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Implications of Single-Particle Experiments for Track Theory, Therapy and Radiation Protection

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EXTENDED ABSTRACTS

Proceedings of the 5th International Workshop: Microbeam Probes of Cellular Radiation Response

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The extended abstracts that follow provide a summary of the Proceedings of the 5th International Workshop: Microbeam Probes of Cellular Radiation Response, held in Stresa, Lago Maggiore, Italy, on May 26–27, 2001, which was organized by INFN, Laboratori Nazionali di Legnaro, Italy and Università degli Studi di Milano, Dipartimento di Fisica, Italy.

There is increasing interest in the use of microbeam systems (*1*, *2*), which can deliver beams of different radiations with a spatial resolution of a few micrometers or less, for radiobiological research. Single-particle microbeams can be used to address such questions as the relative sensitivities of different parts of the cell (e.g. nucleus compared to cytoplasm) and the effects of irradiation on non-hit neighboring (bystander) cells. For particle (e.g. α-particle) beams, irradiation with exactly one (or more) particle per cell can be achieved, allowing questions of risks of very low doses of ionizing radiations, such as radon, to be addressed. Several microbeams are now in operation, and others are being developed. The workshop provided a forum to assess the current state of microbeam technology and current biological applications and to discuss future directions, both technological and biological.

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Implications of Single-Particle Experiments for Track Theory, Therapy and Radiation Protection

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''Because the predominant exposure of cells in humans is to single isolated tracks, a critical question is what effects a single track is capable of producing and with what probabilities.'' ''Most of the current biophysical models. . . make the clear prediction that a single track can produce virtually all of the detrimental stochastic effects of interest.'' ''But one model, in particular (the amorphous track model of Katz and coworkers), disagrees fundamentally that a single low LET track has the ability to cause the cellular changes.'' ''This model leads to very dramatic differences in the predicted risk at low doses. . . '' ''Because of the very major implications this would have if true, there may be strong grounds for critical evaluation of the model'' (*1*).

That critical evaluation is now possible in single-particle experiments that are the subject of this workshop. Thus far, calculations from published equations, from published radiosensitivity parameters, and thus from predictions in real time have yielded agreement with measurements of cell survival after proton and α-particle bombardments, as well as with single α-particle-induced oncogenic transformations (*2*). From their experiments, the authors have concluded that ''the measured oncogenecity from exactly one alpha particle was significantly less than for a Poisson-distributed mean of one alpha particle, implying that cells traversed by multiple alpha particles contribute to most of the cancer risk'' (*3*).

Recall that our predictions are based on the application of the theory to high-fluence experiments with a variety of bombarding ions, up to argon, at energies up to 10 MeV/nucleon.

This theory also provides the motivation for ion-kill dosimetry (*4*), now being investigated as the basis for evaluation of the qualitative effects of high-LET radiations. Ion kill is also suggested as the basis for the differences in tissue response, for the loss of the benefits of fractionation, and for late effects in neutron and high-LET radiation therapy (where overdose can be ruled out as the cause) and also as a basis for space dosimetry in regard to the protection of astronauts from the deleterious effects of cosmic rays. For these purposes, experiments based on the Biostack principle offer the greatest versatility in projectile type and energy (*5, 6*). Since the physical parameter that determines single-particle response is z^*/β, we propose that the response of a tissue or cell to different particles should match at the same value of this parameter.

Single proton bombardments in particular are needed to test both Katz's theory and the assumption that a single (electron or proton) track has the ability to cause cell killing, and transformation, as demanded by the linear, no-threshold extrapolation to low dose which forms the basis of radiation protection affirmations. This is an excellent opportunity for experiment to test both theory and the conventional wisdom.

There is frequently a hidden agenda in physical units and measurements. Thus dose, energy per unit mass, implies multiple random transits of charged particles through a designated target. Cross section is a probabilistic concept, not a geometric concept. It relates to the probability of an interaction between randomly placed targets and random trajectories of projectiles within a channel. The theory of RBE requires knowledge of cellular properties and the full particle energy spectrum in a radiation field, and it is not restricted to a sub-class of secondary interactions, like all secondary protons. Heat and temperature imply thermal equilibrium, which is not achieved in a ''thermal spike''.

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