

Policy on Experimental Tumor Production and Treatment in Rodents

PURPOSE

The purpose of this policy is to provide guidelines for the Virginia Tech research community on experimentally induced neoplasia in rodents. Investigators producing tumors in rodents should use this document as a reference in preparing their animal care and use protocols.

CANCER BIOLOGY AND THERAPY

Cancer studies can broadly be divided into two categories—biology and treatment. *Cancer biology* is the study of how tumors grow and behave. The guidelines presented here are intended to limit the tumor burden an animal experiences to that which does not cause excessive pain or distress. *Cancer treatment* is the study of the response of tumors to chemical, radiologic, or immunologic therapy. In cancer treatment studies, not only must the tumor burden be considered, but the effect of the treatment modality must also be evaluated. The purpose of all cancer treatments, whether radiologic, immunologic, or chemical, is to destroy or disable the cancer cells while minimizing damage to healthy tissues. The success of a treatment becomes a balance between cancer destruction and reduction of side effects.

GENERAL GUIDELINES

1. For all cancer research using animal models, endpoints should be established that minimize the potential for pain and/or distress. The investigator should consult with a veterinarian and must have a plan for pre-emptive euthanasia based on clearly defined endpoints in the protocol.
2. Mice inoculated with tumors should be observed at least twice weekly to assess their physical condition, and observed daily as tumors are nearing their endpoint, including weekends and holidays. Records of observations must be kept and made available if requested.
3. Animals with tumors that have ulcerated or that interfere with their ability to acquire food or water and animals that become emaciated or debilitated will normally require euthanasia. When it is necessary to maintain an animal with an ulcerated tumor, the status of the ulcer and of the animal's overall condition must be assessed daily and in consultation with the Attending Veterinarian.
4. Considering both weight loss and weight gain from tumor growth, tumor burden should not exceed 10 percent of the animal's normal body weight for routine tumor passage for animals involved in therapeutic experiments (10 percent typically represents a subcutaneous flank tumor diameter of 15 mm in a 25 g mouse or 35 mm in a 250 g rat). Calibration curves should be established as part of the characterization of any new tumor system. Without a specific exception justified in the animal protocol, animals should be euthanized before tumors reach this size.

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5. In tumor therapy experiments with adult rodents, it is recommended that weight loss normally should not exceed 20 percent of the animal's body weight at the start of the experiment. For younger animals, failure to maintain weight gain to within 15 percent of untreated control animals should be considered as an indication of toxicity. Baseline body weights must be recorded for each animal on tumor studies at the start of the project and, where weight loss is an expected event, the weight of the animals must be recorded periodically. The frequency with which weight will be monitored should be stated in the protocol.

SOLID TUMOR GUIDELINES

Measurable Observation	Endpoint Criteria	Clinical Assessment
Tumor Size	Not to exceed 10% of normal body weight ^{(1), (2)}	Frequent weighing (3-5 times/week)
	Estimated tumor mass not to exceed 10% of body weight ^{(1), (2)}	Frequent measurements of solitary tumor (1 cm ³ = 1 gm)
Physical Characteristics of Tumor(s)	Evidence of necrosis Evidence of sepsis Evidence of metastasis	Physical examination: scabbing, ulceration, exudate, anorexia, hypothermia, etc.
	Evidence of local invasiveness	Restricted ambulation, inability to access food or water
	Neurologic impairment ^{(1), (2)}	Circling, blindness, dementia, convulsions
Tumor Location	Impairment of normal bodily functions	Inability to access or ingest food and water, inability to ambulate and keep clean and dry

(1) Tomasovic SP, LG Coghlan, KN Gray et al. 1988. IACUC Evaluation of Experiments Requiring Death as an End Point: A Cancer Center's Recommendations. Lab Animal 17(1): 31-34.

(2) Workman P, A Balmain, JA Hickman et al. 1988. United Kingdom Coordinating Committee on Cancer Research guidelines for the welfare of animals in experimental neoplasia. Laboratory Animals 22:195-201.

HEMATOLOGIC TUMOR GUIDELINES

In the case of leukemias and internal, disseminated, metastatic, or other occult (not readily visualized) tumors, determination of the tumor burden may be difficult. The development and/or use of appropriate biochemical and pathological laboratory methods to determine the onset of leukemia before the appearance of clinical signs is required. These methods should be described in the protocol.