Medical Accelerators

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There are almost a million cases of cancer a year in the United States. Roughly half a million people die of cancer a year here. This is about half of what happens with heart disease and cardiovascular disease. Every year cardiovascular diseases account for more deaths than all the U.S. citizens who have died in all the wars that the United States has ever been in.

You may argue then that we shouldn't be working on cancer. Instead, we should be working on cardiovascular diseases. But, in the last decade the rate of cardiovascular deaths has come down by approximately 10 percent because of better diet, more exercise, and all the other factors that we know about now. On the other hand, the number of cancer deaths has increased at a steady rate of several percent per year. This is why it's worth working on the cancer problem.

Table I shows the mortality rates for different cancers. Notice that the largest cancer rate in men is lung cancer, followed closely by prostate cancer. The largest incidence of cancer in women is breast cancer, followed closely by cancer of the rectum.

It's important and relevant that these are all rather deep-seated cancers and cannot be gotten at by methods that only deal with the surface. Figure 1 illustrates that cancer is a disease that is very much a function of age. This is the reason that we are more concerned about cancer now than people were 100 years ago. A century ago they died of other things before they had time to get cancer.

There are three general methods of treating cancer: surgical, medical (using chemotherapy and drugs), and radiation. With all the advances that are going on in gene therapy and related techniques, I suspect the long-range answer to cancer therapy are the techniques using chemotherapy and drugs. Eventually, people may understand how to treat all the many kinds of cancer using those

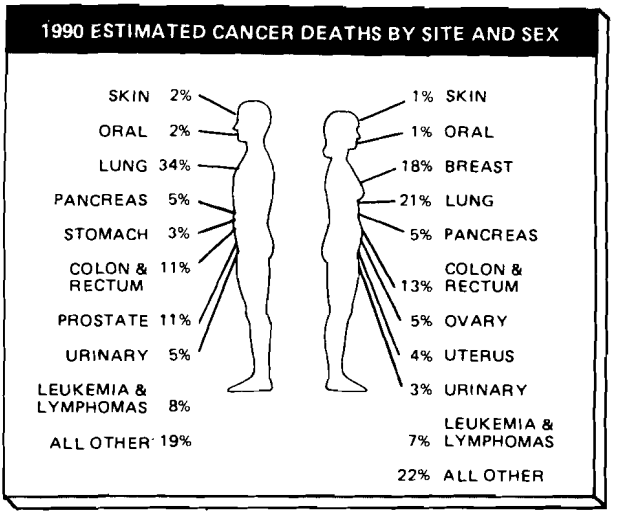


Table I: Mortality rates for different cancers.

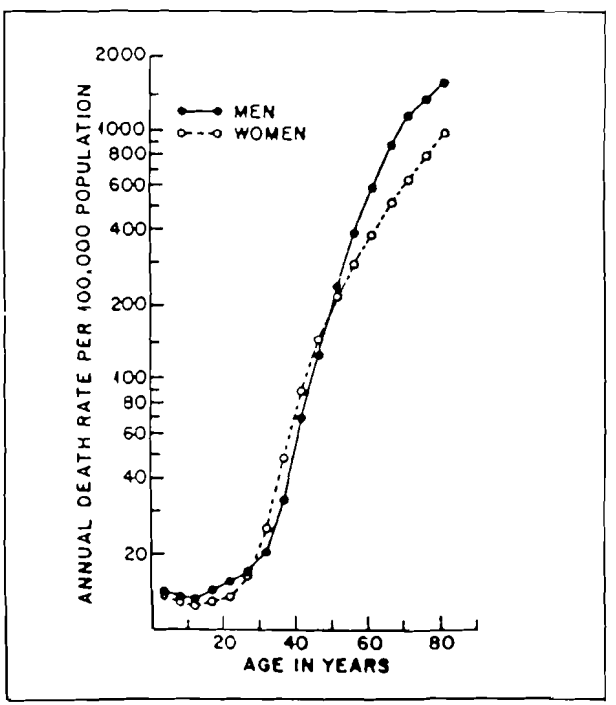


Figure 1: Cancer death rate as a function of age.

techniques. But when half a million people die each year, there's a lot that can be done in the meantime. That's where radiation comes in.

Radiation treatment began almost as soon as Roentgen discovered x-rays. People soon started sticking their hands in the way of x-rays machines. As a result, many of the x-ray pioneers died of cancer.

The modern x-ray tube became practical when Coolidge invented the sealed-off tube in 1916 for General Electric. From 1920 to the 1940s, people did x-ray therapy using these x-ray tubes. That period is now referred to in medicine as the ortho-voltage era.

After the end of World War II, when there had been such striking advances in electronics, people began building electron linear accelerators for this purpose. Betatrons had also been recently invented. For some years, betatrons were very much used for cancer therapy.

Nowadays the x-ray accelerator market is totally dominated by linacs. More than a thousand linacs have been sold for this purpose. For scale note that there are 7000 hospitals in the United States. That is a large market.

The problem with x-rays is that they burn a great deal. The absorption is largely in the skin area. While x-rays are fairly effective biologically, it is difficult to irradiate a deep-seated tumor.

Early in the history of therapy, Ernest Lawrence, the inventor of the cyclotron, and his brother John Lawrence, who is a physician, treated some people with neutrons. These were very preliminary studies. There is no good way to understand the results from the work of the Lawrence brothers.

After World War II there were also great advances in particle accelerators. During that period people began using neutrons for therapy in a serious way, but neutron therapy didn't accomplish very much until Fermilab began doing it in 1974. The Fermilab facility has now treated approximately 2000 patients with neutron therapy. The system uses the existing proton linac for medical purposes between injection pulses into the main accelerator complex. The Fermilab program employs facilities thrown together from other sources. A shielded treatment cave was built around an existing freight elevator. The patient is aligned and positioned at ground level and then taken down to the treatment level on the

elevator. The preliminary concept was much more grand, but it was clearly too early to build such a facility.

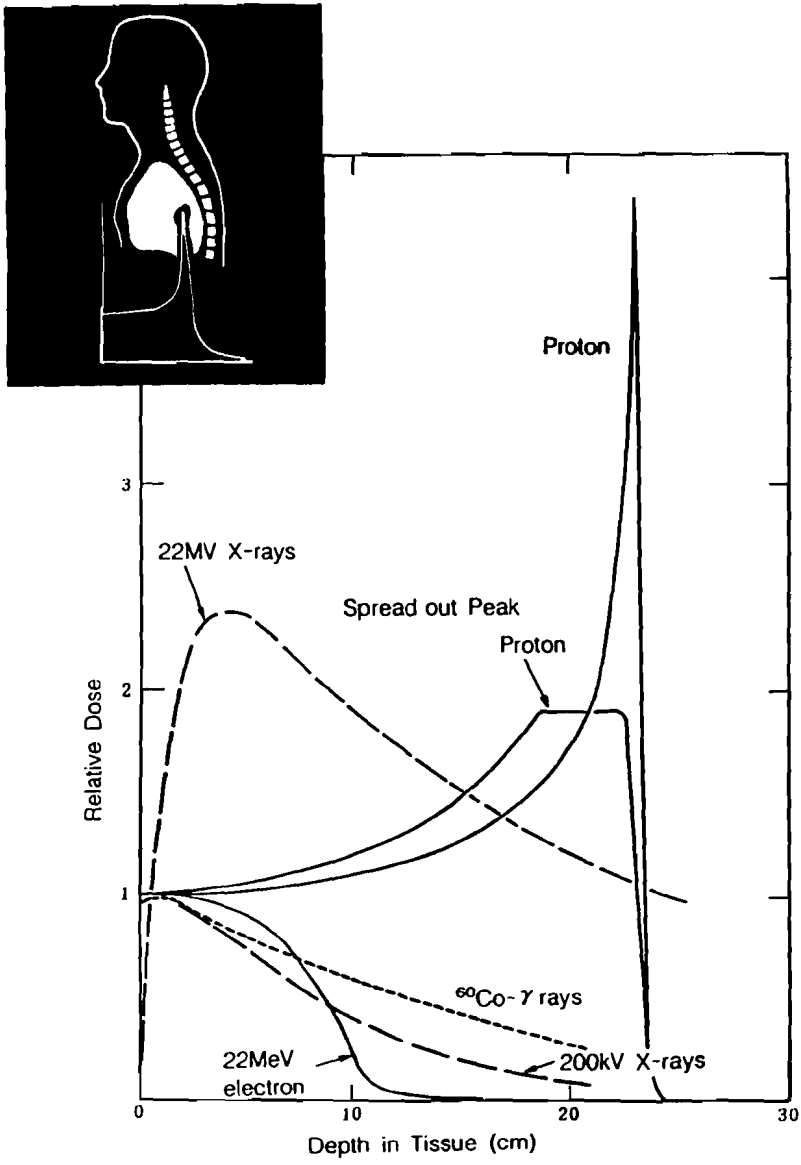
Our original plan also was to use protons for treatment because our Linac accelerates protons. When we approached the medical people in the area, they were not ready to do treatments with protons. As a result, we developed a neutron therapy facility instead.

Neutrons have far greater biological effectiveness than x-rays. They zap tumors better than photons, x-rays, or electrons. The problem is they wander around. They do not have a clean dose distribution. Finally, the cost to build a neutron facility is relatively high.

Nonetheless, there's a lot of interest in such therapy. Dr. Arlene Lennox has made a proposal to Rush-Presbyterian-St. Luke Hospital to build a linear accelerator specifically for neutron therapy in the basement of one of the buildings at the complex. There's very serious consideration of that proposal. An industrial firm would do the actual construction of the accelerator.

An additional way to do this is with charged particles. Consideration of this possibility began in 1946 when Robert R. Wilson, the founding director of Fermilab, wrote a famous paper proposing the use of protons for medical treatment. The advantage of using protons is that they stop in a very definite place. They do not wander around in tissue as neutrons do. When they stop they deposit much of their energy near the end of their track in the peak shown in Fig. 2. The figure compares proton energy loss to 22-MeV x-rays, cobalt gamma rays, and electrons. In the latter cases, most of the dose is distributed close to the surface. The horizontal scale is the depth. Notice that the proton has an exaggerated peak where almost all the energy is deposited at the end of the track. This is the Bragg peak, named after its discoverer, a British physicist. Usually in therapy the peak is spread out somewhat by absorbers. With this technique the distribution can be flattened to cover a larger depth on each pulse.

The obvious way to do an irradiation with protons is to use the highest energy to irradiate the back of the tumor, then to step the energy down and come forward in the tumor. That process continues until the whole tumor had been irradiated. At the same time collimators would be used to mold the beam transversely to the shape of the tumor.



Comparison of depth dose distribution for X–, γ–ray and electron beam with proton beam

Figure 2: Energy loss of protons compared to 22-MeV x-rays and electrons.

That approach has been developed and used experimentally at the Harvard Cyclotron Laboratory. That is an accelerator that Wilson started to build, and then left when he went to Cornell. The studies have been done in a collaboration between Harvard and Massachusetts General Hospital. Several thousand patients have been treated with good results. The proton energy is too low to reach deep-seated tumors.

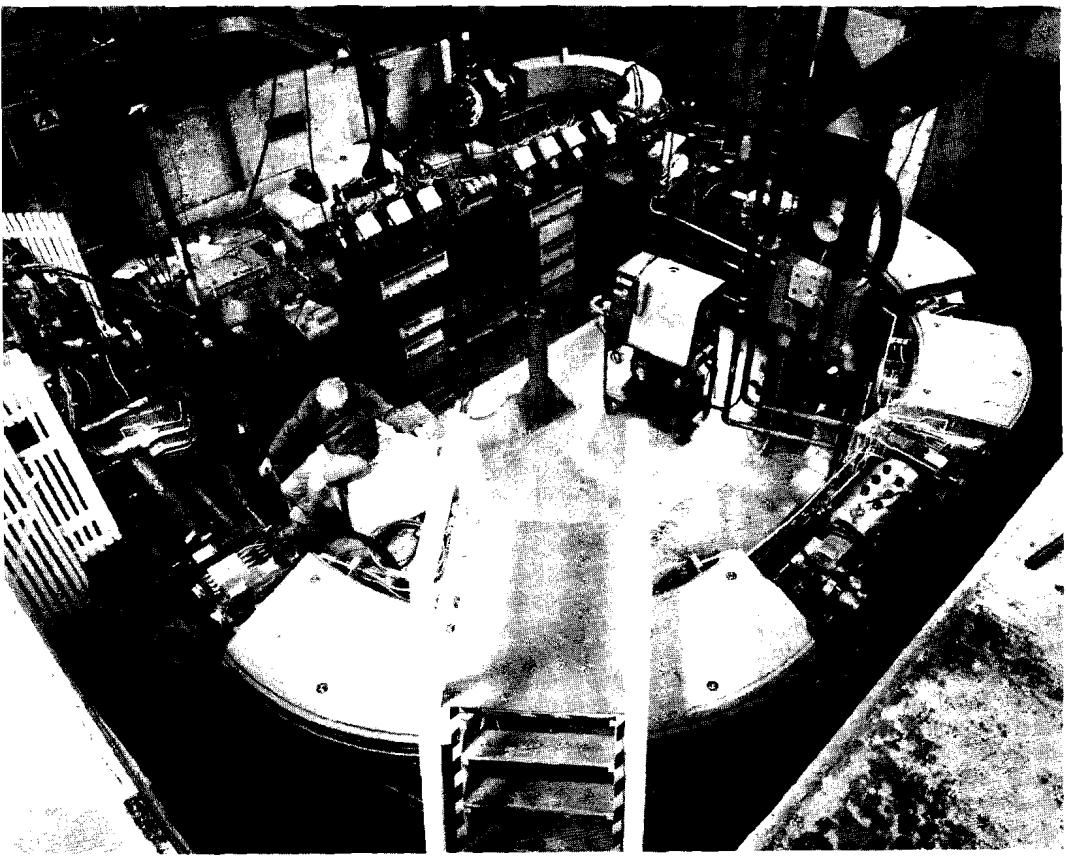
At the University of California, Berkeley, scientists and physicians have been doing therapy with heavier particles, that is, heavy ions, for many years. Figure 3 compares the biological effectiveness, the dose distribution, and the cost for all these different particles.

A team working as Los Alamos did some therapy with pi mesons (pions). That type of work is still being carried on at the cyclotron in Zurich, Switzerland. The difficulty with using heavy particles and pions is that the cost is extremely high to produce those particles. It was for that reason that, when interest in charged-particle therapy returned in 1985, protons were the direction in which to go. At that time, Loma Linda University Medical Center approached Fermilab about collaborating in the construction of a proton accelerator for cancer therapy. After agreement was reached, Fermilab and Loma Linda went through a long design process, resulting in the accelerator and treatment facility I will now describe.

Figure 4 shows the accelerator that has emerged from this collaboration. It is about 20 feet across. Since this photograph was taken the injector has been installed over the accelerator. At Loma Linda the beams will come out to four separate treatment rooms as well as to a research beam for calibration and dose studies. There will be more bending magnets in the beam transport lines than there are in the accelerator. The entire facility is approximately 200 feet long, and is two levels below ground. Three treatment rooms each have rotating gantries that bring the beam to the patient from any angle. The gantries are 30 feet in diameter, and take up about three floors. All of this is to go in a building which is now almost complete at Loma Linda. The accelerator will be installed during the winter of 1989-90. The gantries that rotate the beam are being built close to Loma Linda in Riverside, only about 10 miles away. The dipole magnets for the beamline are being built in Palo Alto and delivery should begin soon. The power supplies are being built in Toronto and are now being delivered.

PARTICLE	BIOLOGICAL EFFECTIVENESS	DOSE DISTRIBUTION	COST
Photon	Fair	Poor	Low
Electron	Fair	Poor	Low
Neutron	Good	Poor	High
Proton or Helium	Fair	Good	High
Heavy Particle	Good	Good	Very High
Pion	Good	Good	Extr. High

Figure 3: Comparison of cost for different particles (including heavy ions).



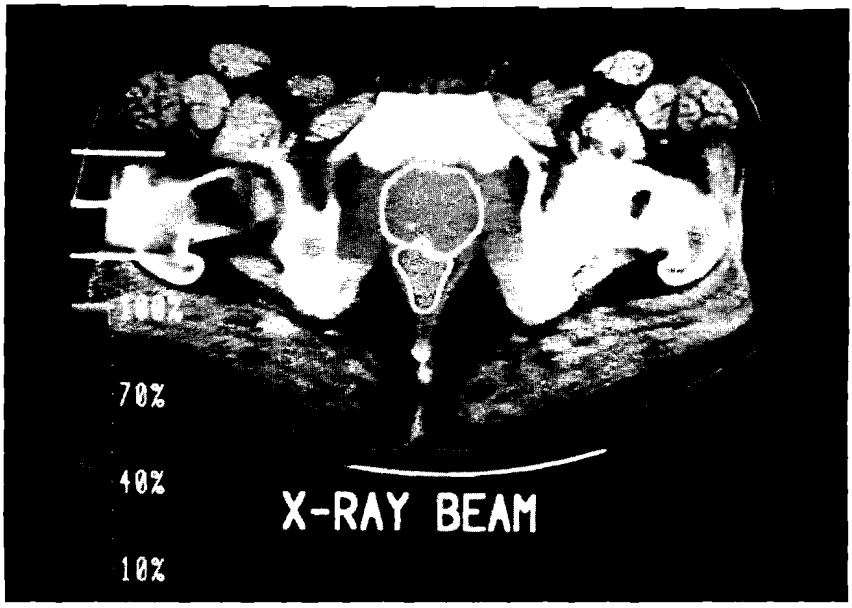
gure 4: Picture of Loma Linda accelerator.

The next several figures show how this treatment method works. They are simulations of typical treatments of a given tumor. Suppose I use an x-ray beam and treat a tumor in the hip area. The rectum, which is nearby, is much more sensitive to radiation than most other tissue, something like a factor of three. If an x-ray beam coming from one side is used, almost all the dose is deposited in the area coming in and very little actually gets to the tumor. Compare this with using a proton beam and coming in from one side (Fig. 6). By far the largest part of the dose is deposited in the tumor area when the proton beam is used. Much less of the beam is deposited on the way in. Note that this is not just one shot of protons. It is a careful gradation of energy coupled with scattering masks to help shape the dose distribution. Obviously there is a large advantage to using protons.

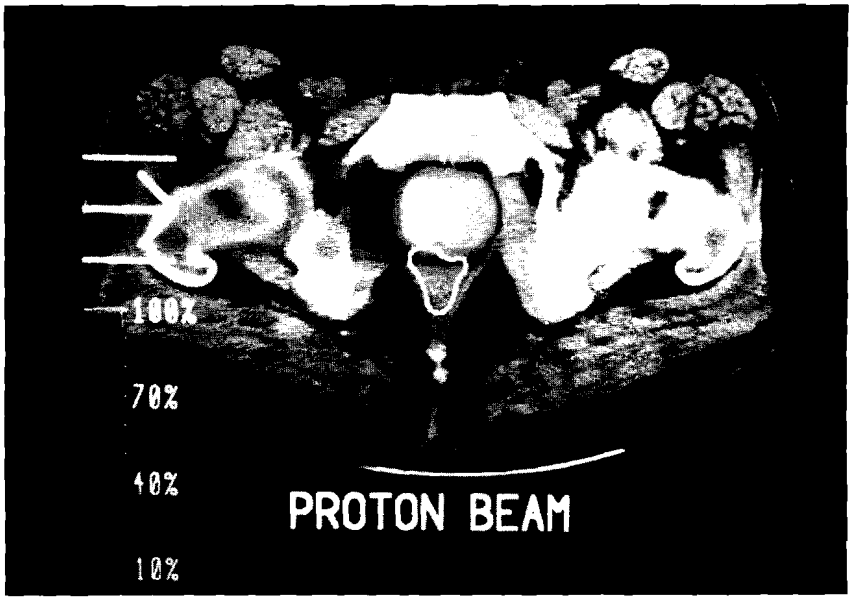
Now, what's usually done with x-rays to try to ameliorate the depth distribution is to come in from several different angles. These are called "portals" in the medical world. Coming in from two directions with x-rays does a better job of hitting the tumor (Fig. 7).

The same thing can be done with protons. That attack produces much better results (Fig. 8). The only difficulty is that there is a high-radiation area just touching one part of the rectum. That can be taken care of by coming in through three portals. Figure 9 shows what can be done with the x-ray beam using three portals. The situation is better except a fraction of the sensitive area has still been irradiated. If a three-portal approach is used with all the appropriate masks and careful control of the energy, it's possible to do an almost perfect job of confining the energy to the tumor site (Fig. 10). This is the advantage of proton therapy with the Loma Linda-Fermilab accelerator.

The accelerator has been commissioned at Fermilab. The machine produced a beam and has run very reliably. So far it has not run at the design intensity. There are two major reasons for the lower intensity. One is that the final radio-frequency power supply for the injector was a year late in delivery (on a six-month job!). The system we threw together just didn't have enough power to do the job. We are sure that we'll get a lot more injected particles when enough power is put in. The second reason the intensity is low is that we used a borrowed power supply for the magnets that had a lot of ripple and we have had considerable beam loss as we accelerate arising from that ripple. That will not



'igure 5: Simulation of hip dose near the rectum - one x-ray.



gure 6: Proton beam from one side.

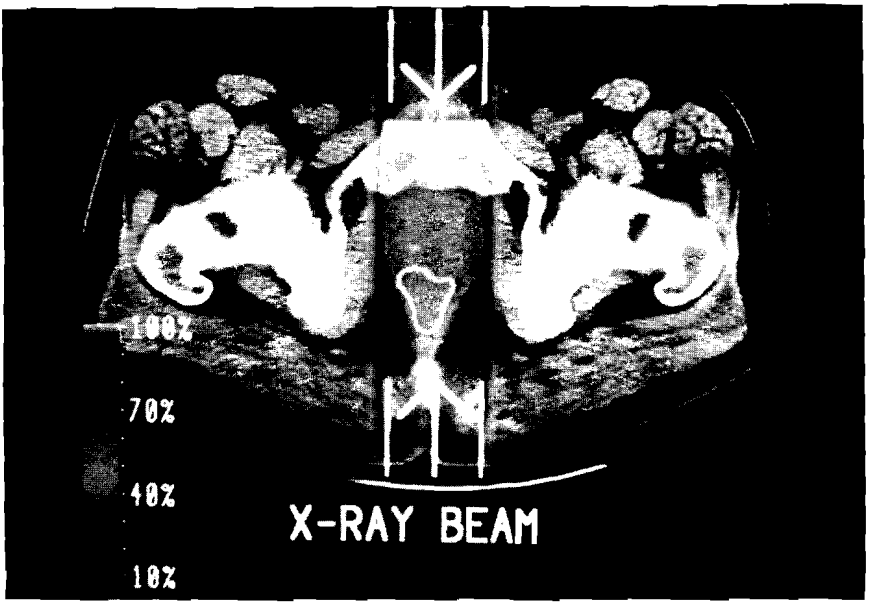


Figure 7: X-rays from two directions.

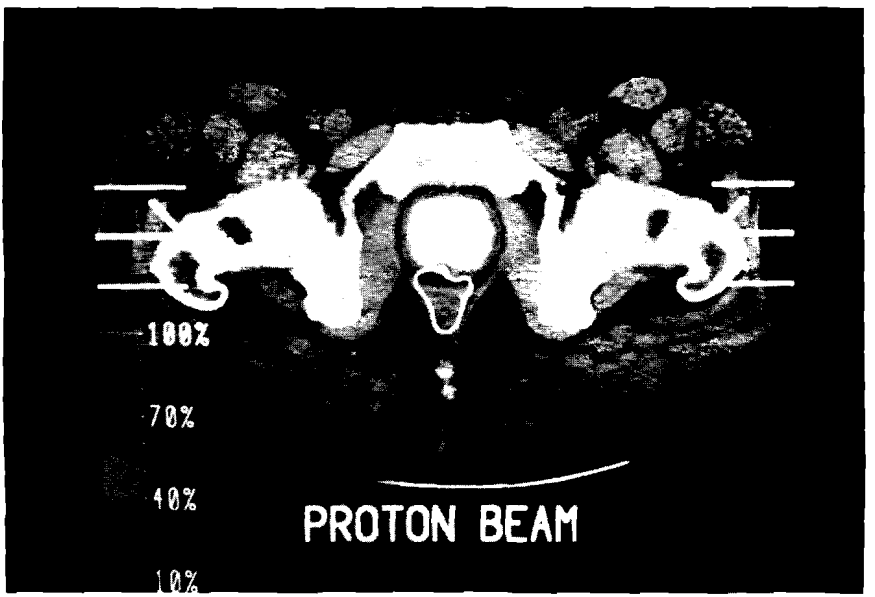


Figure 8: Protons from two directions.

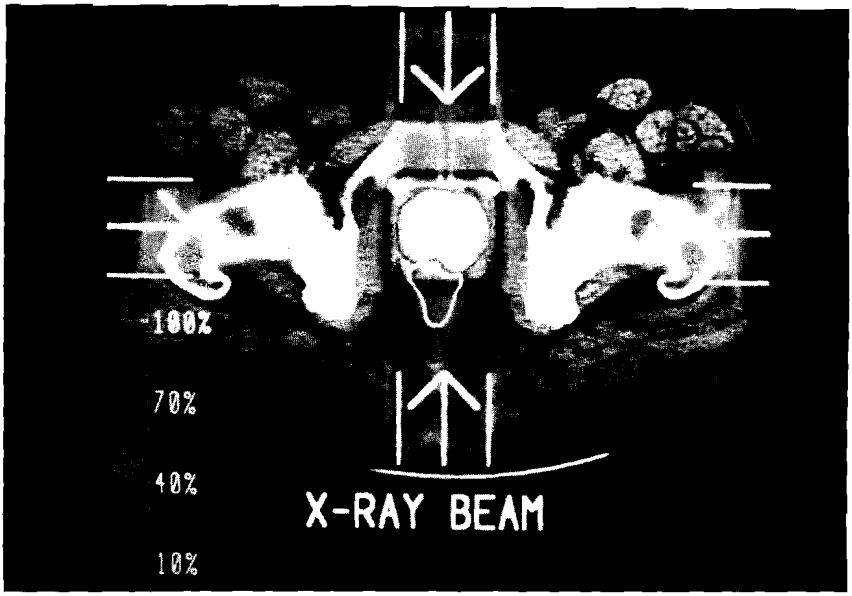


Figure 9: X-rays — three portals.

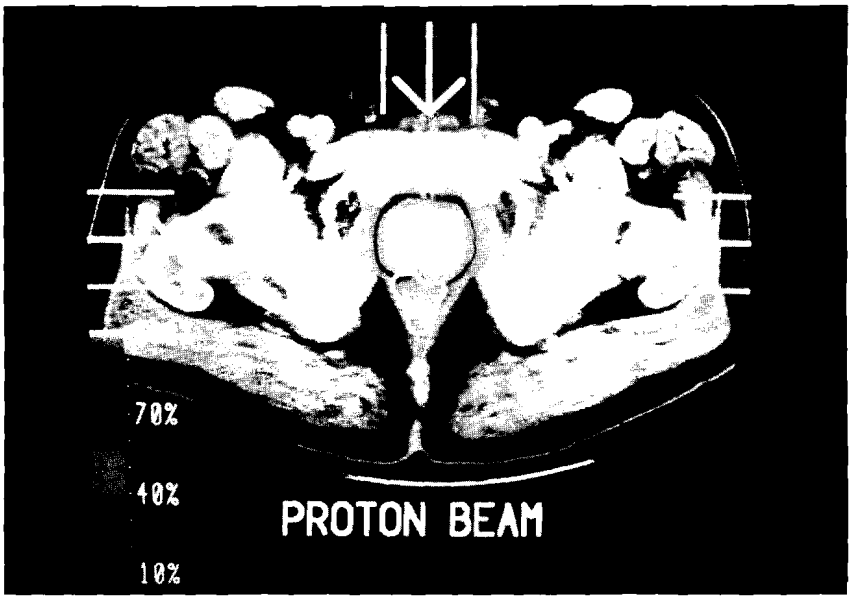


Figure 10: Protons — three portals.

get fixed until the accelerator is installed at Loma Linda because the final power supply is being built in industry and will be delivered directly to Loma Linda.

Early in the game Fermilab and Loma Linda took into account the possibility of commercialization. Loma Linda enlisted an industrial partner Science Applications International Corporation. SAIC is in charge of the re-commissioning at Loma Linda. If it should be your heart's desire to buy a proton accelerator, the place to go to see about that would not be Fermilab, but Science Applications International. Their plan is to provide such accelerators for hospitals that want them in all the different varieties that are desired.

I want to close by noting something that I've learned in the three years I've worked on this project. These comments aren't meant to denigrate hospitals or physicians in any way. This project is terribly high tech. Here at Fermilab we keep saying that's easy and we've done it. But that's not at all true for people in hospitals. That's because they have been trained to do different things from us and they think about their work in a different way. A physicist's approach is sometimes to turn on a new power supply and see where the smoke comes out. You don't do that with patients.

Hospitals like Loma Linda do have particle accelerators and experience with them, but these accelerators arrive at the hospital and are installed in a day or less. Then someone from the company tells them which button to press for on and which for off. If the hospital staff gets in trouble, they have a telephone number to call for service. That is very different from the experience they will have with the proton therapy accelerator.

The Fermilab-Loma Linda machine is going to be a difficult device for a hospital to learn how to deal with. It is a new order of magnitude of operation for them, and they will need staff to help them with the accelerator because it will take several people to keep it going.

In addition there is an enormous amount of peripheral equipment that must come together to make it a useful machine. The reason that there wasn't any great interest in proton therapy for many years was that no one knew exactly where the boundaries of the tumor were anyway. Not until there was CT scanning and magnetic resonance imaging could one really find the outline of the tumor very precisely. All those devices need to be present and be used in con-

junction with the accelerator in a computerized system in order to optimize the treatment plan. Not only are all of those elegant devices required, the CT scanners and MRIs and positron emission tomography, and so on, but there is an enormous investment needed in software to do all the simulations and treatment planning. By now Fermilab and Loma Linda together have gone a fair way toward doing much of this. I hope this project will bring a new era of treatment that will prove itself in a reasonable length of time.