

The Rationale for Fractionation in Radiotherapy

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The use of radiotherapy as a cancer treatment is common, so an appreciation of the biologic effects of radiation at a cellular level is essential to help nurses prepare their patients for the challenging journey ahead using appropriate lay language. The four Rs of radiotherapy (repair, redistribution, reoxygenation, and repopulation) are well established with regard to the principles of radiotherapy; however, these concepts appear undeveloped in nursing literature. The current article aims to succinctly explain how radiation impacts cancer and provides rationale as to why radiation treatment is delivered during a number of sessions. Through receipt of this knowledge, oncology nurses will be better equipped to communicate more efficiently and effectively with their patients.

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Using radiation to treat cancer is not a recent innovation; in fact, radiotherapy was used successfully for the first time in 1899 to cure a patient with basal cell epithelioma (Abeloff, Armitage, Niederhuber, Kastan, & McKenna, 2008). Despite yielding success, early treatments often involved very large single doses in a bid to completely eradicate tumors; this was met with many complications, including extensive skin toxicities. Henri Coutard was the first to use smaller doses of radiation therapy delivered over several weeks to overcome the acute toxicity induced by a large single fraction. By about 1934, Coutard's work became the basis of what is known today in clinical oncology as fractionation (Souhami & Tobias, 2008).

Cellular kill occurs when critical targets within the cell are damaged by radiation and the cell is unable to repair the damage. DNA is most likely to be a critical target for the biologic effects of radiation (Damrot et al., 2009). That has been established following measurement of DNA damage after radiation, which consistently correlates with cell death (McMillan, Tobi, Mateos, & Lemon, 2000). Studies also indicate that cells that are inhibited from repairing DNA damage, or that are naturally deficient in DNA repair enzymes, show distinct radiosensitivity (Kühne et al., 2004).

Direct and indirect damage can break bonds in DNA. These broken bonds can result in damage to one or both strands of DNA. Single-strand DNA breaks are repaired relatively easily using the opposite strand as a template. Therefore, single-strand breaks are not strongly related to cell killing. Double-strand breaks, however, represent the most important factor in de-

termining cell kill. In double-strand breaks, the chromatin is destroyed in two places, which ultimately results in cell death because the cell is unable to repair the damage. Radiation also can work by inducing apoptosis, which is also known as programmed cell death (Rothkamm, Krüger, Thompson, & Löbrich, 2003). Radiation is, therefore, an established and appropriate method to kill cancerous cells.

Radiation's Effect on Cell Replication

The biologic basis of fractionation in radiation therapy takes advantage of what are known as the "four Rs" of radiobiology: repair, redistribution, reoxygenation, and repopulation.

Repair

Cells have complex mechanisms responsible for repairing radiation-induced damage. One of the clearest demonstrations of the cell's ability to repair radiation damage is the phenomenon called sublethal damage repair (Heideker, Lis, & Romesberg, 2007). Following radiation exposure, cells can repair any sublethal or indirect damage. As explained earlier, direct DNA damage can be rare; the more exposures to small doses of radiation, the more likely direct DNA damage will accumulate (Pajonk, Vlashi, & McBride, 2010). With sufficiently high doses comes increased cell destruction, but this comes with a price of increased toxicities to normal cells and tissue, as well. Small doses of radiation will allow normal cells to repair, thereby reducing toxicity. According to Corner and Bailey (2008),