Surgery and radiation therapy are the most important tools for achieving local tumor control in patients with solid tumors. Both modalities are geographically oriented and abide by the principles that 1) microscopic tumor extension must be anticipated and addressed and 2) critical normal tissue structures must be spared. The decision to treat with surgery versus radiation is based on tumor control, preservation of normal tissue structures and financial considerations. New technical developments in both surgical and radiation oncology have expanded the boundaries of what can be treated with curative intention. Despite these advances, combining radiation therapy and surgery is sometimes required to achieve an optimal outcome.

This lecture will focus on cancers where new radiation therapy treatment alternatives are now available. Additionally, new paradigms for combining radiation therapy and surgery will be discussed.

Intensity Modulated Radiation Therapy (IMRT)

Cancers of Urogenital Tract: Intensity modulated radiation therapy (IMRT) has been used for treatment of unresectable or incompletely resected cancers of the canine urogenital tract. A report of 20 dogs with carcinoma of the urinary bladder, ureters, urethra and/or prostate demonstrated an overall median survival time of over 400 days. Acute complications of therapy were common but generally mild; late side-effects, including urethral stricture and ureteral obstruction, were rare. The treatment was effective and better tolerated than previous reports of pelvic irradiation.(1)

Improvement in tumor control and decreased radiation effects are attributed to using a combination of IMRT and image guided radiation therapy (IGRT). With IMRT the intensity of each beam is controlled through collimator leaves (MLC) that move during treatment, allowing the dose to be sculpted around important normal structures. This technique requires a treatment planning system that uses an inverse planning algorithm. Inverse planning requires that the planning target volume (PTV) and critical normal tissue structures be identified and contoured into the planning system. Optimization objectives for each structure are entered, and the algorithm attempts to meet all objectives and deliver the prescribed dose to the tumor while meeting normal tissue constraints (Figure 1). This procedure is enhanced by applying IGRT, which accounts for the variability in tumor/bladder/prostate location within the body between treatments.

IMRT has also been shown to decrease acute effects associated the treatment of nasal tumors and oral tumors (personal communication, Ronald Carsten). Ocular structures and salivary glands can be spared and dose escalation could lead to improved tumor control. IMRT requires that patients be immobilized in a fashion that can be consistently repeated for each fraction. IMRT is administered using small doses per fraction in a schedule that generally ranges from 3-5 weeks in veterinary patients. Normal tissue structures such as spinal cord, heart and bladder are very tolerant of small doses/fractiion. IMRT is appropriate for treating residual microscopic disease post-surgery. It can also be used for the treatment of gross tumor.
Stereotactic radiation therapy (SRT)

Bone tumors; SRT for limbsparing provides excellent tumor control and can be used in almost any location. For osteosarcoma, standard chemotherapy is also administered and survival times are comparable to patients treated with amputation and chemotherapy. Patient selection is important because extremely lytic tumors are vulnerable to early fracture and pre-emptive stabilization may be indicated. SRT has also been used for the treatment of axial osteosarcoma.

SRT is a non-surgical technique using highly focused radiation beams that requires some sort of stereotactic imaging system to confirm fiducial location. A number of different systems have been developed for SRT including the Body Gamma Knife, Cyberknife and linear accelerator based systems, such as the Varian Trilogy™ (Figure 2).

Biologically SRT differs from fractionated radiation therapy because normal tissue structures are spared through avoidance rather than from administering small doses per fraction. SRT treatment is generally delivered in 1-5 fractions, minimizing anesthesia effects to the patient and making it convenient for the owner. Acute effects are minimal and tumor associated signs such as discomfort or dysfunction often improve rapidly.

Brain and Pituitary Tumors: These tumors are amenable to treatment with SRT. Median survival in 19 dogs with meningeal appearing tumors treated with SRT (594 days) is consistent outcome data from fractionated radiation studies (personal communication, Lynn Griffin). Over a dozen cats with acromegaly have been treated at Colorado State University over the last 3 years (Figure 3). The endocrinopathies associated with the syndrome have resolved or become much easier to manage. A few of the cats have become hypothyroid, but there have been no other adverse effects. Median survival has not been reached. A clinical trial has opened up at Colorado State University to evaluate SRT for the treatment of canine Cushing’s disease.

SRT has also been used to treat thyroid tumors, tumors of the mediastinum, rib tumors, soft tissue sarcomas of the head and body region, feline vaccine associated sarcoma, melanoma, and feline oral squamous cell carcinoma.

Combining Surgery and Radiation Therapy

Combining surgery and radiation therapy can improve treatment outcome in tumors that are difficult to control with a single modality treatment. Surgery can remove bulky disease, but can fail at the periphery of the tumor if microscopic tumor remains. Fractionated radiation therapy is not effective for large tumors, but can spare surrounding normal tissue while killing residual disease. Combining the two allows the surgery to remove bulky disease while the radiation eliminates local microscopic disease and regional nodal disease. Much has been written about the sequencing of these modalities. From a biological aspect, radiation before surgery requires a smaller radiation field and the vascular supply of the tumor is not compromised by surgery. Vascular compromise could increase hypoxia, which makes radiation treatment less effective. Also, radiation first can sometimes make a non-resectable tumor into a tumor with surgical options. Treating with radiation first may be associated with an increase in surgical complication. Surgery before radiation therapy provides optimal tumor staging/grading and patients can physically and psychologically benefit from having reduced tumor burden. Radiation dosimetry must also be considered in the decision making process. For instance, sparing the colon may be easier if radiation is performed before resecting a peritoneal tumor. Conversely, a large soft-tissue sarcoma over the ribs of a cat may be easier to irradiate if the tumor has been removed and electrons (more superficial) treatment can be used for the radiation.
treatment. Therefore each patient should be individually evaluated and the surgeon and radiation oncologist should work as a team to determine the most appropriate sequencing.

When combining surgery with stereotactic radiation therapy, SRT must be delivered first. *SRT cannot be used to treat microscopic residual disease.* SRT relies on having a target (the tumor) and avoiding normal tissue structures. SRT is still a relatively new treatment in both human and veterinary medicine. However, it appears that SRT may be more effective against bulky tumors than fractionated radiation therapy. The optimal way to combine SRT with surgery is not known. It may take from 4-6 months for a tumors to shrink following SRT. Tumors should be observed regularly over this period and if it appears the tumor has stopped shrinking, then surgery should be considered.

Reference List


![Figure 1. IMRT treatment plan of a prostate/urethral tumor. Note that the prescribed dose (in red) is targeted to the prostate and urethra while the dose to the colon is restricted. The top right view is a dose volume histogram that provides detailed information regarding dose to specific structures.](image-url)
Figure 2. A. Patient on carbon fiber board with customized acrylic straps for immobilization. B. Utilizing on-board kV imaging to align patient before treating.

Figure 3. Treatment plan for a cat with acromegally. Note multiple beams providing sharp drop-off in dose from the target.