Radiation therapy techniques in carcinoma treatment.

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Radiation therapy works by damaging the DNA of cancerous cells. This DNA damage is caused by one of two types of energy, photon or charged particle. This damage is either direct or indirect ionization of the atoms which make up the DNA chain. Indirect ionization happens as a result of the ionization of water, forming free radicals, notably hydroxyl radicals, which then damage the DNA. In photon therapy, most of the radiation effect is through free radicals. Cells have mechanisms for repairing single-strand DNA damage and double-stranded DNA damage. However, double-stranded DNA breaks are much more difficult to repair, and can lead to dramatic chromosomal abnormalities and genetic deletions [1].

Targeting double-stranded breaks increases the probability that cells will undergo cell death. Cancer cells are generally less differentiated and more stem cell-like; they reproduce more than most healthy differentiated cells, and have a diminished ability to repair sub-lethal damage. Single-strand DNA damage is then passed on through cell division; damage to the cancer cells DNA accumulates, causing them to die or reproduce more slowly.One of the major limitations of photon radiation therapy is that the cells of solid tumors become deficient in oxygen. Solid tumors can outgrow their blood supply, causing a low-oxygen state known as hypoxia. Oxygen is a potent radiosensitizer, increasing the effectiveness of a given dose of radiation by forming DNA-damaging free radicals [2].

Tumor cells in a hypoxic environment may be as much as 2 to 3 times more resistant to radiation damage than those in a normal oxygen environment. Much research has been devoted to overcoming hypoxia including the use of high pressure oxygen tanks, hyperthermia therapy (heat therapy which dilates blood vessels to the tumor site), blood substitutes that carry increased oxygen, hypoxic cell radiosensitizer drugs such as misonidazole and metronidazole, and hypoxic cytotoxins (tissue poisons), such as tirapazamine. Newer research approaches are currently being studied, including preclinical and clinical investigations into the use of an oxygen diffusion-enhancing compound such as Trans sodium crocetinate (TSC) as a radiosensitizer.

Charged particles such as protons and boron, carbon, and neon ions can cause direct damage to cancer cell DNA through high-LET (linear energy transfer) and have an antitumor effect independent of tumor oxygen supply because these particles act mostly via direct energy transfer usually to causing double-stranded DNA breaks. Due to their relatively large mass, protons and other charged particles have little lateral side scatter in the tissue-the beam does not broaden much, stays focused on the tumor shape, and delivers small dose side-effects to surrounding tissue. They also more precisely target the tumor using the Bragg peak effect. See proton therapy for a good example of the different effects of intensity-modulated radiation therapy (IMRT) vs. charged particle therapy.

This procedure reduces damage to healthy tissue between the charged particle radiation source and the tumor and sets a finite range for tissue damage after the tumor has been reached. In contrast, IMRT's use of uncharged particles causes its energy to damage healthy cells when it exits the body [3].

The exiting damage is not therapeutic, can increase treatment side effects, and increases the probability of secondary cancer induction. This difference is very important in cases where the close proximity of other organs makes any stray ionization very damaging (example: head and neck cancers). This x-ray exposure is especially bad for children, due to their growing bodies, and they have a 30% chance of a second malignancy after 5 years post initial RT.

References

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