing degrees. An X-ray image of the head, for example, will clearly reveal the bones of the skull, which absorb a lot of radiation, but not much of the brain, which shows up as just a uniform patch of gray. With higher soft tissue contrast, however, individual areas can be clearly distinguished, including any tissue abnormalities — such as a tumor. The technique could therefore reveal the size and position of a lesion at an early stage, enabling doctors to determine the right treatment, including the precise dosage of radiation therapy. The same applies to mammograms. Here, too, the new technique could improve the contrast of blurry images of breast tissue.

This improved performance is based on the fact that phase-contrast imaging not only measures X-ray absorption, but also shifts in the phase of the waves. Like visible light, X-rays can be regarded as both particles and waves. Whereas pure absorption-based radiography records whether X-rays penetrate anatomy or not, phase-contrast imaging measures the effect that passing through bodily tissue has on their phase — in other words, how much the (X-ray) waveform is shifted with respect to its original position. The same principle makes air bubbles visible in water, for instance, due to the different refractive indices of the two media. This phase shift is very revealing because it varies depending on the nature of the tissue through which the radiation is refracted. This effect is very small, though, and must be amplified.



Gratings for sharper images

However, until recently this was impossible with conventional X-ray systems. The first approaches to this problem emerged over 20 years ago and involved the use of special crystal optics. The method only works with monochromatic radiation, however, like that generated by an expensive synchrotron source. The difference between the radiation produced by this type of particle accelerator and that from a conventional X-ray source is similar to the difference between laser light and an incandescent light bulb. The waves of light emitted by a laser oscillate exactly in time with one another — that is, they are perfectly in phase. In similar fashion, the X-ray light from a synchrotron is almost completely synchronous. By contrast, the X-ray sources used in hospitals produce too much interference, because they radiate a spectrum of wavelengths in all directions. This is why the scientific world declared in 2004 that phase-contrast imaging was impossible with conventional X-ray sources.

But scientists hadn't reckoned with physicist Franz Pfeiffer, Professor of Biomedical Physics at the TUM. Back in 2004, Prof. Pfeiffer was researching at the Paul Scherrer Institute in Switzerland, where he went on to publish his revolutionary findings in 2006. Pfeiffer also used synchrotron radiation for his initial research, but in conjunction with a Talbot-Lau interferometer, a piece of equipment primarily found in atomic physics rather than X-ray physics. His groundbreaking idea was to also use the interferometer with a normal X-ray tube. His first phase-contrast images showed a fish at an unprecedented level of precision.

Pfeiffer's Talbot-Lau interferometer consists of three gratings made of silicon. These look like small plates with slits cut into them at intervals of only a few micrometers. The first grating's slits are filled with gold. It is placed between the X-ray source and the object under examination, and its job is to make the chaotic radiation emitted by the X-ray source as synchronous as possible. The gold absorbs the X-rays, while silicon lets them pass through, resulting in a large number of quasi-coherent X-ray waves. When these waves strike tissue, they alter their phase. The second grating consists purely of silicon. Its job is to recombine the individual partial waves — a process known to specialists as interference.

At the same time, the part of the radiation that passes through the silicon undergoes an additional —and in this instance exactly known — phase shift. This is what makes it possible for the phase information contained in the X-rays to be deciphered by means of the third grating. Like the first grating, the third one consists of silicon and gold. To measure wave intensity, this grating is moved relative to the second grating, and a detector records the signals. The measured values are compared to measurements made without the object. The difference between the two is the phase contrast, and it is visible in the image as levels of gray.

In 2006, shortly after Pfeiffer had published his image of a fish, he started working with Siemens. His initial encounter occurred at a trade fair for X-ray systems. Siemens researchers, including Dr. Eckhard Hempel, at that time with the company's Healthcare Sector, immediately recognized the potential of Pfeiffer's development. The remaining partners came on board in 2008, the year the project was launched. "Integrating phase-contrast X-ray imaging in a conventional X-ray system for human diagnostics was a radical idea — and it still is," says Hempel. "But we succeeded in showing that it works. And that's why we won in the BMBF Innovation Competition for the Advancement of Medical Technology."

Low Radiation. The project's goal is an instrument that will seamlessly integrate into everyday hospital procedures. To do that, it must be no larger than a conventional system and must not exceed the time or cost of today's examinations. With this in mind, the Karlsruhe Institute of Technology is enhancing the gratings, and the University of Erlangen-Nürnberg is improving the detectors. Siemens researchers, meanwhile, are working with Pfeiffer's team on integrating the interferometer into an X-ray system. The demands placed on the components pose special challenges. Medical imaging requires the use of high-energy X-rays, so the gratings' slits have to be finer than those in Pfeiffer's system — in this case, no more than 2.5 micrometers across. Similarly, the gaps between the gratings, X-ray source, and detector could be freely modified in Pfeiffer's original setup. In the new system, all these components will have to fit into less space.

In 2004, experts declared that phase-contrast imaging was impossible — but Pfeiffer proved them wrong.

The detectors will also have to be adapted to the new specifications. As with a digital camera, the images from the new X-ray system are made up of pixels. The more radiation and the greater the number of pixels, the better the image quality. In the interest of patients, however, radiation dosage must be minimized. Finding the optimal combination here is the job of researchers led by Prof. Gisela Anton of the University of Erlangen-Nürnberg. They aim to improve the detector and the parameters of the grating structure so that the best image can be achieved with the least possible radiation exposure.

The project is scheduled for completion in 2012, but that won't be the end of the research. Unlike absorption radiography, which can draw on many years of experience, the field of phase-contrast X-ray imaging is largely unexplored. "That's what's so fascinating," says Anton. "There's so much to investigate." For her and the other scientists, the biggest motivation is knowing the benefit that this new technique will bring to doctors and patients alike. For as soon as phase-contrast imaging works in clinical practice — and none of the partners sees any reason to doubt this — it will likely open up a host of new diagnostic possibilities. ■ *Helen Sedlmeier*