C^{12}, Ray Kaempfer has shown that subunit exchange definitely occurs. The heavy ribosomes, which were resolved from their light counterparts on sucrose gradients, sedimented at 86*S* instead of the usual 70*S*. After 3.5 generations of growth on light medium, all single ribosomes had become half-heavy. The 50*S* and 30*S* subunits were conserved.

Although Kaempfer's data clearly establish the existence of subunit exchange, they do not permit one to determine how often the subunits separate. Masayasu Nomura reported experiments which suggest that separation of the subunits must occur each time a ribosome completes a polypeptide chain, since formyl-methionyl-tRNA will bind only to 30*S* subunits. Binding of f-met-tRNA is inhibited by 50*S* and 70*S* particles. Valyl-tRNA, on the other hand, would not bind to 30*S* subunits in the presence of poly-AUG, but would bind if both 30*S* and 50*S* subunits were present.

Additional evidence consistent with the concept of subunit exchanges comes from David Schlessinger's laboratory. Using "fragile" strains of *E. coli*, which can be lysed almost instantaneously, Schlessinger and his co-workers have shown that the 70*S* ribosome is almost nonexistent in vivo. Instead, ribosomes occur either as components of polysomes or as free 50*S* and 30*S* subunits. This distribution would be expected if the initiation of polypeptide chains could only be effected by means of free 30*S* subunits, as Nomura reports.

Another approach to the analysis of ribosome function is exemplified by Nomura's experiments on reconstitution. Nomura has recently fractionated the "meniscus proteins" from *E. coli* ribosomes, that is, the proteins which are stripped from ribosomes by treatment with CsCl and which band at the top of the CsCl gradient after equilibrium centrifugation. He then recombines the meniscus proteins with the ribosomal cores, separately and in various combinations. Assays for biological activity of these partially reconstituted particles have already revealed much information about the function of some of the proteins. For example, the basic meniscus proteins from the 30*S* subunit are required for amino acid incorporation and for tRNA binding, but the acidic meniscus proteins are not. In contrast, the acidic meniscus proteins from the 50*S* subunits are required for those functions, but the basic meniscus proteins are not. Many other combinations have been tested, as Nomura reported. The method of reconstitution is an extremely powerful tool, which is certain to play an important role in future research on ribosome structure and function.

Genetic approaches to the study of ribosome function have not been neglected; but, as summarized by Joel Flasks, the efforts to find ribosome mutants in microorganisms have met with surprisingly little success.

Several other aspects of ribosome function were considered by David Apirion, Jesse Salb, and Kivie Moldave. Apirion summarized genetic studies on lincomycin- and erythromycin-sensitive mutants of *E. coli*, which apparently affect the 50*S* subunit of the ribosome. He suggested that tRNA binds at the site that is sensitive to these antibiotics. He also reported that ribosomes from cells grown anaerobically appear to bind lysine tRNA in a different manner from that of the controls. Salb compared the ribosomes of mitotic HeLa cells, interferon-treated cells, and microsomes from normal rat liver. All have a relatively low ability to support protein synthesis in vitro, and all can be activated by treatment with trypsin. The possibility that an extra protein on the ribosomes is responsible for the inhibition is strengthened by the observation that 50*S* subunits derived from interferon-treated cells show one more protein band than the controls, when analyzed by acrylamide gel electrophoresis.

Moldave has continued his studies on the effect of ribosomes on RNA transcription. Using a crude preparation of DNA with endogenous RNA polymerase prepared from lysates of *E. coli*, he finds that ribosomes will increase both the amount of RNA made in vitro, the length of the reaction, and the average size of the product. Some of the newly synthesized RNA is freed from the DNA template, and becomes attached to the ribosomes. Chloramphenicol does not alter these effects of ribosomes. Similar effects can be obtained with 30*S* subunits alone. It is therefore clear that protein synthesis is not required for the stimulation of transcription mediated by ribosomes. Experiments are now in progress to determine whether the initiation factors required for protein synthesis are also required in this system.

The 3rd day of the conference was primarily devoted to discussion of nonribosomal ribonucleoproteins. Ru Chih Huang presented her latest data on the RNA which she finds covalently bound to protein from chick embryo nuclei. Animo acid analysis shows that the protein which is bound to RNA is not a basic protein. The presence of β-alanine in the hydrolyzates suggests that the RNA is linked to the protein through dihydrouracil. Studies are now being done on the protein-bound RNA made by chromatin in vitro.

Dai Nakada described the recombination of MS2 protein with MS2 RNA. The normal virus contains 180 molecules of protein per molecule of RNA. When purified RNA has been combined with 6 to 20 molecules of viral protein in vitro, it will still serve as a template for protein synthesis, but the ability to code for noncoat proteins has been preferentially suppressed. This system will undoubtedly be of value in studying the control of translation.

Hewson Swift summarized information on various types of nuclear ribonucleoproteins that have been observed with the electron microscope. The size of the large particles seen in the Balbiani rings of dipteran polytene chromosomes, for example, implies that they are not ribosomes. In two anucleolate mutants—one in the frog, *Xenopus*, and one in maize—many particles larger than ribosomes can be seen. The amorphous masses that form in place of true nucleoli contain no granules, but they do contain RNA. These observations are a useful reminder that the nucleolus may be a more complicated organelle than many scientists currently envision it to be.

EDWIN H. MCCONKEY
Institute for Developmental Biology, University of Colorado, Boulder 80302

Dosimetry: High-Energy Radiation Therapy

Almost two decades have passed since the initiation of the therapeutic use of high-energy radiations with both the high-energy x-rays and electrons from the betatron. Radiation dosimetry, including the distribution of dose produced by these radiations in tissue, is central to their preferred use in therapy. The significance of this development was reflected in the response to the symposium on high-energy radiation

therapy dosimetry, held in New York, 15–17 July 1967.

The symposium was designed to cover all aspects of high-energy radiation dosimetry progressing from fundamental considerations of the absorption of x-rays and electron to problems in their therapeutic application. Topics included the theory and application of a variety of dosimetry methods, calibration of both energy and dose for these radiations, problems and developments in the planning of actual radiation therapy of patients, and a discussion of the problems and experience in correlation of biological effects with dosimetry. Consideration was also given to the direction of future developments in dosimetry and in further computerized service in radiation treatment planning.

Fundamental problems involved in the absorption of high-energy x-rays and electrons were discussed by M. J. Berger (National Bureau of Standards, Washington, D.C.); Dr. Harder (University of Wurzburg, Germany), and N. Kessaris (Sloan-Kettering Institute, New York). Berger reported on the use of the Monte Carlo method to simulate the processes involved in the absorption of high-energy electrons. This was a cascade calculation involving both electrons and secondary bremsstrahlung photons with the two types of radiation acting as sources for each other. The results included the energy dissipation as a function of depth and beam size, charge deposition as a function of depth, and also the spectral distribution of the electron flux at various depths. Kessaris described calculations of the same parameters for electron beams and their application to the relation between absorbed dose and cavity ionization as a function of depth in tissue. Kessaris had solved the transport equation for electrons by the moments method under the continuous slowing down assumption for two beam geometries: a plane infinite beam and a pencil beam, both incident on an infinite water medium. D. Harder described his approach involving the use of special transport equations. He found that application of the Fokker-Planck equation yields a similarity rule, according to which the coordinates for equal spatial distributions of the differential flux density and of the dose are scaled by the average path length in cases where the parameter Zm_0c^2/E_0 (for $E_0 \gg m_0c^2$), or Z (for $E_0 \ll m_0c^2$), is equal. E_0 and M_0c^2 are the initial energy and rest energy of the electron, respectively, Z is the atomic number of the slowing-down medium, and c is the velocity of light. Experimental observations from transmission, range, backscatter, and dose distribution measurements support the theoretical conclusions.

The problem of accurate measurement of absorbed dose over a large array of points in and around a tumor is an ever-present one in the therapeutic use of high-energy radiations. The status and recent progress with several types of radiation detectors were reported on: film dosimetry (J. Dutreix, Villejuif, France), thermoluminescence dosimetry (F. H. Attix, NRL, Washington), ferrous-sulfate chemical reactions (R. J. Shalek, University of Texas, Houston), and calorimetry (A. Pinkerton, Sloan-Kettering Institute, New York). The science and technology of the calorimetric method for absorbed dose as well as of energy flux measurement for high-energy electrons and x-rays have reached a high degree of precision using quasi-adiabatic techniques for laboratory instruments. In fact, radiation calorimetry seems to be in the process of becoming the scientific standard of measurement of absorbed dose. J. R. Cameron (University of Wisconsin) described measurements on the thermoluminescent response of lithium fluoride to high-energy electrons and gamma rays.

It is obviously important that the specification of dosimetry in the treatment of patients be uniform in medical institutions throughout the United States as well as internationally. In a paper presented by J. G. Holt (Memorial Hospital) the development and results of intercomparison and calibration of dose among several medical institutions over the past decade were described. Use of ionization chambers, of the Fricke ferrous sulfate dosimetry, and lithium fluoride thermoluminescence under carefully specified conditions have proved invaluable in maintaining uniformity of dosage among institutions over this period of time. In particular, development of methods of mailing both the Fricke and thermoluminescent dosimeters by these medical institutions represents a significant achievement in dosimetry. M. Ehrlich (NBS, Washington) reported on the plans of the bureau to establish a standard calorimeter for absorbed dose, as well as a program of uniformity checks. These will be limited to electron beams appropriate to biological and medical work, and to institutions within the United States. The Fricke dosimeter is to be used initially as the measuring instrument. Cells containing the dosimeter, and placed in specially designed polystyrene blocks, will be shipped to a given institution, exposed, and returned to NBS for evaluation. W. A. Jennings (National Physical Laboratory, Teddington) and W. H. Henry (National Research Council of Canada, Ottawa) reviewed the policies of their national standards laboratories on calibrations of high-energy electrons and x-rays. Jennings spoke briefly on the use of cavity ionization chambers followed by a derivation to arrive at absorbed dose for machines operated up to 8 Mev and based on 2-Mev x-ray exposure calibrations. Jennings indicated that the National Physical Laboratory is considering the possibility of a program similar to that of the National Bureau of Standards measuring absorbed dose directly rather than carrying out exposure calibrations. It is only in the highly developed countries that have sophisticated institutional and national Laboratories that absorbed dose calibration techniques are employed. In general, these laboratories offer only limited services to hospitals outside their national borders. However, the International Atomic Agency has recently inaugurated a program of absorbed-dose intercomparisons for institutions and hospitals in developing countries. This program was described by R. Loevinger (IAEA, Vienna). It makes use of the thermoluminescence of lithium fluoride sent by mail. The present service is limited to calibrations of cobalt-60 gamma rays.

The use of high-energy electrons in particular requires accurate and reliable calibration of energy, since the penetration of electrons in the patient is directly dependent on their energy. Methods of energy calibration were reported by L. H. Lanzl (University of Chicago) and W. Pohlit (Biophysics Institute, Frankfurt). Lanzl discussed both magnetic and nuclear threshold methods. At energies above a few Mev, magnetic methods are needed for which the peak energy as well as the whole spectral shape is required. Techniques have not yet been devised to consider this method as an "absolute" method except for energies below a few Mev, and where both object and image lie within the region of the uniform mag-

netic field. Techniques are expected to be improved during the next several years so that absolute magnetic methods should be possible. The major problem area is the fringe field effect in the sector type of magnetic spectrometer. Nuclear threshold reactions are used extensively as a secondary method for the energy calibration of the upper end of the spectrum. Above 20 Mev, however, simpler and more precise threshold techniques need to be established. The (γ, 2n) oxygen reaction is about the only practical one in use. W. Pohlit reported on empirical methods of specifying the energy of electron beams in water-like substances through the use of range measurements with a constant absorbing layer while varying the initial electron energy.

An entire session was devoted to the important problem of the actual planning of patient treatment and details of the methods employed for the prediction of dose distribution and for corrections for patient structure and the different absorption properties of the various tissues involved. Pohlit described methods developed at Frankfurt for the calculation of electron dose distributions in inhomogeneous materials, that is, soft tissues interspersed with air or bone. The energy transport by electrons and the type of inhomogeneity are characterized by several parameters. He illustrated in many practical situations that the slowing down of electrons is the dominant effect while scattering can be treated as a correction. Although a given institution may have a technique for detailed treatment planning, this technique often is not carried out because of a variety of factors such as cost, needed personnel, and other factors. However, A. Dahler spoke on the comprehensive electron beam treatment developed and employed at the Memorial Hospital for Cancer and Allied Diseases, New York, which regularly corrects for inhomogeneities. Individualized planning uses tissue compensators, polystyrene wedges, masks, and molds. The concept of absorption equivalence thickness (AET) is employed in regions of body inhomogeneities. In vivo dosimetry in patients was also described by Dahler. P. Almond (M. D. Anderson Hospital, Texas) reported on extensive measurements made directly in various tissues (bone, lung, fat, and other tissues) in dogs and other mammalian systems on the basis of which a precise correction system had been developed. M. Brenner (Abo Akademi, Finland) also described detailed measurements on the phenomena of inhomogeneous distributions at interfaces of materials of different density and atomic number involved in the absorption of high-energy electrons. J. Ovadia (Michael Reese Hospital) reported on treatment planning methods employed at his institution.

A problem of long standing in the therapeutic use of high-energy electrons has been the question of whether there is a qualitatively different biological response to them as compared to experience with x-rays. There have been numerous subjective clinical as well as some experimental indications of a variation in biological response to electrons of different energies and in different scattering conditions. B. Markus (Universitats-Hautklinik, Gottingen, Germany) described measurements with *Drosophila* eggs and with other biological systems which indicate a dependence of biological response on depth in absorbing material, corresponding to the change in energy spectrum of the primary and scattered electrons. E. Robinson (University Hospital, Baltimore) reported on experiments with human kidney cells maintained in tissue culture. These were exposed to electrons at different depths in absorbing material, and analysis of the survival curves indicated no demonstrable dependence on electron energy. Relative to conventional x-rays he reported a relative biological effectiveness of 0.87 for this system which is similar to the quantitative difference found with other biological systems for high-energy x-rays and electrons relative to the lower energy x-rays often employed in patient therapy. Another report was given by J. H. Kim (Sloan-Kettering Institute) describing experiments with human tumor cells exposed in vivo to electrons under different energy and scattering conditions. The criteria examined were survival curves, clonal size distribution, and extent of recovery from sublethal radiation. With respect to all of these criteria no variation in biological response with electron energy was found. Experiments by Dutreix (Gustav Roussy Institute, France) and by Wambersie (University of Louvain, Belgium) with *Saccharomyces cervesiae* also indicated no biological dependence on electron energy. It appears that, although there are still differences found by responsible investigators, for most biological systems tested there is no basis for expecting a qualitatively different biological response to electrons as compared with x-rays.

H. H. Rossi (Columbia University) discussed the concept of microdosimetry and the interpretation of biological response in terms of dose distribution on the micron scale. He described the relevant parameters for representation of microdose distributions and discussed specific instances in which interpretation of the biological response was possible by consideration of the microdose distribution. D. K. Bewley (Hammersmith Hospital, London) discussed experiments carried out with neutrons and heavy particles where the density of ionization is much greater than achieved by the use of x-rays and electrons. On the basis of particular features of the biological response to heavy ionizing radiations he was able to define possible future limitations in the extent of the use of high-energy radiations. A major limitation is the dependence of biological response on oxygen concentration which is maximal for x-rays and electrons but is minimized for more heavily ionizing radiations. W. Roesch (Battelle Memorial Institute) discussed the interpretation of survival curves for irradiated biological systems in terms of "target" and "hit" theory.

In the final session, D. Harder described fundamental developments in transport theory concepts with possible future applications to biological dosimetry. Another indication of the future was given in the report of a practical linkage system which makes computerized treatment plans available to collaborating hospitals as developed by Memorial Hospital (J. G. Holt and R. F. Phillips). The remote terminal consists of an ordinary teletype machine by means of which all input and output data are transmitted by regular telephone wires. Hospitals both in San Francisco and New York City make use of this system for routine treatment planning.

During the banquet, H. S. Kaplan (Stanford) reviewed the significant advances in the radiation treatment of cancer and the relation to this of high-energy radiation dosimetry. He indicated directions of future advances in radiation therapy and specific needs from medical physics and radiation dosimetry in this continuing development. D. W. Kerst (University of Wisconsin)

reviewed aspects of the early history of concepts involved in betatron acceleration, as well as items in the early development and operation of the betatron.

The symposium, planned by the Subcommittee on Radiation Dosimetry of the American Association of Physicists in Medicine, was sponsored by the Association, the New York Academy of Sciences, and the Office of Naval Research. Additional financial support was provided by the American Roentgen Ray Society and several accelerator manufacturers.

The proceedings will be published by the New York Academy of Sciences.

LAWRENCE H. LANZL
University of Chicago, Chicago, and *International Atomic Energy Agency, Vienna*

JOHN S. LAUGHLIN
Memorial Hospital and *Sloan-Kettering Institute, New York*

Calendar of Events—January

National Meetings

4–6. **Human Factors in Automotive Engineering** Design, Ann Arbor, Mich. (Society of Automotive Engineers, Continuing Education Program, 485 Lexington Ave., New York 10017)

7–12. American **Chemical** Soc., New Orleans, La. (Meetings Manager, 1155 16th St., NW, Washington, D.C. 20036)

8–9. National Specialists Symposium on **Orbital Resonance**, Redondo Beach, Calif. (G. S. Gedeon, Systems Group, TRW, Inc., One Space Park, Redondo Beach 90278)

8–12. Automotive **Engineering** Congr. and Exposition, Detroit, Mich. (W. I. Marble, Soc. of Automotive Engineers, Meetings Div., 485 Lexington Ave., New York 10017)

9–11. **Chemical Marketing**, Hopatcong, N.J. (Saul Gordon Associates Center for Professional Advancement, P.O. Box 66, Hopatcong 07843)

10–13. National Soc. of **Professional Engineers**, winter mtg., Washington, D.C. (P. H. Robbins, NSPE, 2029 K Street NW, Washington, D.C. 20006)

11–12. Wires for **Electrical Conductors**, Philadelphia, Pa. (American Soc. for Testing and Materials, 1916 Race St., Philadelphia 19103)

14–18. Society for **Cryo-Ophthalmologists**, Miami Beach, Fla. (J. G. Bellows, Executive Sceretary, 30 N. Michigan Ave., Chicago, Ill. 60602)

15–16. **Medical Library** Board, Washington, D.C. (Medical Library Assoc., Inc., 919 N. Michigan Avenue, Chicago, Ill.)

15–17. **Noise Measurement and Control**, Hopatcong, N.J. (Saul Gordon Associates Center for Professional Advancement, P.O. Box 66, Hopatcong 07843)

15–17. **Paint, Varnish, Lacquer**, and Related Products, Cincinnati, Ohio.