toward [Halley containing] pristine material of the solar system present during its formation," he said. "What we know of interstellar dust, but that's very little, is compatible with the Halley results [as well]," he added. Whether interstellar dust simply agglomerated on the frigid fringes of the solar nebula to form Halley, or interstellar dust vaporized in the heat of the solar nebula and then recondensed remains to be seen.

Geiss emphasized that a productive application of the Halley analyses would be to use them to identify which of those particles now being collected in the earth's stratosphere are comet dust. Some of these relatively large interplanetary dust particles have been proposed as possible comet dust. But Robert Walker of Washington University in St. Louis points out that to produce more than the present circumstantial evidence linking the two, extensive analyses must be performed on stratospheric dust at the size scale of Halley dust. All the Halley particles whose impact-vaporized remains were analyzed by spacecraft instruments do not equal one 10-micrometer stratospheric dust particle, he notes. The analytical tools to duplicate the Halley analyses in the laboratory are only now becoming available.

Even before researchers could see that Halley is made of enticingly primitive material, it was obvious that there must be a great deal more cometary material in the solar system than once thought. Until the spacecraft got close enough to pierce Halley's shroud of dust and gas, most astronomers presumed that unseen comet nuclei were bright or at least not too dark and therefore relatively small, typically a few kilometers across. But instead of being bright and 6 kilometers in diameter, as recently predicted, Halley's nucleus is black and about 16 kilometers long and 8 kilometers wide.

On the basis of the old assumptions, Paul Weissman of the Jet Propulsion Laboratory had calculated that the Oort cloud, the tenuous halo of comets circling the sun far beyond Pluto, contained 2 Earth masses of cometary material. Incorporating the blackness of nuclei as well as other recent developments into his calculations, Weissman now estimates that the Oort cloud contains 25 Earth masses of comets. That makes it easier for comets to have supplied Earth's reservoirs of water and other volatile gases through bombardment early in the history of the solar system. It also means that comet impacts created a larger proportion of the impact craters on Earth, a possible cause of biological extinctions. And, notes Weissman, comets may constitute a significant fraction of interstellar material, which was assumed to be almost all gas and microscopic dust. ■ RICHARD A. KERR

Synchrotron X-rays Probe Coronary Arteries

Although not yet up to clinical quality, images of coronary arteries in three patients at Stanford encourage hopes for a safe and inexpensive diagnostic technique for heart disease

THE first images of coronary arteries in human patients taken by means of a new technique that requires the intense radiation from a synchrotron light source have been reported by researchers at Stanford. Although the images are not yet of clinical quality, the technique is considerably less invasive and potentially less expensive than coronary angiography, the x-ray method now in widespread use for detecting trouble spots in the system of arteries that supply blood to the heart.

It is conceivable that geographically scattered regional centers housing compact synchrotron x-ray sources could someday provide coronary artery imaging services for those diagnosed as having heart disease. Long-term serial studies for establishing the natural history of coronary atherosclerosis and its response to treatment, as well as widespread screening of those at risk for this disease but not yet evidencing any symptoms are other possibilities.

Coronary angiography requires that a catheter be inserted into a patient's peripheral artery (in the thigh, for example), after which it is pushed through the arterial system toward the heart. The tip of the catheter is moved to the point in the aorta where either the left or right coronary artery has its origin, according to which is to be imaged, and a concentrated dye containing x-ray absorbing iodine is injected into the artery. The x-ray image therefore shows where blood is flowing normally in the coronary arteries and where the flow is reduced or blocked altogether because of atherosclerosis.

Although coronary angiography generates images of high quality, it poses some risk to the patient. In a presentation in October to the annual users' meeting of the Stanford Synchrotron Radiation Laboratory (SSRL), where the experiments were done, Edward Rubenstein of the Stanford University School of Medicine* noted that complications occur in about 1% of patients. These include heart attacks and strokes when the insertion of the catheter dislodges from the walls of arteries atherosclerotic deposits that then travel to the coronary arteries or to the brain. Fatalities occur about 0.1% of the time.

In addition to the risk, coronary angiography is expensive and requires a 2-night stay in a hospital. The average cost is about $3500. Nonetheless, because coronary angiography is essential before heart surgery, almost one million procedures are done each year in the United States, so that providing this service is a multibillion dollar enterprise. Although heart disease remains the leading cause of death in the United States, coronary angiography is plainly an unsuitable technique for screening large numbers of nominally healthy people in an effort to find those who are developing life-threatening conditions.

Conventional coronary angiography requires injection of the concentrated dye because of the low sensitivity of x-ray imaging systems to the dye. Synchrotron radiation has three features that combined with electronic x-ray detectors and computers make possible an attractive alternative to angiography. The first is that synchrotron light comes in a smooth, continuous spectrum; the second is that the light is very intense; and the third is that the beam is naturally highly collimated.

Because the beam is collimated, researchers can use a crystal monochromator to select by Bragg diffraction any wavelength of interest from the broad spectrum, and the high intensity guarantees enough x-ray photons at the selected wavelength to be useful. By recording image intensities with an electronic detector at two wavelengths, one just above and one just below an x-ray absorption edge for iodine (or another chemical element) in a dye and subtracting the logarithms of the intensities from one another on a computer, it is possible to eliminate nearly all contributions to an image except those due to the dye.

*In addition to Rubenstein, the researchers are Robert Hofstadter, Herbert Zeman, and John Otis of Stanford University; Albert Thompson of the Lawrence Berkeley Laboratory; George Brown of the Stanford Synchrotron Radiation Laboratory; John Giacomini, Helen Gordon, Robert Kernoff, and Donald Harrison of the Stanford Medical School; and William Thomlinson of the National Synchrotron Light Source.

With the dramatically enhanced contrast resulting from this digital subtraction technique made feasible by synchrotron radiation, the dye need only be injected into the central venous circulation by means of a catheter inserted into a vein. The dye eventually reaches the coronary arteries in much diluted form. With veins, there is little risk of the type associated with catheterization of an artery, and hospitalization is also unnecessary. At the SSRL users' meeting, for example, Stanford medical physicist Herbert Zeman told a questioner that the three patients studied were each "fitted" with a catheter inserted through the right jugular vein at a local hospital and taken in an ambulance to SSRL, where they were able to walk around while waiting for the images to be made.

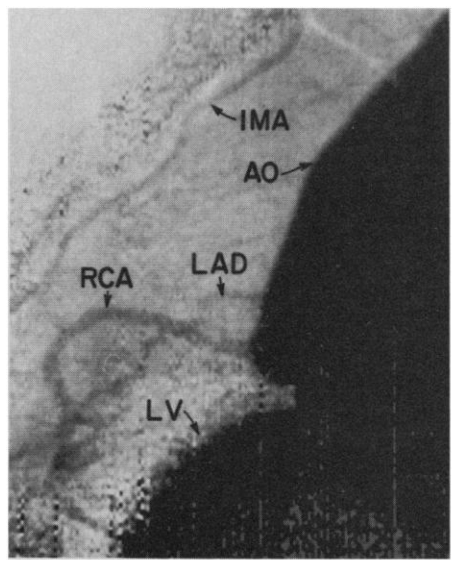
Experiments began at SSRL in 1979 with artificial objects (phantoms) and excised pig hearts and progressed to anesthetized dogs 3 years later. By last May, the dog images were nearing clinical quality, and researchers decided to try human subjects. Three male volunteers ranging in age from 41 to 52, one who had had coronary angiograms following a heart attack and two after episodes of angina, were selected. The goal was to determine if the new technique, which Rubenstein called synchrotron radiation-based transvenous angiography, could find features known to be present from conventional coronary angiography.

In sum, the images were not of clinical quality, partly because of the increased x-ray absorption of the human body, which is thicker than that of a dog and which lowered the signal-to-noise ratio. The spatial resolution of the digital images, 0.5 millimeter, was also poorer than that of conventional coronary angiograms on x-ray film. Nonetheless, the main coronary arteries were imaged, including the left anterior descending artery and the right coronary artery. It was also possible to identify grafts of the saphenous vein and internal mammary artery that had been made to bypass an obstructed coronary artery. In one patient, the image showed a flaw in a saphenous vein graft that subsequently caused a recurrence of angina and had to be surgically corrected.

A major difference between the images made by the synchrotron radiation technique and conventional coronary angiograms is due to the insertion of the catheter through a vein. Because of this otherwise positive feature, the dye finds its way into the aorta as well as the coronary arteries, so that the arteries cannot be seen where they cross the aorta. For example, the circumflex artery that passes behind the heart is hard to see, especially behind the left ventricle.

In a second presentation at SSRL, Zeman discussed some computer image enhancement strategies to deal with this difficulty. The idea is to suppress large features in the image, such as the aorta, so that smaller features, such as the arteries, are made clearly visible. The method remains to be perfected, but Zeman reported that in one early test it was possible to see part of the circumflex artery in a dog.

According to Rubenstein, improvements in the present synchrotron radiation–based method for obtaining images should be sufficient to bring them to clinical quality. The main thing needed is to increase the x-ray intensity, which will raise the signal-to-noise ratio and, in conjunction with a new electronic detector, will enhance the spatial resolution by a factor of 2 to a value of 0.25 millimeter.



Transvenous coronary *angiogram recorded in a human subject using synchrotron radiation. The structures visualized include the ascending aorta (AO), the left ventricle (LV), an internal mammary artery (IMA), the left anterior descending coronary artery (LAD), and the proximal right coronary artery (RCA).* [*Courtesy of the* Proceedings of the National Academy of Sciences, U.S.A.]

At present, two silicon crystals intercept an x-ray beam 123 millimeters wide and 3 millimeters high that emerges from a specially designed port on the synchrotron source. The crystals are oriented to diffract two spatially separated beams of x-rays, each 0.5 millimeter high, that converge toward the patient, one with a wavelength just below and one just above the iodine K absorption edge. Two rapidly rotating drums, each with ten flat facets, alternately pass one beam then the other. A linear position-sensitive detector records the intensities of x-rays passing through the patient at each wavelength in a total of 4 milliseconds, thereby generating one line of the full two-dimensional image. The patient sits on a chair moving vertically at a comfortable rate of 6 to 12 centimeters per second. In this way, the image is built up a line at a time with no blurring due to motion of the heart.

Improvements slated for the next round of experiments at SSRL next month include the use of germanium rather than silicon crystals. Germanium will diffract roughly twice as many x-ray photons because of its higher atomic number. The group will also eliminate the rotating drums, which will raise the x-ray intensity reaching the patient by another factor of 2.5. To accomplish this, a new dual detector is being built at the Lawrence Berkeley Laboratory that will record x-rays at both wavelengths simultaneously. A future version of this detector will also achieve the 0.25-millimeter spatial resolution. Rubenstein estimates that the x-ray intensity must be raised by a factor of 8 to obtain images of clinical quality. The extra intensity over that made possible by the instrumental improvements is available at Brookhaven National Laboratory's National Synchrotron Light Source, and experiments there are planned for next fall.

If image quality improves so that it is at least equal to that of conventional coronary angiography, the question arises as to how to make the technique available to physicians and their patients in a practical way. Clinical practice is incompatible with the large synchrotron light research facilities that now serve dozens of users with diverse needs simultaneously, and the cost of traveling to such centers could upset any economic advantage that the synchrotron technique might otherwise have. Helmut Wiedemann of SSRL has been looking into the feasibility of a compact synchrotron x-ray source and finds the numbers interesting.

Such a source might be 10 meters in diameter and might cost $30 million to build and put into operation, which is too large and too expensive for most hospitals. An alternative is a network of regional centers. Twenty centers of this type, which could handle as outpatients the 1 million or so patients now undergoing coronary angiography, would cost "only" $600 million. Typical operating costs for synchrotron sources, says Wiedemann, are 10% of the construction cost or $60 million annually. If correct, these figures compare favorably with the yearly expenditures on coronary angiography. ■ ARTHUR L. ROBINSON

ADDITIONAL READING

E. Rubenstein *et al.*, "Transvenous coronary angiography in humans using synchrotron radiation," *Proc. Natl. Acad. Sci. U.S.A.* **83**, 9724 (1986).