August and September, spewed oil along stretches of shore along the Kolva River near Kolva village, damaging grazing areas for cattle and reindeer. A team of scientists from the Institute of Biology in the Komi Scientific Center in Syktyvkar reported last November that the bottom of the Kolva River was denuded of life. A "complete absence of benthos from bottom sediments," the researchers stated, suggests the ecological condition of the waterways in Usinsk is "critical." Any additional pollution from further run-off "should be expected to disrupt the food web at every level," says stream ecologist Anne Hershey of the University of Minnesota, Duluth.

The spill is the latest insult to an ecosystem already weakened by previous oil spills, and observers fear the Komi's inhabitants may lose a valuable resource—commercial fishing for salmon, whitefish, flounder, and perch—if the health of the watershed is further degraded. According to the World Bank, the fish catch in the Usinsk region had declined from 68 tons in 1976 to 8.4 tons in 1994. In a recent study, Komineft concluded that recent spills have decreased the fish populations in several Usinsk streams by 70% to 75%, a level that begins to threaten even subsistence fishermen. If the dikes break, oil swept into the Kolva River could contaminate the much larger Pechora River, "threatening salmon and important fishery spawning grounds," concludes a World Bank report.

Even if the oil is cleaned up, however, the taiga marshes are likely to remain damaged. "One of the absolute hallmark rules is that if you spill oil in a marsh, you'll do more damage getting the oil out than the oil does itself," says Jerry Galt, an oceanographer with the National Oceanic and Atmospheric Administration's hazardous materials response division in Seattle. "Some of the marshes will be destroyed for a very long time," he says. That will pose the greatest problem for reindeer herders, who will be forced to drive their herds along a different route between summer and winter grazing areas.

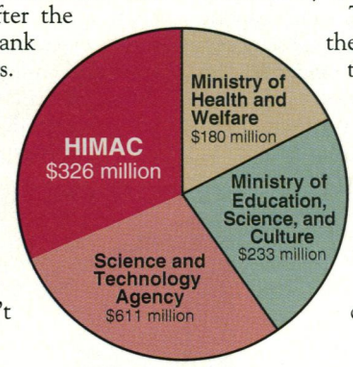
Russian authorities at first were reluctant to come to grips with the spill, and Komineft's official estimate of its extent—14,000 tons—is seven times smaller than independent estimates. But the World Bank's McKay says he has seen a change in attitude in recent months. Russian officials "are much more willing and open now," he says. That new attitude is essential, McKay says, for Russian scientists to gain access to the threatened regions to monitor water quality and the spread of oil into cattle and reindeer grazing areas. Armed with that information, experts may be able to predict whether next spring will signal a time of renewal or resignation for the residents of Komi.

–Richard Stone

JAPAN

Chiba's Heavy-Ion Accelerator Battles Cancer and Critics

CHIBA, JAPAN—The world's only heavy-ion accelerator dedicated to cancer therapy has performed well in its clinical debut, say researchers at Japan's National Institute of Radiological Sciences (NIRS): In late March the institute reported that the first three patients to undergo treatment were able to return to work after the therapy significantly shrank their primary head tumors. Although these preliminary results are far from conclusive, they are welcome news to the Japanese government, which put up $326 million to build the facility and is spending $45 million a year to operate it. But they won't damp down a controversy about the wisdom of putting so much money into an unproven therapy. Nor do they erase concerns about the way clinical trials, involving thousands of patients over the next several years, will be evaluated.



Hefty slice. The program that funded HIMAC is part of a $2.4 billion anti-cancer effort in the past decade.

The project was recognized as a costly scientific gamble ever since the government, in the early 1980s, decided to build an accelerator-based cancer therapy center as part of a national 10-year plan to combat cancer. Completed last year, the Heavy-Ion Medical Accelerator in Chiba (HIMAC), outside Tokyo, is designed to tackle hard-to-treat cancers of the head and neck, brain, and lungs (*Science*, 3 September 1993, p. 1270). Previous experiments with particle beams, including tests conducted in the United States, indicated that the technology shows promise in treating such cancers. But some Japanese cancer researchers have questioned whether this promise is sufficient to justify the huge investment in HIMAC—a third of the 10-year plan and 13% of all cancer-related research spending in Japan over the past 10 years (see pie chart).

Cancer researchers elsewhere will be watching the clinical trials closely. Already, provincial officials in Hyogo prefecture, west of Osaka, are planning to build a facility similar to HIMAC as part of a multibillion-dollar science park, and researchers in Germany will soon start treating a handful of patients on an experimental basis. And although there are at present no plans to fund trials in the United States, Joseph Castro, professor of radiation oncology at the University of California, San Francisco, says he is hopeful of restarting the work if HIMAC and the European programs yield promising results. Castro led a 15-year series of tests using an accelerator at Lawrence Berkeley National Laboratory that was shut down in 1993.

This international interest in the therapy rests on the theory that particle beams should be more effective than x-rays and gamma radiation in attacking some types of tumors. That's because the charged particles generated by two synchrotrons can be focused more precisely than other forms of radiation. In addition, the mass and charge of heavy ions allow them to pack more of a wallop to the cancerous tissue. Last month's results at HIMAC involved three patients irradiated with two streams of carbon-12 ions—one vertical and one horizontal—that converged on their tumors for 90 seconds, three times a week for 6 weeks. In all three cases, according to NIRS scientists, the tumors shrank significantly with minimal side effects.

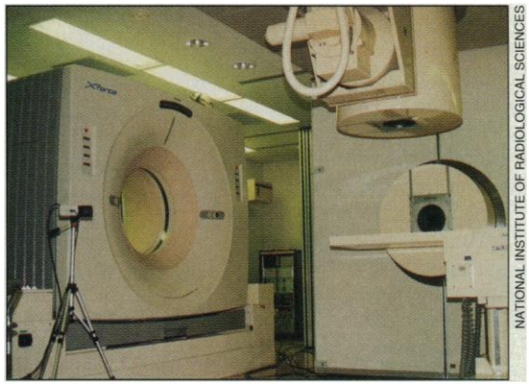
These are the first of what is expected to be a stream of results from HIMAC. NIRS is building a $129 million, 100-bed hospital on an adjacent site to accommodate up to a thousand patients a year for full-scale clinical trials. And researchers hope to move beyond head tumors as they get more experience with the machine. "The range of applications will expand as experience with the technique is gained," says Kozo Morita, director of charged-particle therapy at NIRS, noting plans to extend trials to uterine, liver, and prostate cancers.

Working the system. Japan is leading the way in part because of its approach to funding science, in particular its affinity for large projects. Decision-making in Japan is widely perceived by outsiders as a painstaking process of consensus-forming, but as the history of HIMAC shows, funding agencies often operate more like individual fiefdoms, making little effort to integrate their plans with other agencies. "Each ministry is practically an independent nation," says Takashi Sugimura, president emeritus of the National Cancer Center in Tokyo.

Sugimura should know. He served as vice chair of a committee of cancer experts who advised a government panel that nominally oversaw a national anti-cancer program, including setting priorities and coordinating activity. But rather than drawing up a set of priorities that was translated into an overall program, says Sugimura, individual ministries each came up with their own proposals and lobbied for funding.

HIMAC wasn't proposed by the Japanese cancer community, although researchers did not oppose its construction. Rather, it grew out of an idea by Yasuo Hirao, an accelerator physicist. HIMAC is funded by the Science and Technology Agency, which supports mostly big projects in the physical sciences, and STA came out a big winner in the government's anti-cancer sweepstakes.

Cancer researchers have since grumbled privately about the size of the investment in HIMAC, but given how the decisions were made, it's not clear that the money would have been available for other types of cancer research anyway. "It was not a zero-sum game," notes Toshinobu Sato, deputy director of the Ministry of Health and Welfare's Division of Disease Control. That view is seconded by Masaaki Terada, director of the National Cancer Center Research Institute, the center's research arm. "It was not money we felt we could compete for," he says, adding that most biologists like himself working on the molecular bases of cancer knew very little about HIMAC during its initial planning.



High-powered concerns. Results from clinical trials could quell doubts about the wisdom of building HIMAC.

Now that it's up and running, doubts about its value are beginning to be heard publicly. Norio Suzuki, professor of experimental radiology at the University of Tokyo School of Medicine, says that he expects HIMAC to clarify the pros and cons of heavy-ion versus other radiotherapies, "but whether [the advantages] justify the money spent is very difficult to say at this point." Makoto Kondo, assistant professor of radiology at Keio University School of Medicine, is more blunt. "I don't think particle-beam therapy is very promising," he says.

Kondo gives two reasons. Despite the beam's greater precision compared with x-ray therapy, Kondo says the increased power of the heavy-ion beams increases the possibility of harmful side effects. Most importantly, he believes there are few patients who can benefit from the heavy-ion therapy. The small tumors best suited for heavy-ion treatment can be treated in their early stages with more conventional and less costly methods, he says, while the precision of a machine like HIMAC "loses its value" if the cancer has already spread.

Some cancer researchers also worry that HIMAC's presence will distract the government from the need to improve existing cancer therapies. Masanori Fukushima, an oncologist in the Department of Internal Medicine and Laboratory of Chemotherapy at Aichi Cancer Center in Nagoya, says it is "foolish" to be spending such money on advanced—and still unproved—technologies when the relative scarcity of trained radiologists and equipment often means that "many patients cannot receive appropriate radiotherapy."

Trials on trial. In line with the government's commitment to the facility, Morita says that his institute has strengthened its normal procedures for conducting the clinical trials. All patients will have to pass two stages of consent, he says, acknowledging that they understand they have cancer—cancer patients in Japan often aren't told they have the disease—and that the HIMAC treatment is experimental. He also hopes to set new standards for the operation and review of the clinical trials.

But Fukushima, Kondo, and others question whether those new procedures will be adequate to protect both patients and the integrity of the data. "These patients aren't going to be thinking of this as an experiment," he says about the difficulty people have in distinguishing between experimental and conventional therapy. They are also worried about the objectivity of the review committees typically gathered to assess clinical trial or research results. "They don't bring in people who might oppose the views of the researchers," Kondo says. "The conclusion [of the review] is decided from the outset," he argues.

Concerns about the rigor of clinical trials and their evaluations were heightened earlier this year by the handling of a recent report summarizing some 20 years of experiments involving fast-neutron radiation tests done at another NIRS facility. An investigation by the Tokyo-based *Asahi Shimbun* newspaper found that a review committee received data on only 500 of 2004 patients. Some members stated that they never saw data comparing fast-neutron and other therapies, although the report concluded that fast-neutron therapy was more effective than x-ray and gamma radiation in some cancers and less effective in others.

The chair of the review committee, Sumihiko Sakamoto, professor of radiology at Tohoku University School of Medicine, declined to discuss the matter. NIRS' Morita confirmed that reviewers were given data on only 500 patients treated solely with fast-neutron therapy, saying that it provided a clearer picture of the results. And he says the NIRS report, only one-and-a-half pages of text and three pages of tables, was an interim internal memo not intended to be taken as a report from the evaluation committee. Morita says a book-length report on all the fast-neutron trials, including more rigorous reviews, is due next year.

While Morita agrees with some of the points Fukushima and Kondo have raised about the quality of cancer treatment in Japan, he disagrees with their criticism of the assessment process. "They haven't been out here to discuss the protocols we have set up," he says. And NIRS officials say that HIMAC will be a boon not only to cancer researchers but also to those in the physical sciences. "This is an unusual facility," says Kiyomitsu Kawachi, director of accelerator physics and engineering for NIRS. He says the unusual capabilities of the machine have experimentalists lining up for nighttime and weekend slots that won't be occupied by clinical trials.

Local governments are equally excited about HIMAC's potential. This year Hyogo Prefecture expects to start building a facility for proton-radiation therapy that will also provide heavy-ion therapy if the HIMAC trials are deemed successful. The facility, to be completed in 1999, is expected to cost $350 million. It will be part of the Harima Science Garden City, now anchored by STA's $1 billion Super Photon ring-8 GeV synchrotron radiation facility, which will be the world's most powerful synchrotron when completed in 1998. "The prefecture wanted a facility that would be international class and at the leading edge of the technology," says Shuji Kimura, former head of the Hyogo Medical Center for Adults. Other prefectures are reported to be watching what happens at HIMAC and Harima closely.

Although HIMAC's supporters are glad to hear expressions of faith in its potential, they are quick to remind people that the benefits of heavy-ion cancer therapy remain unproven. "The world does not yet have enough data on the use of carbon-12 therapy," says NIRS' Morita. But 30 years from now, Morita predicts, heavy-ion treatment will be a standard clinical therapy, and the wisdom of the investment will be a matter for historians, not scientists.

–Dennis Normile