irradiated clusters were subsequently disassociated and processed for survival fraction. Figure 6 shows the dose response curves for V79 multicellular clusters exposed to chronic and acute ^{137}Cs gamma irradiation at 10.5°C. The shouldered dose response curves are characteristic of the response of mammalian cells to radiations with low linear energy transfer (LET). It is clear that the response of the multicellular clusters is dependent on the dose rate. The chronic dose rates are similar to the dose rates encountered with incorporated radionuclides, therefore, the α and β coefficients for the chronic irradiation can be taken as representative of the coefficients one would expect for the response to cross-dose from low-LET radiations emitted by the radionuclides.

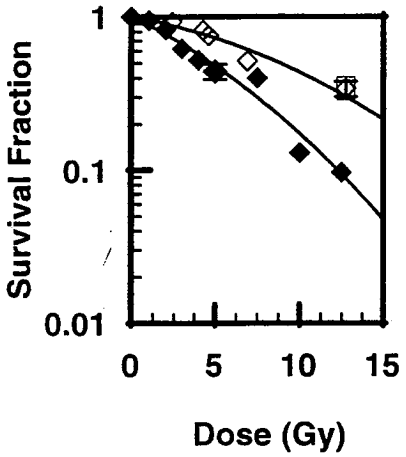

Figure 6. Survival of V79 cells following acute (◆) and chronic (◇) irradiation of multicellular clusters with ^{137}Cs gamma rays. Irradiations were carried out under the same conditions as those maintained in the radionuclide studies. A least squares fit of the data to the linear-quadratic model ($SF = Exp(-\alpha D-\beta D^2)$) yielded the following:

$SF(chronic) = Exp(-4.4x10^{-2} D - 3.9x10^{-3} D^2)$
$SF (acute) = Exp(-1.18x10^{-1} D - 5.6x10^{-3} D^2)$

where the α and β coefficients are in Gy^{-1} and Gy^{-2}, respectively

C.2i. *Mutagenesis and Survival Studies with External Gamma Rays: The Question of Hypoxia in the Clusters.* In this experiment, the protocol used in the above acute gamma ray experiment was followed except that immediately prior to irradiation, cells in half the tubes were resuspended to replace depleted oxygen while the cells in the remaining tubes were continued as pellets. Cells in all tubes were plated to evaluate colony-forming ability. Fig. 7A shows that the cells that remained in clusters were somewhat more resistant to killing by acute gamma irradiation relative to those that had been resuspended. Curve fits to the linear quadratic model resulted in α(susp) = 0.24 Gy^{-1}, β(susp) = 0.0022 Gy^{-2}, α(pellet) = 0.12 Gy^{-1}, and β(pellet) = 0.0070 Gy^{-2}. Fig. 7B shows that the same is true for induction of mutations at the HPGRT locus. Least squares fits to the number of mutants per cell plated *F* yield: *F*(susp) = $3.9x10^{-5}$ per Gy and *F*(pellet) = $2.5x10^{-5}$ per Gy. For this latter arm of the experiment, the Banbury Protocol was followed (*81*). The oxygen enhancement ratio (OER) for survival was about 1.4, and for mutation was approximately 1.6.

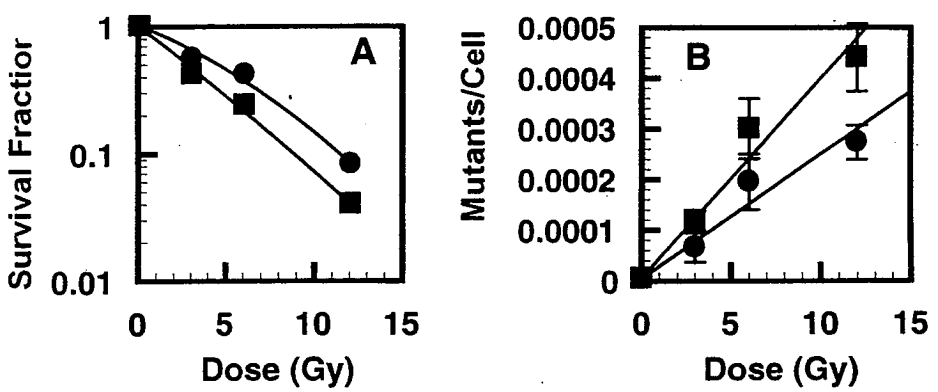

Figure 7. Response of V79 cells following acute irradiation with ^{137}Cs gamma rays at 10.5°C when clusters are maintained at 10.5°C for 72 h and then irradiated intact (■) or after dissociating (□). Two endpoints are examined: A) cell survival, and B) mutations at the HGPRT locus.

This experiment demonstrates that, after the 72 h incubation, hypoxia is present in the clusters. However, it appears to be uniform throughout the pellet since differentially hypoxic populations would result in a two- or more component exponential response to uniform irradiation. This is an important point because differential hypoxia would make data interpretation difficult. The OER is substantially less than 2.5 to 3.0, the maximum range expected for anoxia (Ref. (*82*), pg. 135) so the clusters are not completely hypoxic. In fact,