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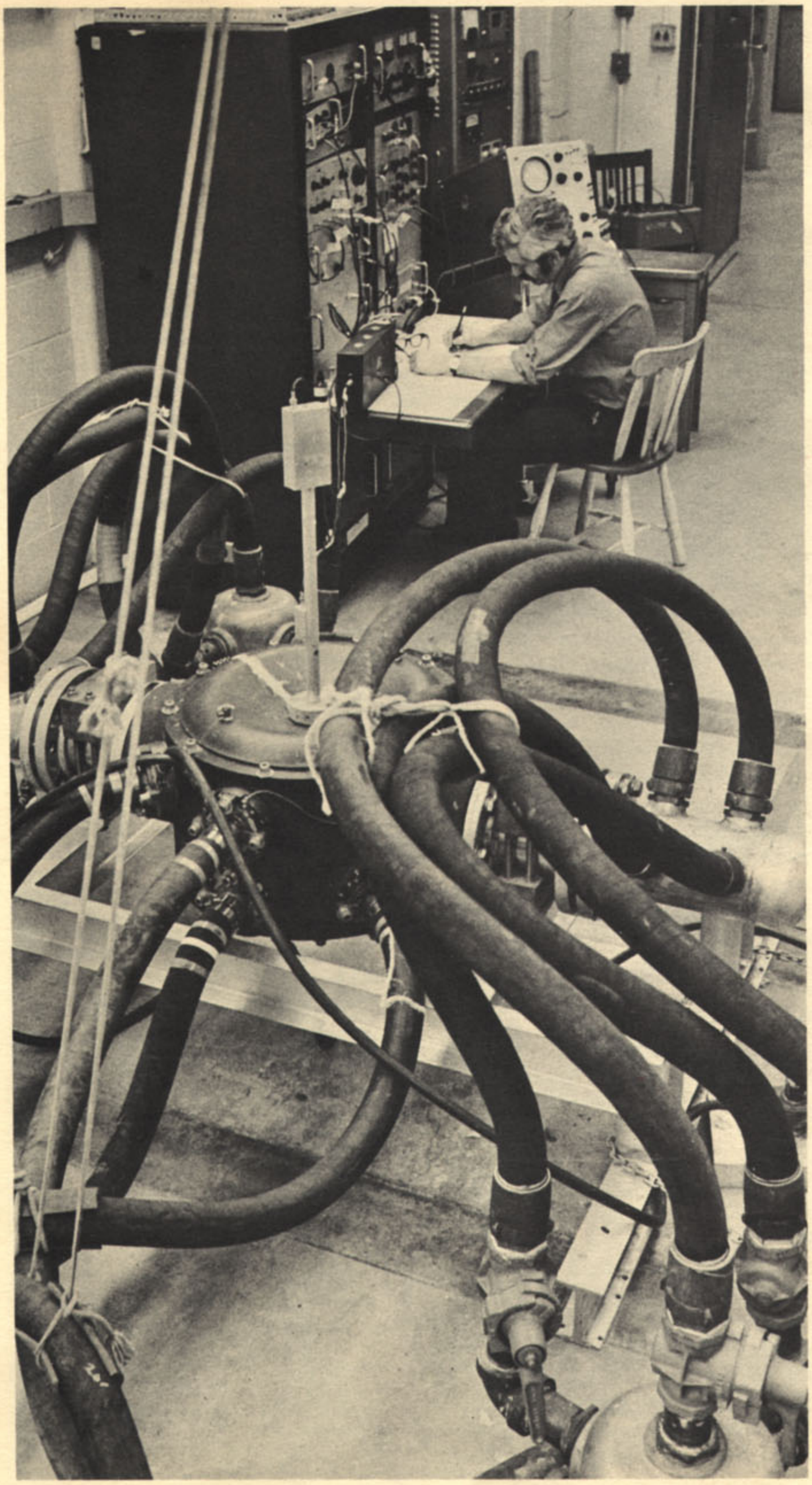

Basic Research Leads To Radio Signals From Cancer Tissue

Sometime in June, a truck will pull up at Downstate bearing a 14-foot-high machine for the biophysics laboratory of Dr. Raymond Damadian, Assistant Professor of Medicine and of Biophysics.

The machine is a nuclear magnetic resonance instrument, which is more at home in physics or chemistry laboratories than in medical institutions. But to Dr. Damadian, the device is very much a medical instrument. He regards it as the prototype of a machine-to-be that could fulfill a long-standing dream of physicians: a quick, foolproof method of early cancer detection.

Already, Dr. Damadian is planning to build a much larger nuclear magnetic resonance device, one that will be big enough to hold a human being. That machine, Dr. Damadian believes, will prove that nuclear magnetic resonance (NMR) is the tool that doctors have been looking for in their quest for a method of detecting cancer early, when treatment is most effective.

All that Dr. Damadian has to support his belief now is a series of tests in which NMR successfully distinguished cancerous cells from healthy tissue in the test tube. But several years of work with NMR, together with its proven power in chemistry, have convinced Dr. Damadian that the technique will work on something as complex as the human body. He hopes to start proving his belief by building and operating his planned

Dr. Raymond Damadian conducts research on cancer detection in the National Magnet Laboratory at the Massachusetts Institute of Technology. The heavy black hosing connected to the high field magnet in the foreground carries water from the Charles River to cool the magnet.

"Nuclear magnetic resonance may give researchers a new insight into one of the most mysterious processes in biology: the transformation of a normal, controlled cell into the uncontrolled, malignant cancer cell."

larger machine in the next two years.

If Dr. Damadian is proven right, his work will be an example of two uncommon events—the translation of basic biophysical research directly into medical practice, and the union of sophisticated research instrumentation with clinical medicine.

Those who know him regard the youthful, mustachioed, and intense Raymond Damadian as the kind of man who is capable of uniting two such diverse disciplines. Trained as a physician and as a biophysicist, he came to his difficult chosen line of research fully equipped. When that seemingly esoteric research led back to a practical medical use, he was quick to seize the opportunity.

Dr. Damadian began his research efforts in 1963 at the Biophysical Laboratory at Harvard University. There, he and other researchers began investigating one of the biggest mysteries of the living cell—how cells manage to concentrate certain molecules while excluding others.

The generally accepted theory is that the cell's outer coat, the cell membrane, contains "pumps" that somehow manage to exclude the molecules that are not needed for the cell's functioning while pumping essential molecules into the interior of the cell.

But Dr. Damadian and a small group of other scientists have attempted to prove that it is not the membrane "pumps" but the way the cell's contents are organized that governs the coming and going of molecules. They have amassed evidence aimed at proving their theory: that the cell's contents (consisting mostly of water, with other molecules dissolved or suspended in it) are organized into a fairly systematic molecular structure when the basic laws of physics and chemistry are taken into account. The theory says that the molecules are held in place by electric charges on atoms in the structural backbone of the cell. "In effect," Dr. Damadian says, "the cell may be regarded as an ion exchange resin bead with respect to the way it takes in and expels molecules, much like the ion exchange resin beads that take up and expel molecules in the commercial ion exchangers that soften water for household use."

If an atom fits in this structure, the cell holds it. If the atom doesn't fit, it passes out of the cell. In either case, says the theory, membrane "pumps" have little to do with it.

During the three years of basic research that followed his arrival at Downstate in 1967, Dr. Damadian began to think of applying his theory to cancer. There were two reasons. First, it is known that when a normal cell changes into a wild-growing, cancerous cell, the internal organization and structure of the cell break down. Therefore, on theoretical grounds it should be possible to detect the difference between a cancerous cell and a normal cell purely from its chemistry instead of from its appearance in a microscope.

The second reason followed directly from the experiments on his theory. Cancer cells are known to contain increased amounts of the atom potassium. Both from his experiments and from his theory, Dr. Damadian knew that changes in potassium were related to changes in the "structure of the water" inside the cells. It was this change in water structure that was detected in the NMR.

"The success of these experiments with cancer tissue constitutes a major triumph for the theory," says Dr. Damadian, since the theory "predicted precisely the nature and extent of the cancerous changes to be expected." Furthermore, he says, "they illustrate once again the practical dividends of basic research for its own sake," since this application to cancer was in no way anticipated when his research into the molecular basis of cell structure first began.

Nuclear magnetic resonance is the basic tool in his research. In NMR, radio waves are directed at an atom which is in a strong magnetic field. Under the right conditions, the atom absorbs the energy in the radio waves briefly, and then emits energy to return to a resting state.

The kind of energy each atom absorbs depends on a number of things, including the molecule that the atom is in. The NMR characteristics of an atom change even when its molecule changes only slightly. Therefore, by studying NMR changes, Dr. Damadian can study changes that occur to molecules within cells—for example, the kind of changes that occur when a cell turns cancerous.

Specifically, he has found that NMR can easily tell the difference between, say, a normal liver cell and a cancerous liver cell, simply by studying a single kind of atom in water molecules within those cells.

In a recent scientific paper on his work (*Science*, March 19, 1971), Dr. Damadian said that he has concentrated on hydrogen atoms—protons—in water molecules. What he measured was these protons' "relaxation time"—that is, the amount of time required for a proton to give up the energy added by the radio waves.

Dr. Damadian worked with six different kinds of normal tissue taken from rats—skeletal muscle, liver, stomach, kidney, brain, and small intestine. He also tested two types of cancer found in rats.

NMR showed striking differences between those tissues. For example, the relaxation time for protons in water molecules in normal liver tissue was .250 seconds. The relaxation time for protons in water molecules in a cancer of the liver was .860 seconds.

Dr. Damadian says that it should be possible to tell all cancerous tissues from normal tissues by using NMR. He plans to run a long series of tests on a number of different tissues using his NMR machine, which will be as-

Counterclockwise from top left: Dr. Damadian inserts a tissue sample into the end of the NMR probe; the probe is inserted into the magnet; the duration of the radio frequency pulse is set on the spectrometer.

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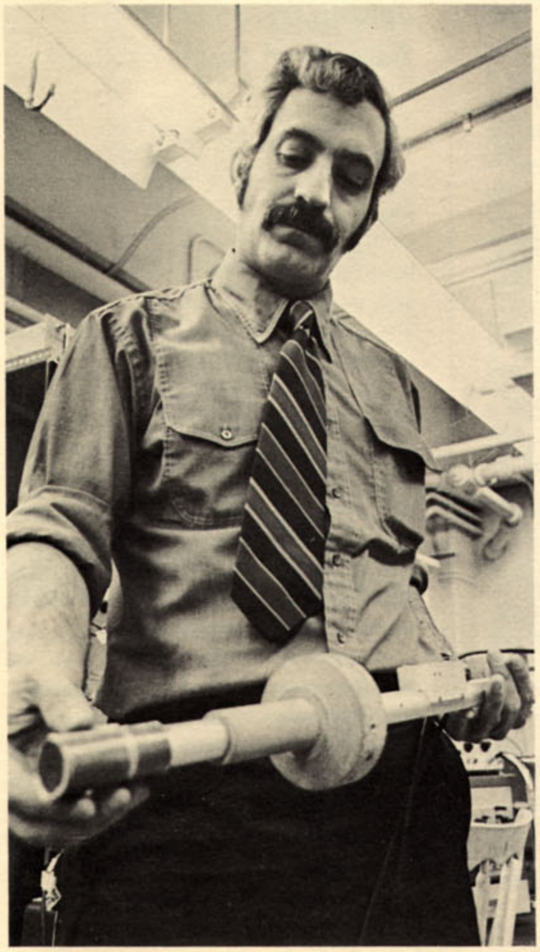
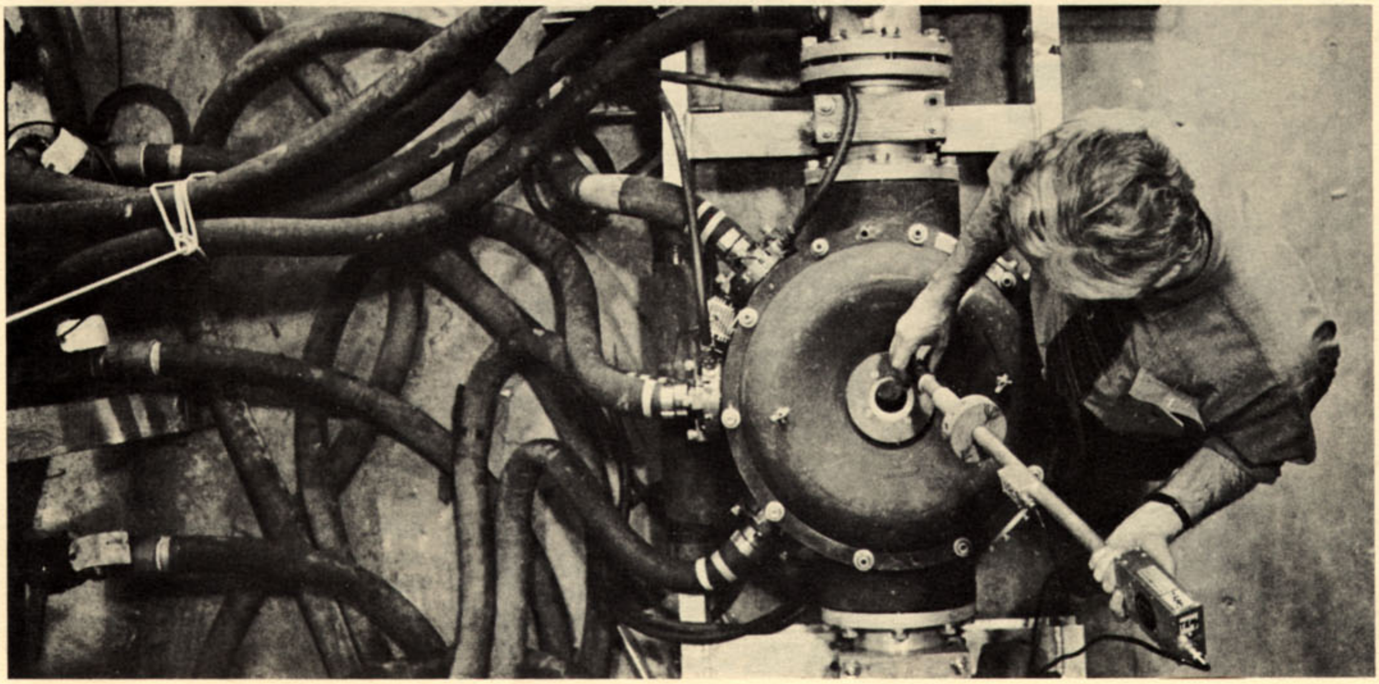




"By analyzing all these atoms with nuclear magnetic resonance, researchers could build a spectrum that would identify each cell in the same way that a fingerprint identifies a person."

sembled at Downstate in June, when his new high field magnet arrives. At present, he is conducting his NMR experiments at the National Magnet Laboratory at the Massachusetts Institute of Technology, where the high field magnets necessary for his research are available.

The proposed NMR device for detecting cancer in humans would not have to be highly elaborate, Dr. Damadian says. It would consist of a large coil to emit radio waves and a movable magnet to create the magnetic field required. The coil would be wrapped around the patient's chest, while the magnet passed back and forth across the body. A detector would pick up NMR emissions for analysis

Several kinds of analysis might be possible, Dr. Damadian says. For example, many different kinds of atoms could be studied in the same cells. By analyzing all these atoms with NMR, researchers could build a spectrum that would identify each cell in the same way that a fingerprint identifies a person. Analyzing these spectra could then enable a doctor not only to detect a cancer within the body, but also to pinpoint the cancer's location, Dr. Damadian believes. For that kind of analysis, he says, a computer would be needed, since the number of different spectra might be too great for any one man to handle. The computer would compare the signals coming from the patient's body with the spectra stored in its memory.

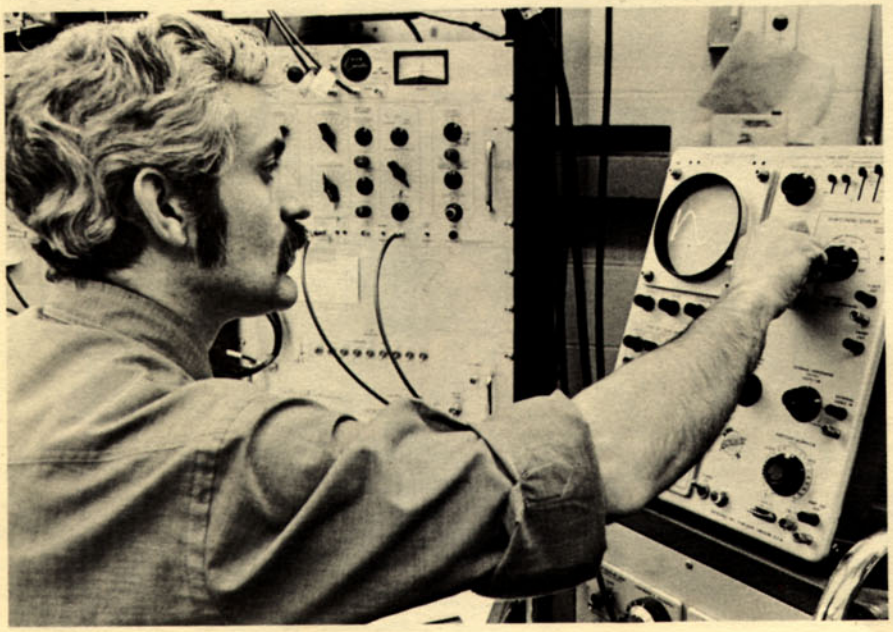
Dr. Damadian has begun to compile a catalogue of NMR responses from different tissues, both normal and cancerous. One of the first uses of this kind of catalogue, he hopes, will be quick identification of suspicious tissues removed by surgeons during exploratory operations.

Dr. Damadian also believes that NMR may give researchers a new insight into one of the most mysterious processes in biology: the transformation of a normal, controlled cell into the uncontrolled, malignant cancer cell.

To study the transformation, Dr. Damadian says, biologists can simply use some of the chemicals that are known cancer-causers to induce the cancerous transformation in the test tube. Then they can perform periodic

(continued on page 16)

Radio frequency signals are recorded on the oscilloscope for quantitative discrimination between tumor and normal tissue.



Jewish Ceremonial Art Subject of Doctor's Book

It's not unusual to hear that a doctor has written a book. Downstate has many authors on its staff. However, it is unusual to hear that the book has nothing to do with aches and pains, nothing to do with DNA and ACTH, and nothing to do with mental aberrations.

Dr. Abram Kanof, Professor of Pediatrics, has written a book entitled *Jewish Ceremonial Art and Religious Observance.* Of coffee-table size and arty price, the handsome book contains numerous color photographs of mosaics, jeweled wine cups, seder plates, coins, linens, and illustrated Hebrew manuscripts.

According to the author, the attractive appearance has a disadvantage, however. Dr. Kanof woefully points out, "My chief concern is that people will just want to look at the pictures and not read it. It's the written matter that I value most highly."

In its explanation of Jewish ceremonial objects, their use, and the ceremonies in which they are utilized, the book contains the history of many Jewish religious practices. Dr. Kanof explained that he had been working actively on the writing of the book for about four years. But his interest in ceremonial objects as art began about 20 years ago, when he became a member of the Board of the Jewish Museum and later its chairman.

"I started collecting ceremonial objects and I also became interested in the psychological importance of ceremony and the history of ceremonies. I was brought up to believe that all of the Jewish ceremonies were of Jewish origin," he states. "I realized as I read and studied that most religious ceremonies have a common source in the ancient heathen periods but that these practices have been revised and given a new meaning by the monotheistic religions of today."

"Medical schools have only recently begun to offer some training in genetics, and I think guidance in genetics is something that the physician of the future is going to be pressed to provide for his patients."

tected in this manner is still small compared to the total number of genetic defects known and suspected. While medical science has not yet developed the techniques for repairing the bad genes, the clinical advances in detecting genetic diseases and in treating them have been numerous, considering that only two decades ago scientists did not know for sure how many chromosomes there are in the human cell. The positive identification of 23 pairs, or 46 altogether, was not made until 1956.

"If the defect is a biochemical deficiency, experiments are being tried with supplemental medications. If it is an Rh blood difficulty between mother and child—which is a genetic problem—we can now transfuse the child in utero," explains Dr. Solish. There are great hopes for treating sickle-cell anemia now that we know the basic conditions governing it.

"Medicine is centering more and more on preventive aspects," he concludes. "Genetic counseling fits into that trend very well, and it's a field that holds a great deal of hope for the future. We've already reached the point where there really is something we can do about many genetic defects."

RADIO SIGNALS *(from page 4)*

NMR checks to determine which molecules in the cell are changing and what changes occur.

And so, although Dr. Damadian is now placing most of his emphasis on a practical medical use of NMR, he still leaves room for the basic scientific research on which he started.

Dr. Damadian is a Career Scientist of the Health Research Council of the City of New York. His research is supported by the Health Research Council of the City of New York, the New York Heart Association, and the National Institutes of Health.

INTENSIVE CARE *(from page 13)*

If she hasn't been trained for it, she may not even know that a change is occurring."

In addition to the ICU staff, the doctors feel that the backup facilities available to them in the State University-Kings County complex are very important to their success. These include the cardiac surgeons and other diagnostic and treatment facilities that are available.

While the doctors believe that a pediatric ICU is "a must in any hospital where sick children are admitted," Dr. Ehrlich points out that there are many smaller community hospitals—probably a dozen in Brooklyn—that deliver babies but do not have a pediatric service, much less the more extensive facilities. The large nursing staff required, the scarcity of pediatric specialists, and the extremely expensive equipment required would make such a unit prohibitive as well as impractical for hospitals that have a comparatively small patient load.

Therefore, Dr. Torres would like to see the State University-Kings County unit designated as a regional center where seriously ill children or babies born with congenital heart defects could be transferred by ambulance, or maybe even helicopter, for the intensive care they need. "There is no question that our pediatric intensive care unit can save lives that might otherwise be lost," he says.

Credits

Photos by Bob West

Ceremonial objects on pages 5-7 from *Jewish Ceremonial Art and Religious Observance* published by Harry Abrams, Inc., New York

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