RADIATION AGING BY HIGH LET RADIATION: THE IMPLICATIONS OF ASSUMING CELL NUCLEUS IRRADIATION IS THE RELEVANT PARAMETER

by

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A companion paper to
"The Mechanism of Radiation Carcinogenesis"
(Document 1-A)

by

John W. Gofman and Arthur R. Tamplin

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Introduction

In the companion paper to this one, Gofman and Tamplin have provided an explanation of R.B.E. for high LET radiation carcinogenesis based upon the uneven distribution of high LET radiation among the cells of a tissue at moderate radiation doses (1).

There is considerable evidence to suggest that the crucial events in carcinogenesis may occur in the cell nucleus, rather than in the cytoplasm. It is of interest to explore the consequences for R.B.E. if this is true.

We shall assume that energy delivered in the nucleus affects only the nucleus; energy delivered in the cytoplasm does not affect the nucleus. To what extent relevant free radicals, or other radiation-produced entities will migrate between cytoplasmic and nuclear volumes is unknown. We shall calculate the extreme case where no cytoplasmic-nuclear exchange of relevant radiation energy occurs. This, as we shall see, may considerably raise the potential R.B.E. of high LET radiation for carcinogenesis in comparison with low LET radiation.

Description of the Physical Parameters

Assume (1) an idealized cubical cell

(2) Cell diameter = 2x nuclear diameter
(3) Cell volume = 8x nuclear volume

Next, assume a cubical array of cubical cells, and particles incident along a normal axis of the cell.

Thus the fraction of cells in which the particle will traverse the nucleus is directly the ratio, $\frac{(\text{nuclear cross-section})}{(\text{cellular cross-section})}$

But, since cell cross section = 4x nuclear cross section, it follows that 1/4 as many nuclei are traversed by $\alpha$ particles in this idealized array as are cells.
The essential difference here, therefore, in contrast to the cellular treatment of Gofman-Tamplin is that \( \frac{1}{4} \) as many nuclei are traversed, for any given number of \( \alpha \) particles, as they estimated for cells.

Number of cells per gram = \( 1.91 \times 10^9 \) (For \( 523.7 \mu^3 \) volume)

For 5 MEV \( \alpha \) particles

8.05 \( \mu \) cell diameter. (\( 523.7 \mu^3 \) volume)

5 MEV \( \alpha \) particle Range = 45 microns in tissue.

Cells traversed per \( \alpha \) particle (5 MEV) = \( \frac{45}{8.05} \) = 5.6 cells.

1.25 \( \times \) \( 10^7 \) \( \alpha \) particles correspond to 1 rad

Then \( (1.25 \times 10^7)(5.6) = 7.0 \times 10^7 \) cells traversed

Therefore 1 rad provides \( \alpha \) particles traversing,

\[ \frac{7.0 \times 10^7}{1.91 \times 10^9} = 0.0366, \text{ fraction of the cells.} \]

If \( \frac{1}{4} \) as many nuclei are traversed, as are cells, then

\[ 0.0366 = 0.00915 \text{ is fraction of nuclei traversed} \]

Consideration of the Bragg ionization means \( \frac{1}{2} \) the nuclei traversed receive 2x the energy received by the other half.

Therefore, 0.00458 of nuclei receive 2x the dose of the remaining 0.00458 of nuclei (Call the doses \( x \) and 2x)

Let us now calculate dose to nuclei, for 1 Rad to the cells

\[ (0.00458)(x) + 2(0.00458)(x) = 1.0 \]

\[ 0.01374x = 1.0 \]

\[ x = 72.8 \text{ rads} \]

Therefore 2x = 145.6 rads.

Therefore, for 1 Rad of 5 MEV alpha particles delivered, we have the following population distribution:
0.00458 of nuclei receive 145.5 rads
0.00458 of nuclei receive 72.8 rads
0.99084 of nuclei receive 0 rads

Now, we can calculate effective aging for the distribution, assuming delivery of radiation in the 8th year of life. Gofman and Tamplin have used (their Figure 1a) 1 Rad = 0.29 years.

So, 0.00458 of nuclei are aged (145.6)(0.29) = 42.2 years
0.00458 of nuclei are aged (72.8)(0.29) = 21.1 years
0.99084 of nuclei are not aged at all.

For the low LET radiation,
we have, for 1 Rad, 6.25 \times 10^7 1 MEV \beta-particles
Range = 4000 microns
Cell diameter, for \( \frac{\text{volume}}{523.7} \) volume, in the cubical array will be 8.05 microns
Therefore \( \frac{4000}{8.05} \approx 500 \) cells traversed
So (6.25 \times 10^7)(5 \times 10^2) = 3.125 \times 10^{10} cells traversed
But 1/4 as many nuclei are traversed,
So 7.81 \times 10^9 nuclei are traversed
But there are \( \frac{10^{12}}{523.7} \) = 1.91 \times 10^9 cells, or nuclei
Therefore \( \frac{7.81 \times 10^9}{1.91 \times 10^9} \approx 4.1 \) times, each nucleus is traversed

So, the low LET radiation can be considered approximately uniform.

And, aging therefore = 1 \times 0.29 = 0.29 years

We can now calculate the expected cancer incidence, as did Gofman and Tamplin for chronological age of 40 years.
### Table: Cancer Rates and Expected Cancers

<table>
<thead>
<tr>
<th>Effective Age (years)</th>
<th>Fraction of Nuclei</th>
<th>Cancer Rate (Cases/10^9/year)</th>
<th>Expected Cancers (Fraction x Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 MEV α particles</td>
<td>82.2</td>
<td>0.00458</td>
<td>~15500</td>
</tr>
<tr>
<td>(1 Rad)</td>
<td>61.1</td>
<td>0.00458</td>
<td>4950</td>
</tr>
<tr>
<td>Low LET Radiation</td>
<td>40</td>
<td>0.99084</td>
<td>550</td>
</tr>
<tr>
<td>(1 Rad)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>40</td>
<td>1.0000</td>
<td>550</td>
</tr>
</tbody>
</table>

Therefore, for 5 MEV α particles (High LET), Excess cancers = 88.62

for 1 MEV β particles (Low LET), Excess cancers = 20

R.B.E. = \( \frac{88.62}{20} \) = 4.43

### Conclusion:

It appears that if nuclei represent the relevant parameter, the R.B.E. is much higher than the case estimated by Gofman and Tamplin for whole cells as the relevant parameter. More detailed calculations, at various dose levels, cell sizes, and particle energies will be worthwhile.

### References