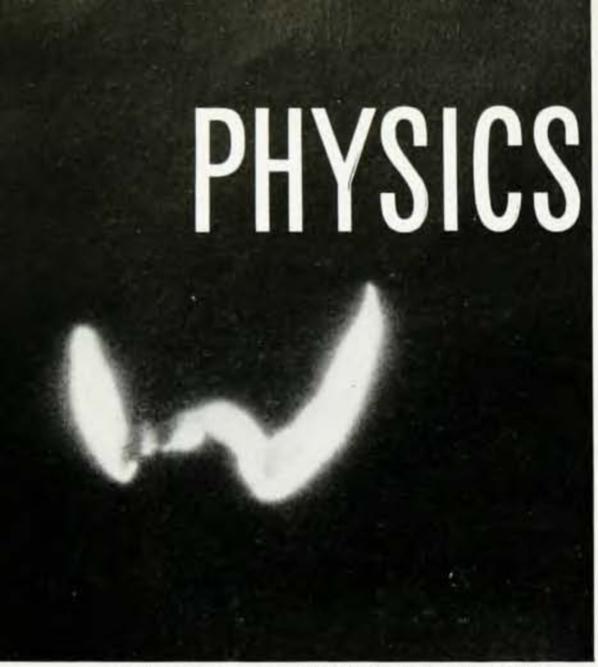
PHYSICS AND CANCER



Reidar Sognnaes, Harvard School of Dental Medicine

by Arthur K. Solomon

The fundamentals of cancer are the fundamentals of growth. Physics offers biology tools and techniques to attack the disease, but both sciences must work together on the basic problems of growth.

The connection between physics and cancer is peculiarly intimate—as intimate as cause and effect. For radiation, a valuable agent in the treatment of cancer, can itself cause cancer. This curious interrelationship exists largely because no one knows what causes growth, whether it be normal or abnormal. The primary problem in cancer is not an exploration of such isolated problems as the connection between radiation and cancer. It is the much larger and much more stimulating problem of understanding the fundamentals of growth.

The first necessary step, therefore, is an examination of the contributions that physics can make to the larger problem of growth, rather than to the more limited and purely applied problem of the treatment of cancer. This is just another way of asking the even more fundamental question: what can physics bring to biology? Precisely because cancer is not yet understood, and precisely because the explanation may lie in any of the areas of biological research, the attack on the problem demands a wide expansion in our understanding of the fundamental processes of biology.

What can physics bring to biology? The answer to the problem is subjective, and the answer of a physicist will probably be quite different from that of a biologist. At the outset the biologist wants techniques; the physicist believe that his greatest contribution is conceptual. And the truth of the matter, no doubt, lies in that broad no-man's land between these extremes.

Techniques of Physics

Today the use of radioactive isotopes is a very fashionable technique. Partly this is the inevitable result of the terrible fascination of the atom bomb, and partly it is the result of the real extension of basic biological knowledge that has already come about from the use of isotopes. Using radioactive isotopes, certain compounds can be traced without minute control of the experimental biological system. The final fate of an essential foodstuff may be determined by labeling it with radioactive atoms, then finding how these are excreted during the animal's lifetime or, after post-mortem, where they have concentrated. A principle such as this can be extended to smaller and smaller systems and leads to an intimate knowledge of some of the basic chemical systems that exist in living matter. It is even possible to make experiments on normal human adults, if the measurements are confined to excretory products and blood. Indeed, some students at Harvard Medical School are earning a small stipend by acting as experimental animals in studies of the uptake of minute quantities of radioactive iron in normal blood.

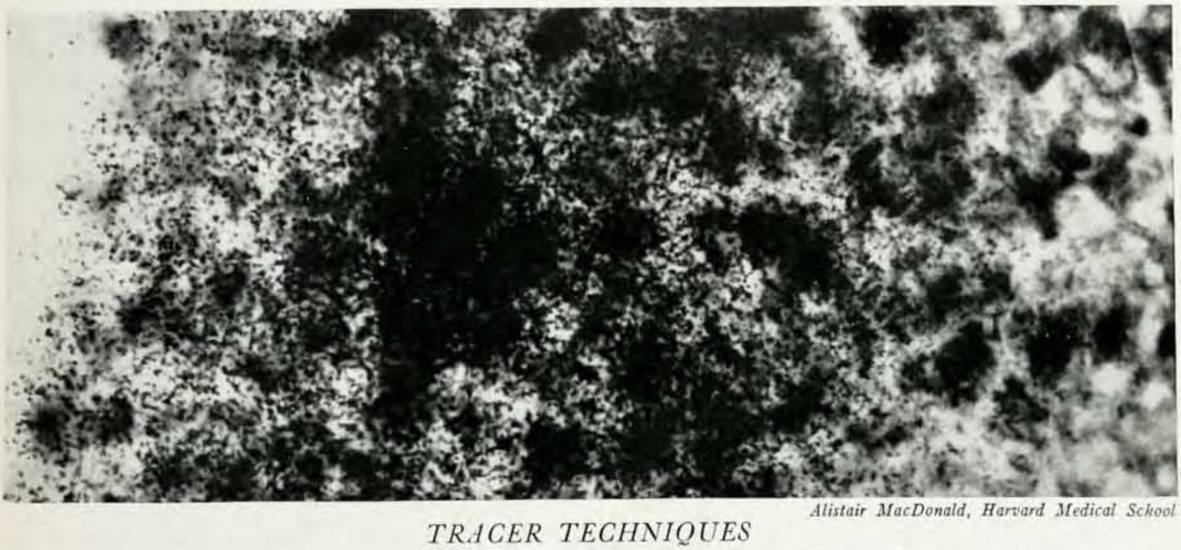
The tracer technique is applicable to studies other than the unraveling of biochemical reactions. Wherever a fluid diffuses through a barrier, wherever a fluid is transmitted through a hollow vessel, radioactive tracers make it possible to measure the diffusion and the flow. And wherever small amounts of material, too small to be detected by normal chemical means, play an important role in a physiological process, tracers help elucidate the pathways.

These successful physical and chemical excursions into the domain of the microcosmos bring to mind that early great contribution and introduction into the microworld that came to biology by way of physics through the lens, the telescope, and the microscope. Physics, pure and applied, has continued to contribute to the development of the microscope from that first incredibly crude instrument used to such good purpose by Leuwenhoek. Today the polarizing microscope and the phase microscope represent the newest development of these instruments routinely available for the use of biologists. To progress even further into the microworld, one must turn to the ultraviolet microscope, the electron microscope, and even to the proton microscope now being developed in France.

The ultimate limit of vision with a conventional microscope is the wave length of the light with which the image is viewed. Therefore, the shorter the wave length, the tinier the object that can be discerned. Since the ultraviolet microscope uses shorter waves than the visible, a consequent decrease in the lower visual limit may be expected. In modern physics all particles have characteristic wave lengths, the heavier and faster the particle the shorter the wave. But even a particle as light as an electron has a characteristic wave length many times shorter than the wave length of light. Thus the electron microscope can 'see' objects far smaller than those visible in the best conventional microscope. It may be possible to see even smaller objects by the use of heavier particles at the same speed, as, for example, the proton, 1800 times heavier than the electron. If the technical difficulties involved in the construction of a proton microscope can be solved, we may penetrate further into ultimate structure.

Variables and More Variables

It is always easier to talk about the specific contributions that techniques make to a sister science than to explain the conceptual differences between sciences. This is particularly true since one man's opinion can never truly represent the whole profession. In general the approach of the physicist is simple and direct because his problems can usually be set up in simple and direct terms. In the main his variables are controllable. But coupled with the



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TRACER TECHNIQUES

Opposite page: Radiophosphorus shows up in the enamel of a monkey's tooth (from which all but the enamel has been drilled away) in this 60-hour exposure.

Above: Carbon-14 spots its presence on film placed over a section of liver tissue. Magnified 600 ×.

dry precision of the experimental approach are the vast imaginative powers of theory. The first floor of the physical structure is built on the solid foundation of experimental fact; the lofty towering spire comes directly from the fancy of theory. Theory must be mathematically developed and exactly stated, and it remains tenable only so long as no new experiment comes to tumble the structure down again.

In sharp contradistinction to physics, all biological processes are very dependent on a large number of interrelated variables. The simplest sample to be studied is that smallest fraction of living tissue which will still carry out the functions that are being investigated. An attempt to apply too stringent a control of the variables may mean destruction of the experimental system. Many reactions that can be carried out in the normal animal liver cannot be reproduced if the liver is ground up and placed in a glass vessel to provide an environment and a temperature that can be accurately controlled.

In the past, the biologist has never failed to produce theories to account for his experimental results; the theories, however, can rarely be developed in exact mathematical terms. This is particularly true because so few biological experiments can be set up so that the variables can be controlled at the will of the investigator. The complexity of biology is, indeed, the complexity of life, presenting a multitude of problems that can barely be attacked at all. Such complexity does not yield readily to mathematical treatment. Our understanding of biology rests on a knowledge of the basic chemistry and physics of biological systems. Surely it is logical to call in the physicist and chemist themselves in a joint attack on the problem of growth so that we can deploy the best talents available for the steps ahead. Perhaps the greatest of their contributions will be the concept and discipline of these more exact sciences.

Tools for Treatment

In the light of the larger problems of growth, the physicist's contribution to the study of cancer has been modest. The present and immediate contributions are those which physics can make to the healing of disease, and these are now, as they have been in the past, very limited. The treatment of sick people does not in general lead to a knowledge of what made them sick.

The present-day use of radiation therapy is merely an extension of the familiar use of radium and x-ray in the treatment of cancer. The action of radiation in the body is not completely understood, but there is reasonable agreement that it is the effect of ionization (in which atoms or molecules acquire an electric charge) along the path of radiation. Ionization by x-rays cannot be localized at one specific point along the path of the x-ray in tissue: thus treatment of deep-seated tumors with x-rays irradiates not only the tumor but also the skin and intervening tissues. A more specific method of introducing the radiation directly at the tumor would be a great help.

It now seems clear that such an effect can be achieved by using electrons as irradiating agents. The electron cannot penetrate tissue to the depth reached by x-rays, but the ionization is much more intense, and increases just at the end of the electron path. The great energy required to propel the electrons deep into tissue has only recently become available with the development of the synchrotron, a tool in nuclear physics devised to provide an intense beam of high-energy electrons. Its use in biology stems from the ability of these electrons to produce a local region of dense ionization deep inside the body with very little exposure at the skin. A good deal of research is needed to show just how effective such dense, localized ionization can be: research not only in the physical, but also in the clinical sense, since it is often impossible to know where the radiation should be directed even when it can be controlled.

The Long Way

The physicist and the doctor both tend to be cautious now in predicting the future effect of newly developed tools, because of their joint experience with radioisotope therapy. In the early days before the war it was thrilling to devote long cyclotron hours to the bombardment of phosphorus for the treatment of a leukemic patient. Early results were promising: the radioactive phosphorus seemed to concentrate in the bone morrow where white blood cells are made. Since leukemia is characterized by the over-production of white blood cells, it was sensible to hope that radiophosphorus could deliver enough radiation in the right places to control this over-production. Although control of this sort was exercised, our initial optimism has given place to the realization that, in general, the average prolongation of life of leukemic patients is no greater with radiophosphorus than with the more conventional x-ray treatment.

Some initial striking success has been obtained with the use of radioactive iodine in the treatment of thyroid cancer. Since the thyroid picks up iodine preferentially, it seemed, by the same rationale that applied to phosphorus treatment, that thyroid cancer might be controlled by delivering the iodine radiation directly into the thyroid itself. But not all thyroid cancers take up iodine; indeed, the more vicious the cancer, the less likely it is to accumulate iodine. Nonetheless, a few cases have been controlled by iodine treatment, particularly patients who have had surgical thyroid removal, and who are still troubled by malignant transplants of small fractions of thyroid tissue at different places throughout the body. Such small amounts of malignant tissue have, on one case at least, been successfully controlled for a period of years. Thyroid cancer, however, is a relatively rare form of cancer, and the percentage of thyroid patients who respond to radioactive treatment is small. To sum up: The use of radioactive isotopes in the treatment of cancer has not yet proved itself on an appreciable scale, despite repeated efforts.

One other fashion in which radioactive isotopes may produce a great impact on cancer is in diagnosis. It has already been shown that breast cancers pick up appreciably more radioactive phosphorus than do surrounding sections of normal tissue, presumably because the tumorous tissue is growing so much faster than normal that it incorporates all of its structural elements very rapidly. If this abnormality in phosphorus uptake can be used to diagnose and to locate not only breast cancers, but other and more deep-seated lesions, then, indeed, it will have proved itself of great value in the treatment of cancer.

Until that time, realistic appraisal of the cancer problem brings us back to our starting point: The real contribution of physics to cancer lies in the joint prosecution, by the physicist, by the chemist, by the biologist, of basic research on the problems of growth.

NEWS and VIEWS

Optical Society

The winter meeting of the Optical Society of America, held at the Hotel Pennsylvania in New York City on March 4–6, may be best characterized in terms of the diversity of subjects covered in the fifty-six papers presented. Often scientific meetings have some central theme or outstanding series of papers which determines their flavor, but these Optical Society meetings seemed to cover the broad field of optics, and its many applications, in an unusually thorough fashion. That this was popular fare was attested by the registration of over 500, and the fact that each of the eight sessions was well attended, several of them reaching the "standing room only" state.

The first day's sessions were devoted to colorimetry and spectrophotometry. An invited, introductory paper by Arthur C. Hardy on the early history of recording spectrophotometry was followed by contributed papers which described the techniques employed in large laboratories such as those of the Eastman Kodak Company and the National Bureau of Standards, and papers recounting specific uses, for example the descriptions by S. Q. Duntley and E. A. Edwards of the spectrophotometry of living human skin and its application as a research tool in medicine.

The second day of the meeting featured two invited symposia, one on optical and spectroscopic methods of flame temperature measurements which described techniques of great importance in combustion research and engineering, and the other on the various optical problems associated with wind-tunnel studies and the interferometry and special photographic methods employed in studying supersonic flow. A contributed paper which proved to be of considerable general interest was the one in which Hans Mueller described his new operational theory of optics—a phenomenological theory that is based on empirical laws rather than the usual wave hypothesis. In the field of physiological optics, there was a description by Lorrin A. Riggs and E. P. Johnson of measurements of the electrical response of the retina to light flashes entering the human eye.

The third day of sessions was given over entirely to thirty contributed papers in the wide range from specific techniques of spectrochemical analysis through various items of infrared instrumentation to discussions of methods for the reduction of aberrations in optical systems.

S. S. B.

Harmonic Synthesizer-Analyzer

University of Texas physicists, under the direction of Dr. S. Leroy Brown, have constructed a mechanical harmonic synthesizer-analyzer for solving certain types of mathematical equations. Its principal uses are in: harmonic synthesis and analysis; solving high degree polynomials-complex and real roots; plotting Patterson diagrams for x-ray crystal analyses; impedance diagrams for electrical networks including electric wave filters; and plotting specific polynomials resulting from hyper-geometric series.