Saturday, October 17, 2009 - 10:30 am

INTRODUCTION TO RADIATION THERAPY

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INTRODUCTION

Radiation was discovered in 1895 by Wilhelm Conrad Röntgen and within a year radiation was being used clinically for both diagnostic and therapeutic purposes. One hundred years later, radiation therapy has been firmly established as one of the principal methods of cancer treatment and is used in over 50% of human cancer patients. In veterinary medicine, treatment of cancer with radiation has been uncommon relative to the use of surgery and chemotherapy. The limited use of radiation has stemmed more from a lack of funding and expertise rather than from a lack of medical indications, however. In the last several years in the US, there has been a tremendous increase in the availability of radiation therapy for veterinary patients. In 1994, a specialty board in veterinary radiation oncology was created within the American College of Veterinary Radiology. There are currently about 70 board-certified veterinary radiation oncologists and several residency programs in the US and abroad and a few formal residency programs have been established. The expansion of radiation oncology in veterinary medicine necessitates that veterinary technicians, particularly those working in oncology practice should have a basic understanding of clinical radiation oncology and the management of radiation therapy patients. The goal of this lecture is to introduce some fundamental concepts of radiation oncology including the mechanisms, indications, and toxicity.

WHAT IS RADIATION THERAPY?

Radiation occurs in various forms including photons, which are packets of energy (X- and Gamma- rays), and subatomic particles, which include electrons, alpha particles, protons, and neutrons. Regardless of the type, when radiation interacts with matter, energy is deposited within the medium. The deposited energy excites or ionizes which may lead to the breakage of chemical bonds and the formation of free radicals. Radicals are molecules with unpaired electrons in the outer atomic orbital and are highly reactive with adjacent molecules. These molecular, chemical, interactions form the basic mechanisms by which radiation affects cells. Radiation kills cells primarily by damaging DNA.

Radiation therapy is the use of various types of radiation to treat conditions such as cancer. Three main treatment methods fall under this umbrella including:

1) Teletherapy: Also called external beam radiation therapy is the most commonly used modality. This consists of using a radiation machine to deliver a beam of radiation to the patient. The machines used for radiation include orthovoltage machines, cobalt therapy units, and linear accelerators.
2) Brachytherapy: IS the used of radioactive implants or devices to deliver the radiation directly to the tumor
3) Nuclear medicine: Is the systemic administration of radioactive substances that target tumors. (e.g. I131 for thyroid tumors).

Today's lecture focuses on teletherapy.

RADIATION DOSE AND EFFECTS

Radiation interacts with cells through the transfer of energy. Therefore, radiation dose is measured in units of energy deposited per mass of tissue. Two units have been used to describe radiation dose. The Gray (Gy) is the standard, accepted, unit for radiation dose measurement although an older unit, the rad, is still used by some. The following equations describe the units for radiation dose:

1 Gy = 1 joule/kg
1 rad = 100 ergs/g
1 Gy = 100 rad

The effects of radiation on both tumors and normal tissues depend on dose. In the context of radiation therapy, normal tissues fall into two types, the early responding and the late responding tissues based upon the time frame in which radiation toxicity is exhibited. For early responding tissues, toxicity is seen within weeks of radiation exposure. Damage to late responding tissues is not clinically evident for months or years following treatment. Early responding tissues comprise the continually dividing tissues, whereas late responding tissues are not generally mitotically active. Examples of early responding tissues include epithelial layers of the skin or mucosa and bone marrow. Late responding tissues include for example nervous tissue and bone. Most organs contain cells that fall into both tissue categories.

There are a number of ways in which the radiation oncologist seeks to exploit differences in normal and tumor tissues to improve the therapeutic result. These include:
1. Fractionation
2. Precise tumor localization
3. Planned multimodality therapy
4. Computer treatment planning
5. Positioning
6. Instrumentation
7. Sensitizers/protectants

Fractionation of dose: Since the 1920's it has been know that radiation therapy is more effective and better tolerated when radiation dose is delivered in multiple small treatments as opposed to delivering the dose all at once. Individual radiation treatments are called "fractions." Three variables dictate the response of tissues to radiation. These are 1) total dose, 2) fraction size, 3) duration of treatment protocol.

- **Total Dose:** Total dose is related to both tumor response and toxicity. The higher the dose of radiation delivered, the better the chance of durable tumor control. However, as dose increases toxicity, both late and acute also may increase.
- **Fraction size:** The larger the fraction size the higher the probability of developing a late effect of radiation. When larger fractions are used the total dose has to be decreased to avoid increasing the probability of a late irreversible effect of radiation. Conversely, if the fraction size is dropped the total dose may be increased which may enhance tumor control.

- **Duration of treatment:** The longer the radiation protocol, the fewer and milder the acute effects of radiation. Unfortunately, this may also be associated with more opportunity for the tumor to repopulate during treatment. Particularly for fast growing tumors, giving dose in a short period of time may enhance tumor control. However, this may also increase acute effects.

For each patient treated with irradiation, the radiation oncologist must prescribe a dose and a fractionation protocol. The first consideration is the goal of therapy. Treatment may be either curative or palliative in intent. The decision to pursue curative vs palliative therapy is a decision based upon the biologic behavior of the tumor, the quality of life of the animal, and client wishes and expectations. In curative treatment, the treatment prescription should deliver sufficient dose for a high probability of tumor control and the dose will be delivered with the fractionation protocol preferred by the radiation oncologist.

In palliative treatment the goal is to improve the quality of life of the patient when the tumor is unlikely to be cured by irradiation but is causing considerable discomfort. Palliative therapy protocols prescribe a few large fractions of radiation. Because these patients are not expected to survive long term, the increased probability of late radiation complications associated with large fraction size is unlikely to be of concern. The total dose administered is low enough to prevent significant acute radiation injury. Palliative treatment is particularly helpful in alleviating bone pain caused by a primary tumor or metastases.

The treatment plan: Plans may be generated by hand or computerized treatment planning software may be used. The radiation oncologist must understand how the dose from a radiation beam will be distributed in tissue. The plan will detail the number of beams to be used, the shape of the treated fields, and the dose that will be delivered by each beam, so that the tumor volume is treated to the prescribed dose and normal tissue is spared.

Administering the treatment: The best radiation plans may fail if the treatment is not delivered precisely. The patient must remain still for several minutes after being positioned on the treatment table (also called a couch) and personnel must leave the room during irradiation. Therefore, general anesthesia is required for radiation therapy in animals. The patient must be positioned precisely as planned to avoid missing the tumor or inappropriately exposing normal structures to irradiation. Positioning devices including frames and cradles aid in positioning.

Tools to verify positioning of the patient include simulators and portal radiography. Portal radiographs are taken using the therapy unit. Unfortunately, the high energy of the therapy beam results in poor detail, but the anatomic region included in the treatment may be identified when appropriate radiographic film and screens are used. New radiation therapy units include high quality onboard imaging systems. These systems allow for increased precision of positioning and thus the margin of normal tissue treated may be decreased.

COMBINING RADIATION WITH OTHER TREATMENT MODALITIES

The goal of combining therapies is to increase tumor control while decreasing normal tissue damage, a concept known as therapeutic gain. If altering a treatment regimen increases damage to the tumor and normal tissues equally, there is no therapeutic gain.

Combining radiation with surgery

Both theory and clinical data support a substantial therapeutic gain when surgery and radiation are combined appropriately. Surgery is most likely to fail at the periphery of the tumor where microscopic tumor can be left behind. The large, bulky portion of the tumor can frequently be removed however. Conversely, the cells at the periphery of the tumor tend to be well oxygenated and cycling, rendering these cells most sensitive to irradiation whereas the cells within a bulky mass may be more radiation resistant. The success of combined surgery and radiation requires deliberation of the consequences of surgery, the sequence of administration of the two modalities, and the timing of administration. Communication between the surgeon and radiation oncologist is essential to achieve a high probability of tumor control, function, and cosmesis. A good radiation plan cannot be generated on the basis of a surgical scar and a pathology report describing incomplete margins.

When the likelihood for en bloc resection is low, the goal of surgery is to reduce the tumor burden to subclinical or microscopic levels. If this requires functional or severe cosmetic impairment, surgery may negatively impact therapeutic gain by increasing normal tissue damage. Similarly, therapeutic gain may be undermined when reduction of tumor burden leaves gross disease. In this case the surgery has not reduced tumor burden sufficiently to allow for improved radiation responsiveness. Response may in fact be compromised due to disrupted blood supply and subsequent hypoxia.

The sequence of surgery and radiation should be considered prior to beginning a course of treatment. The sequence of treatments influences field size, wound healing, blood supply, tumor growth kinetics, and metastasis. All of these issues must be considered to determine the optimum treatment plan.

Radiation and chemotherapy

Indications for cancer chemotherapy include a sensitive histologic type, such as lymphomas and leukemias, or a high likelihood of systemic metastasis. Chemotherapy is rarely indicated for the local control of solid tumors. There are two contexts in which chemotherapy can be combined with radiation therapy to improve treatment results. First chemotherapy may be useful in treating systemic disease or metastasis that will not be addressed by local irradiation. Second, some chemotherapeutic agents may act as radiation sensitizers.

Radiation sensitizing agents act synergistically with radiation to increase lethality beyond the level that is expected from purely additive effects. Not all drugs that sensitize cells to irradiation increase the therapeutic gain achieved through radiation alone, however. It is necessary that sensitizers increase tumor sensitivity without increasing the sensitivity of normal tissues to the same degree. Other radiation sensitizers include drugs that target the resistant, hypoxic population of cells within a tumor. Newer targeted therapies including anti-angiogenic agents are also being explored for synergism with irradiation.