SYNCHROTRON RADIATION FOR TRANSVENOUS CORONARY ANGIOGRAPHY*

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The present method of visualizing the coronary arteries is unsuited for long-term, serial assessment of the natural history of coronary atherosclerosis and its response to interventions, and unsuited for screening asymptomatic populations at risk. For these reasons, an effort has been underway at Stanford University to develop a means of visualizing the coronary arteries following the intravenous injection of contrast agents such as iodine. The approach is based on the use of synchrotron radiation, which is generated by a new class of accelerators employed in particle physics.

This field of physics is concerned with the pursuit of information about the ultimate structure of matter. The search focuses on the identification of truly elementary objects, if these exist. The central experimental method has been to observe the consequences of collisions between particles. In conventional experiments, one particle serves as a stationary target and the other as an incoming missile, propelled by energy imparted to it in a linear accelerator. The longer the accelerator, the greater the energy of the incoming particle. The impact is made to occur within the confines of detectors, which provide information about properties such as mass, electric charge, lifetimes, and decay products.

Inferences drawn from such experiments led to speculations about primordial units of structure that cannot not be studied by using stationary target particles and incoming particles from linear accelerators, since the length of the accelerators would need to be so great as to make them impractical devices.

These considerations resulted in the development of the storage ring,

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into which a stream of fast particles, bearing electric charge, is injected, usually from a linear accelerator. The trajectory of the beam of high-speed particles is made to conform with the shape of the oval storage ring by the fields of a lattice of magnets deployed around it.

The original intent of such devices was to bring about head-on collisions between counter-rotating antithetical particles, such as electrons and positrons. Such collisions result in the mutual annihilation of the particles, with the local release of energy equal to the rest masses of the two particles plus the kinetic energy of each. Such miniature fire balls of energy can condense into new, massive particles whose properties are observed as they come into being and then decay. This is the strategy that provided experimental confirmation of the quark hypothesis and led to the formulation of the theory of quantum chromodynamics.

During the operation of the storage ring, intense beams of radiation are produced (1). These are generated as a result of the change in energy of the particles as they slow down while traversing the curved sections of the storage ring. The lost kinetic energy materializes as a beam of radiation emitted in the plane of the orbiting particles. The radiation is characterized by a smooth continuous spectrum extending from the infrared to hard x-rays, a high degree of polarization, and by extreme natural collimation.

The latter property is a result of a relativistic transformation, that is, a physical change which occurs when objects move at speeds very close to the speed of light. When a particle emits light while it propagates at a relativistic velocity, the emission is confined to a beacon-like beam, projected in front of the moving particle. Particles moving at ordinary velocities tend to emit radiation isotropically, that is, more or less equally in all directions. In the case of relativistic particles, the solid angle of the cone into which light is emitted is a function of how fast the particles are moving; the faster they travel the narrower the beam. When they whirl inside a storage ring at energies of several billion electron volts, the solid angle is only a fraction of a milliradian. In other words, the radiation is virtually confined to a plane.

The spectral components of such radiation can be readily separated by passage through a crystal: polychromatic radiation enters the crystal, monochromatic radiation exits it. The "color" or frequency of the diffracted radiation can be selected by adjusting the angle at which the radiation enters the crystal.

The intensity of the radiation produced in storage rings is enormous. For instance, at the Stanford Synchrotron Radiation Laboratory, the flux in the x-ray domain is 100,000 times greater than the radiation that can be obtained from the most powerful rotating anode generators. Thus, the intensity after monochromatization remains high enough to allow the recording of images during very brief, motion-freezing exposures, of the order of a few milliseconds.

The emission produced in a storage ring is known as synchrotron radiation. The name derives from the fact that the orbiting particles (usually electrons) lose energy as they negotiate the curved sections and therefore slow down. To maintain them in orbit at their original velocity, the energy they lose in each curved section must be restored. The energy replenishment is provided by klystrons or radio-frequency generators which supply pulses of electromagnetic energy. The need for precise synchronization of these pulses with the passage of the bunches of electrons emerging from a curved section into a straightaway gave rise to the name synchrotron radiation.

IMAGING WITH SYNCHROTRON RADIATION

The imaging method employed in synchrotron radiation-based angiography is known as iodine K-edge dichromography. The strategy is based upon the interaction between x-ray photons and matter. X-ray photons (at energies less than one million electron volts) are attenuated as they pass through matter by two independent processes: the Compton effect and the Einstein or photoelectric effect.

In the Compton interaction, an incident photon strikes an electron in an atom, transfers part of its momentum to the electron, scatters at an angle of 0–180°, and may then engage in subsequent collisions.

In the photoelectric process, the incoming photon is totally absorbed by the electron and cannot engage in other interactions. The photoelectric process occurs only when the energy of the incident photon matches or exceeds the energy binding the electron to the atomic nucleus. This binding energy is a function of the number of protons in the nucleus and the position of the electron in the orbitals of the atom. In the case of the innermost (K-shell) electrons in iodine, the binding energy is 33.17 keV. The photoelectric effect does not occur unless the x-ray photon matches or exceeds this energy. In K-edge dichromography, two x-ray beams are used, one with energy immediately above and the other with energy immediately below the K-edge energy of iodine (2, 3). If an image is made of a subject in whom there is an iodine-containing contrast agent in the circulation, the x-ray image taken with the energy just above the K-edge value will contain information relating to the Compton and photoelectric effects of the atoms of the body as well as of the iodine. The second image, taken with energy just below 33.17 keV, will contain virtually identical Compton and photoelectric effects arising from the attenuation by atoms of the body and by the Compton interaction of iodine, but will contain no information arising from the photoelectric effect of iodine.

The logarithmic subtraction of the recordings of these two x-ray beams maximally enhances signals arising from iodine and maximally suppresses signals arising from soft tissue and bone. The duration of each exposure is only 4 msec; therefore blurring owing to motion is comparable to that which occurs during conventional coronary angiography. The spatial resolution is 0.5 mm. A transvenous coronary angiogram done on an anesthetized dog is shown (Figure 1).

Overlapping iodinated structures present a problem. Because of the epicardial position of the coronary arteries, projection angles are chosen which allow the visualization of the arteries in positions in which they are well separated from the endocardium. Digital edge-enhancement methods are also employed to reduce the effects of contrast agent contained in overlapping structures.

The radiation does per scan is about one-half a rad. Therefore if five scans are required to provide clinically useful views of the coronary circulation, the total x-ray dose would be 2.5–3 rads. This dose would be increased if greater radiation flux were used to improve signal quality.

FIG. 1. This is a transvenous angiogram done on the anesthetized dog at the Stanford Synchrotron Radiation Laboratory. The left anterior descending coronary artery and the proximal right coronary artery can be seen arising from the ascending aorta. (Reprinted with permission from Hughes EB, Rubenstein E, Zeman HD, et al. Prospects for noninvasive angiography with tunable x-rays. *Nuclear Instruments and Methods in Physics Research* 1985; B10/11: 323.)

The x-ray dose should, however, be considerably less than that of conventional invasive coronary arteriography, which is about 35 rads.

If experiments in human subjects indicate that this method can assess the anatomy of the coronary circulation, then facilities currently available at the Stanford Synchrotron Radiation Laboratory, and soon to be available at the National Synchrotron Light Source at Brookhaven, could be used for the evaluation of the natural history of coronary atherosclerosis and the effectiveness of therapeutic interventions.

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DISCUSSION

James (Birmingham): I was trying to do a quick calculation of the volume of the injection you would make in a dog with an average thousand milliliter blood volume. It seems like it would be 40–50 milliliters. Is that the ballpark of how much you inject?

Rubenstein: It's about 12–18 ml of Renografin-76 for a 25 kilo dog.

Burrows (Boston): This is obviously another very exotic, and exquisite at the same time, technology that we'll have to anticipate being introduced into clinical medicine eventually, along with other high technology. But I have an elementary question. On one of your pictures there was some apparent beading in the coronaries and I'm wondering if that was an artifact of the technique or does it represent some sort of streamlining of the injected material?

Rubenstein: The question relates to the fine detail seen in the coronary arteries of the excised pig heart. The beading is owing to the fact that by accident we injected air along with the contrast agent. The artifacts mimicked atherosclerotic changes, and since we hope to see 0.5 mm structures we have deliberately used this technique to demonstrate objects of this size. I would also like to comment on your remarks about high technology. There are two storage rings in the United States currently capable of doing angiography. One is SSRL at Stanford—the machine that you have seen, the other is NSLS at Brookhaven. The latter device is just coming on line, and should be available for medical studies next year. Although this technology is not currently suitable for screening populations or for use in individuals suspected of coronary disease, we believe that it might be a useful approach for doing long-term studies of the natural history of atherosclerosis and for establishing responses to interventions. So we hope to use the facilities at those two laboratories in that way. There are methods for reducing the size of these machines, making them smaller than they are now and perhaps appropriate on a regional basis for clinical purposes. This issue needs to be addressed by more work.