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Technical Note

Oxygen in S phase of a cell cycle*

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Variation in radiation cell sensitivity through the cell cycle has an important radiobiological implication in cancer treatment. The reasons for the radiation cell sensitivity changes through the cell cycles are not well understood.[1] It is generally agreed that the S phase is radio resistant because of its deficiency of molecular oxygen. This conclusion is based on the oxygen enhancement ratio (OER) and not by measuring the actual molecular oxygen content in each phase of the cell cycle (Table 1).

The OER is calculated by radiation dose delivered under hypoxic and under aerated condition to achieve the same biological end point. The OER at high doses yield a value between 2·3 and 3·5 for X-rays and γ rays.

We abstracted the data from the literature. It is interesting to note in Figure 1, as the cell ages, water proton NMR Spin Lattice relaxation time (T_1) decreases[2] and the mean lethal dose (Do) increases.[3] T_1 is a very sensitive index of molecular oxygen concentration in cells.[4,5] The decrease in T_1 from M phase to S phase cannot be accounted for the mere condensation of chromosome. The obvious reason in the decrease of 50% in T_1 value is due to paramagnetic effect of molecular oxygen. In other words, S phase has more oxygen than M phase of Hela cells. To prove this hypothesis, the OER is plotted against T_1. It is interesting to note that M phase has low OER value. This clearly indicates that M phase does not have high oxygen content.

OER increases with the ageing of the cell cycle. For example, cells in G1 phase have a lower OER than in the S phase. This is because G1 phase are more radiosensitive as shown in Figure 2. The high sensitivity of G1 phase compared to S phase is due to tenderness of chromosomes in early phases of the cell cycles than S phase. It appears that higher the OER indicates higher oxygen concentration. On the other hand, as the cell ages, mean lethal radiation dose (Do) increases. This is due to maturing of the chromosome that makes them more radio resistant.

The biological effects of ionising radiation on cells to be observed, oxygen must be present during the radiation exposure or within microseconds after the radiation exposure or at least during the lifetime of the free radicals generated by the radiation. It is not clear regarding the influence of oxygen resulting in free radicals that causes damage to DNA that is difficult to repair. However, only small quantity of oxygen is required for radio sensitisation, such as a 0·5%

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Table 1. Data abstracted from the literature

Phases of cell	T_1 (ms) (2)	Do (cGy) (3) at 280 kV	OER (3) at 280 kV	OER (3) at 1·25 MeV
M phase (0 minute)	1200	101	2·1	2·0
M phase (30 minutes)	800	101	2·1	2·0
G1 phase	638	118	3·3	3·2
S phase	534	140	3·4	3·0

Abbreviations: T_1, water proton NMR spin lattice relaxation time; Do, mean lethal radiation dose at 280 kV; OER, oxygen enhancement ratio in different phases of Hela cell at 280 kV and 1·25 MeV.

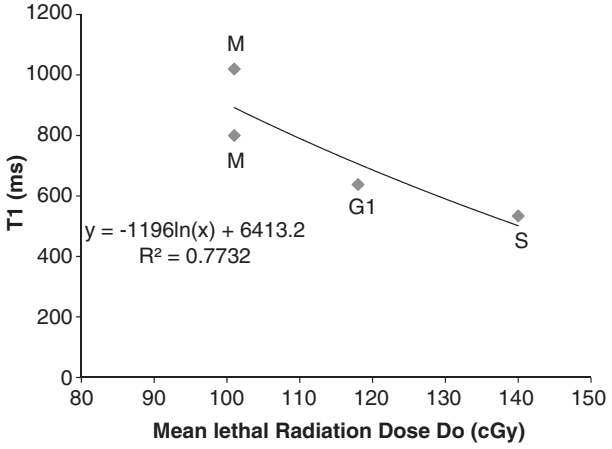

Figure 1. Correlation between T_1 and mean lethal radiation dose in different phases of Hela cell.

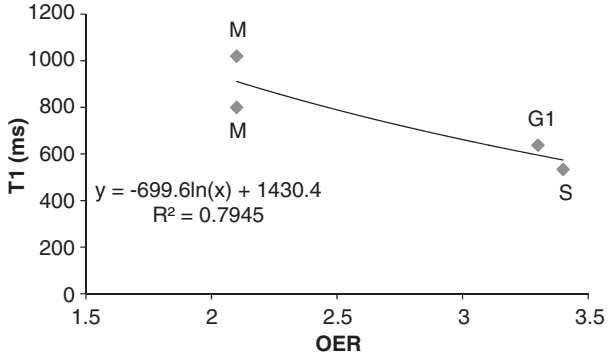

Figure 2. Correlation between T_1 and oxygen enhancement ratio in different phases of Hela cells.

oxygen (pO_2 of about 3 mmHg) results in sensitivity half way between hypoxia and full oxygenation.[1]

Molecular oxygen in addition to dose modifying agent is indispensible in repairing the cell damage produced by direct or indirect hit.

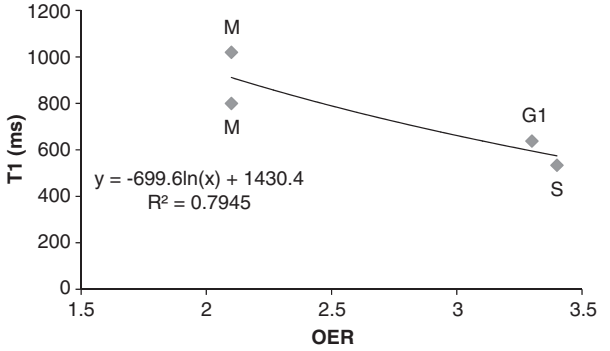

Figure 3. Correlation between T_1 and oxygen enhancement ratio in different phases of Hela cell at 1·25 MeV.

Since S phase has the highest capacity to repair the damage, it is obvious that S phase has more oxygen than M phase. Furthermore, for the synthesis of chromosomes to spit two mitotic cells, S phase need abundant oxygen to carry out their function.

The OER varies through the cell cycles. If M phase has high content of oxygen than the T_1 value would be lower and S phase should have highest T_1. In reality it is reverse. The value of OER is the same for all dose levels. Similarly, it also appears to have little or no significant effect on OER if energy is increased from 280 kV to 1·25 MeV (Figures 2 and 3).

Acknowledgement

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