

# Indications for Multimodality Therapy in Veterinary Oncology

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# Multimodality Therapy

- The use of more than one form of treatment as the primary therapy for cancer
  - Surgery, radiation, chemotherapy
  - Does not include rescue therapy
  - Can consist of simultaneous or staged therapy

# Veterinary Oncology

- Often think of single modality therapy
  - Lymphoma = chemotherapy
  - Solid tumors = surgery
- Radiation is often overlooked or thought of as something to be avoided
- Relax - accept the photon. The photon is good. The photon is our friend.

# Radiation Therapy

- Generally think of radiation as a local therapy only
  - Adjuvant therapy post-op
  - Highly invasive tumors
  - Surgically-unfeasible sites
  - Palliation

# Human Radiation Therapy

- Combination therapy is typical
  - Surgery, radiation, chemotherapy
  - “Chemoradiation” – the combination of radiation and chemotherapy either to improve local control or treat disease on two fronts

# Chemoradiation

- Uses of Chemoradiation
  - Achieve primary control over disease (head & neck cancers)
  - Adjuvant therapy post-op (breast cancer)
  - Regional lymph node therapy (various carcinomas)
  - Chemo for distant disease; radiation for local (sarcomas)

# Chemoradiation

- Principles of Action:
  - **Spatial cooperation**
  - **Additivity**
  - Supra-additivity (referred to improperly as 'radiosensitization')
  - Infra-additivity

# Chemoradiation

- **Spatial cooperation** – radiation affects local disease; chemotherapy affects metastatic disease
- **Additivity** – Both treatments affect the primary tumor without complimentary interaction

# Chemoradiation

**Supra-additivity** – enhanced tumor kill greater than the summation of damage expected from the individual treatments.

- **Infra-additivity** – protection of the tumor due to chemotherapy inhibiting damage caused by radiation

# Chemoradiation

- To achieve spatial cooperation or additivity, chemo and radiation must be used at full dose levels or, in the case of chemo, to at least cytotoxic levels.
  - I often recommend lower doses of chemo when used concurrently with radiation
- Supra-additivity may be achieved with lower doses of chemotherapy.
  - “Sensitization dose”

# Additivity / Supra-additivity



DNA ADDUCT



Single strand break



Additive damage leading to  
increased cell kill

# Veterinary Uses of Chemoradiation

- In general we are thinking of spatial cooperation
  - use of radiation to achieve local control
  - use of chemotherapy to achieve distant control
- If an additive result occurs, so much the better, but this is usually elusive

# Common Indications for Chemoradiation in Veterinary Medicine

- Mast cell tumor
- Lymphoma
- Head & neck tumors
  - Nasal, oral, thyroid
- Various others
  - Anal sac, osteosarcoma

# Mast Cell Tumor

Cutaneous form is a surgical disease +/- radiation +/- chemotherapy

Surgery alone – low to intermediate grade with complete margins

Surgery + radiation – low to intermediate grade with incomplete margins with no evidence of metastasis

Surgery + chemotherapy – Intermediate or high grade tumor +/- complete margins +/- metastasis

# Mast Cell Tumor

- Question:
- How to treat a dog with a non-resectable primary tumor with proven regional lymph node metastases?

# Mast Cell Tumor

- Multimodality approach:
  - Radiation for loco-regional control
  - Chemotherapy for distant metastases plus loco-regional control
  - Surgery if nodes remain enlarged or if primary tumor reduced to a more amenable size
- Example of spatial cooperation with a hope for additivity

# Lymphoma

- In veterinary medicine this is the domain of chemotherapy.
- Radiation can be effective for local relapses, loco-regional relapses, or multiple peripheral node relapses (total nodal).

# Lymphoma and Radiation

- Poorly reported but well known that relatively low doses of radiation are typically effective at inducing rapid, complete remissions.
  - Emergency treatment of pharyngeal nodes
  - Cutaneous relapses
  - Total/partial nodal
- Example of spatial cooperation since original chemo is no longer effective

# Lymphoma - HBRT

- Half-body radiotherapy (HBRT)
  - Recently several reports
  - Soon to be published Cornell data
- Induce similar first remissions with fewer treatments overall
  - Spatial cooperation
  - No additive effect noted

# Feline Nasal Lymphoma

- Chemotherapy and radiation are effective as single therapy
  - Chemotherapy - one year MST
  - Radiation - 18 month MST
  - Combination - 31 month PFI

Example of an additive therapy, possibly supra-additive

# Other Tumors Treated with Multimodality Therapy

- Osteosarcoma
  - Surgery and chemotherapy; role of radiation?
- Anal sac adenocarcinoma
  - Radiation and surgery; role of chemotherapy?
- Thyroid carcinoma
  - Similar to anal sac - full role of multimodality therapy has yet to be explored