Welfare refinement in a mouse model of bone cancer

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Rationale: Bone cancers are extremely painful in humans, so large numbers of mice are used as models to develop anti-cancer treatments. However, there is little information on how this affects animal welfare. We used methods of mouse welfare monitoring and pain-specific assessments to evaluate the appropriateness of current end-point guidelines and any refinement needs in mice with Osteosarcoma.

Methods: Female NOD SCID mice were orthotopically implanted with saline or $1x10^6$ TC71 imageable (bioluminescent) cancer cells (n=10/group).
Welfare Assessment: Daily body weight, food and water intake and nest quality recordings (Fig. 1A). The Mouse Grimace scale (MGS) provided facial expression analysis of changes caused by poor welfare (Fig. 1B).
Pain Assessment: Weekly tactile allodynia (von Frey) and Conditioned Place Preference (CPP) testing. Mice were repeatedly conditioned and tested for preference to CPP chambers previously paired with saline or analgesic (20mg/kg Meloxicam). If painful, mice were predicted to show an increased preference for (exploration of) the analgesic-paired ('pain-relieving') chamber (Fig. 3).

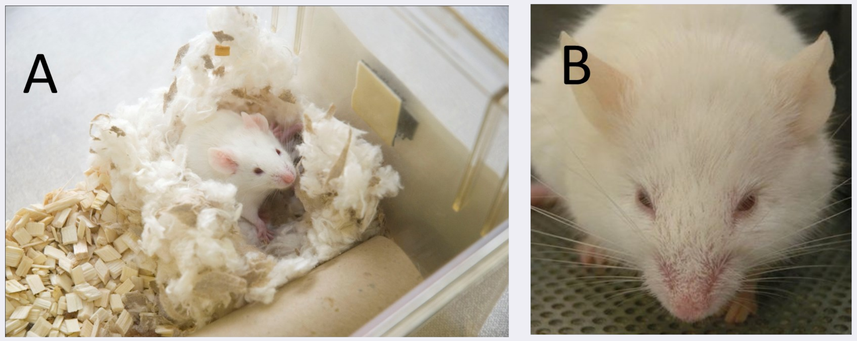

Fig. 1. (A) A nest scoring 4 /5 on the Ness scale (1); (B) Facial expression showing MSG units 'orbital tightening', 'nose bulge' and 'earl flattening' (penultimate day).

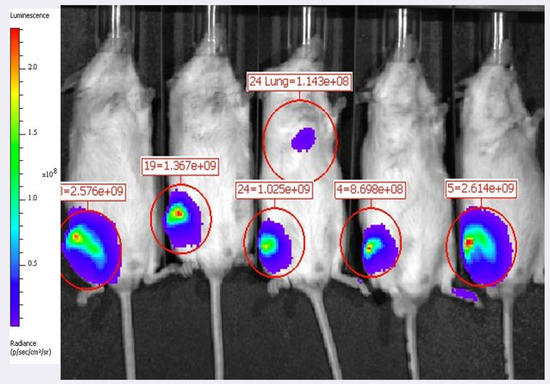

Fig. 2. IVIS image showing Bioluminescent signals. Note the variable signal intensity and lung metastasis (Day 47).

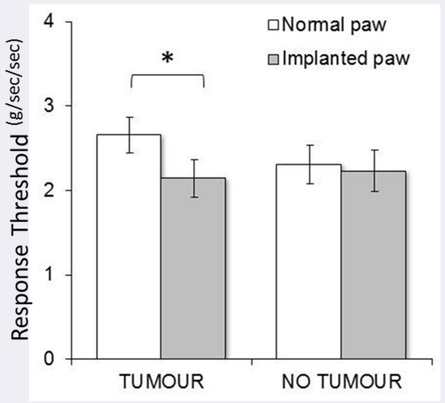

Figure 5. eVF results showing reduced threshold in tumour mice to testing in von Frey testing (indicating tactile allodynia)

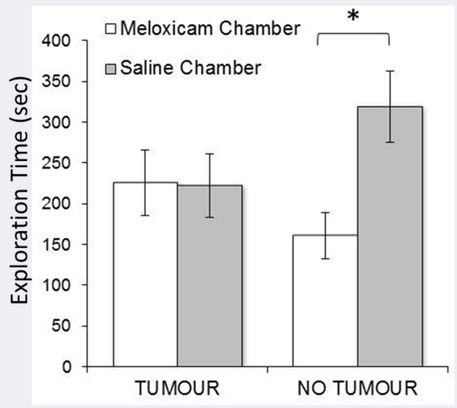

Figure 4. CPP results showing aversion to Meloxicam in control mice. Tumour mice showed no chamber preference

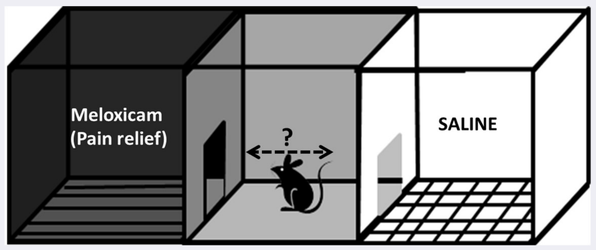

Fig. 3. CPP boxes showing black & white conditioning/choice chambers. Mice were conditioned by being confined to either chamber following meloxicam or saline (counterbalanced design) then chose their preferred chamber on drug-free test days.

Results and Conclusions: There were no significant changes in weight data or nest quality, however, changes in facial expression indicated *malaise* (if not pain) close to the study end-point (Fig 2B). Meloxicam was aversive to control but not tumour mice; possibly indicating some analgesic effects, There was evidence of discomfort (Fig 5) from moderately increased tactile responsiveness (Fig 5) and reduced aversion to meloxicam in tumour mice, but variable tumour growth (Fig. 2) prevented us from being able to firmly establish refinement needs beyond present welfare guidelines.

(1) Hess, S. E., S. Rohr, B. D. Dufour, B. N. Gaskill et al (2008). "Home improvement: C57BL/6J mice given more naturalistic nesting materials build better nests." J Am Assoc Lab Anim Sci 47(6): 25-31.

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