Guidelines for Tumor Induction in Rodents

To provide guidelines and endpoints that avoid excessive pain and distress caused by tumor burden or tumor-associated disease. These guidelines apply to spontaneous as well as experimentally induced tumors. Deviations from these guidelines must have prior IACUC review and approval based on scientific necessity/justification.

Statement

Tumor Induction
- Subcutaneous implantation is recommended in the flank or between the shoulder blades.
- Tumor implantation should be in sites that will not interfere with normal body functions, including ambulation, eating, drinking, and elimination.

Tumor Volume
- Maximum tumor volume should not exceed $2000 \text{ (mm)}^3$ for mice and $4000 \text{ (mm)}^3$ for rats. 
- Total combined tumor volumes of multiple tumors should not exceed these size limits. Deviations from these sizes must have prior IACUC review and approval based on scientific necessity/justification.

Monitoring
- Animals with tumors should be observed at least twice weekly. Once signs of morbidity are noted and/or a tumor has reached 50% of maximum allowable size, animals should be monitored daily. Records of assessments should be maintained in the animal room.

Endpoints
- Tumor size reaches maximum allowable size.
- Tumor interferes with the animal’s ability to eat, drink, or ambulate.
- Tumor becomes ulcerated, infected, or necrotic with a break of overlying skin.
- 20% weight loss of adult body weight from tumor induction, which can manifest via an emaciated appearance. However, the weight loss could drop rapidly (over 2-4 days) or gradually, over a few weeks.
- Palpation of tumor elicits a pain response.
- Respiratory difficulty
- Animal becomes moribund, weak, comatose, unresponsive, or death appears imminent.
- Body condition score (BCS) $\leq 2$ (see attached).

Determining Mouse Body Condition Score

Body condition scoring (BCS) is a useful tool for evaluating overall condition of the mouse. Techniques such as obtaining body weights regularly may be impractical for some studies or for large numbers of animals. When one is studying genetically altered animals, or using any research animal in danger of deteriorating over a long period, or overseeing large colonies with a broad spectrum of ages, BCS offers a useful, rapid, practical, and objective alternative for health assessment. BCS is particularly helpful in cases where pregnancy, organomegaly, or tumor growth (particularly intra-abdominal growth) may interfere with body weight assessment. **Use of this method does not preclude other humane endpoint criteria, but should be used in conjunction with these standards.** At any time, an LAR veterinarian should be consulted if there are any questions. **As an end-point for premature euthanasia, the highest score that will yield**
useful data must be used – for example, if mice can be euthanized when they reach BCS 2 (approx. 10% weight loss) without compromising data, that point should be chosen, rather than the mandatory BCS 1, which can be 25% weight loss or more. If the animal must progress to BCS 1, this will need to be scientifically justified in your animal use protocol.

BCS is simple to perform: when restraining a mouse by the base of its tail using your thumb and middle finger, note its body condition by passing the index finger of the same hand over the sacroiliac bones (back and pubic bones – if this is awkward for you, a two-handed approach can be used instead). This may be done while the animal is on the floor of the cage, or on the wire cage top. This may take some practice, but, once mastered, is quick and easy. This scale is a continuum, and determining where in the spectrum a particular animal falls is accomplished most consistently if it is the same person from the lab who evaluates the animals on a regular basis.

The body condition can be scored on a scale of 1 through 5:

<table>
<thead>
<tr>
<th>BCS</th>
<th>Description</th>
</tr>
</thead>
</table>
| BCS 1 | Mouse is emaciated.  
- Skeletal structure extremely prominent;  
- Little or no flesh cover.  
- Vertebrae distinctly segmented. |
| BCS 2 | Mouse is underconditioned.  
- Segmentation of vertebral column evident.  
- Dorsal pelvic bones are readily palpable. |
| BCS 3 | Mouse is well-conditioned.  
- Spine is a continuous column.  
- Vertebrae palpable only with firm pressure. |
| BCS 4 | Mouse is overconditioned.  
- Bone structure disappears under flesh and subcutaneous fat. |
| BCS 5 | Mouse is obese.  
- Spine is smooth and bulky.  
- Bone structure disappears under flesh and subcutaneous fat. |

A “+” or a “-” can be added to the body condition score if additional increments are necessary (i.e. ...2+, 2, 2-...).

Comments:
BCS1: If a rat or mouse is found in this condition, euthanasia must be performed.

BCS2: At this stage, as the animal progresses from BCS3 to BCS2, more careful observation is warranted. Supportive care (moistened food on the cage floor, plus a water source such as water gel) should be initiated, if it would not interfere with the outcome of the experiment. If data can be obtained once the mouse has reached this point, euthanasia is required.

BCS3: This is optimal rodent body condition.

BCS4: The animal is beginning to gain weight.

BCS5: The animal is obese. The feeding of a lower-fat, lower-protein chow may be considered at this point for optimal health.

References


Contact

Please contact the School of Medicine IACUC office if you have any questions about this guidance.
Phone: 317-278-1826
Email: somiacuc@iupui.edu