

Frequent, Quantitative Bone Planar Scintigraphy for Determination of Bone Anabolism in Growing Mice

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Abstract

Background

To provide insight into bone turnover, quantitative measurements of bone remodeling are required. Radionuclide studies are widely used in clinical care, but have been rarely used in the exploration of the bone in preclinical studies. We describe a bone planar scintigraphy method for frequent assessment of bone activity in mice across the growing period. Since repeated venous radiotracer injections are hardly feasible in mice, we investigated the subcutaneous route.

Methods

Repeated phosphonate tracer bone planar scintigraphy studies of the knee region and μ CT to measure femur growth rate were performed in eight mice between week 6 and week 27 of life, i.e. during their growth period. Three independent investigators assessed the regions of interest (ROI). An index was calculated based on the counts in knees ROI (normalized by pixels and seconds), corrected for the activity administered, the decay between administration and imaging, and individual weights.

Results

A total of 97 scintigraphy studies and 90 μ CT were performed. Repeated subcutaneous tracer injections were well tolerated and allowed for adequate radionuclide studies. Mean scintigraphic indexes in the knees ROI decreased from $87.4 \pm 13.0 \times 10^{-6}$ counts.s⁻¹.pixel⁻¹.MBq⁻¹.g⁻¹ at week 6 to $13.1 \pm 3.9 \times 10^{-6}$ counts.s⁻¹.pixel⁻¹.MBq⁻¹.g⁻¹ at week 27. The time constant of the fitted exponential decay was equal to 23.6 days. Mean femur length assessed by μ CT increased from 12.2 ± 0.8 mm at week 6 to 15.8 ± 0.2 mm at week 24. The time constant of the fitted Gompertz law was equal to 26.7 days.

Conclusion

This study demonstrates the potential of repeated bone planar scintigraphy in growing mice, with subcutaneous route for tracer administration, for quantitative assessment of bone remodeling.

Full Text

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Figures

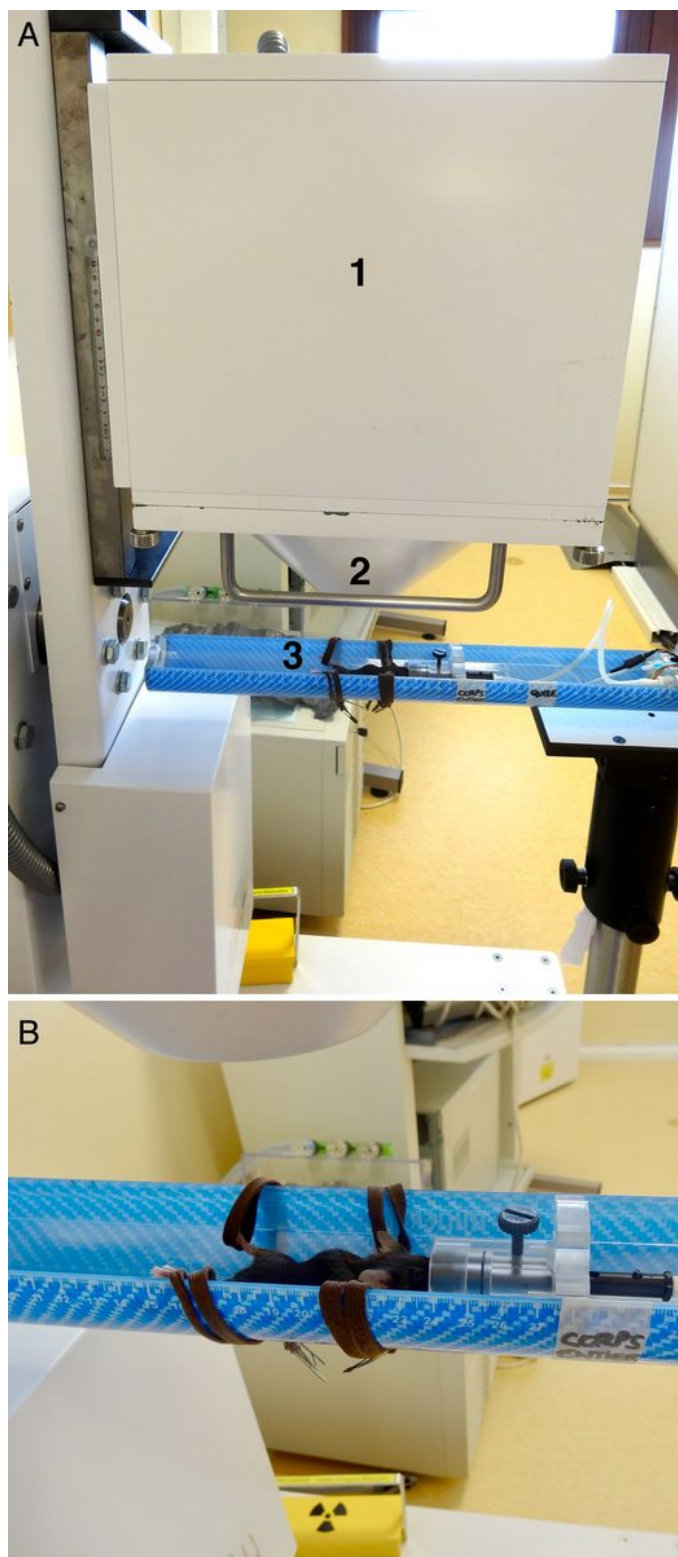


Figure 1

Experimental setup. (A) Side view, showing (1) the head of the gamma-camera, (2) the collimator and (3) the animal inside the bed. (B) Close view of the bed showing the laces used to move away the hind legs, and especially the knees, from the body.

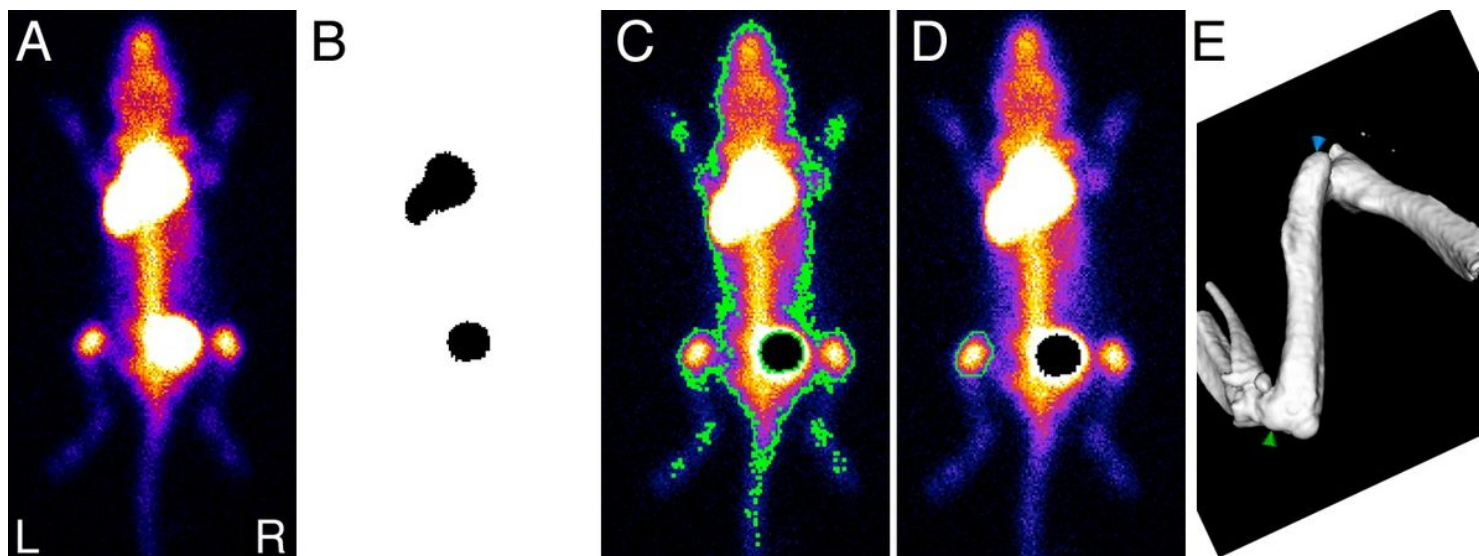


Figure 2

Sequential view of data processing. (A) Typical dorsal view, saturated pixels, allowing visualization from top to bottom the injection site, the bladder and the knees. (B) Automatically applied threshold using maximum entropy method: the injection site (top) and the bladder (bottom) were detected, and masks are used to define corresponding ROI. They are used to get the number of counts inside the injection site and to withdraw the bladder for the next step. (C) Automatically applied threshold using Huang's fuzzy thresholding method to create the whole body ROI (surrounded by a green line). (D) Freehand ROI drawn on the left knee (surrounded by a green line). (E) Isosurface representation of the femur (selected from a typical whole body μ CT acquisition): femoral length was measured between the higher point of greater trochanter (green arrow) and the maximal concavity of lateral epicondyle (blue arrow).

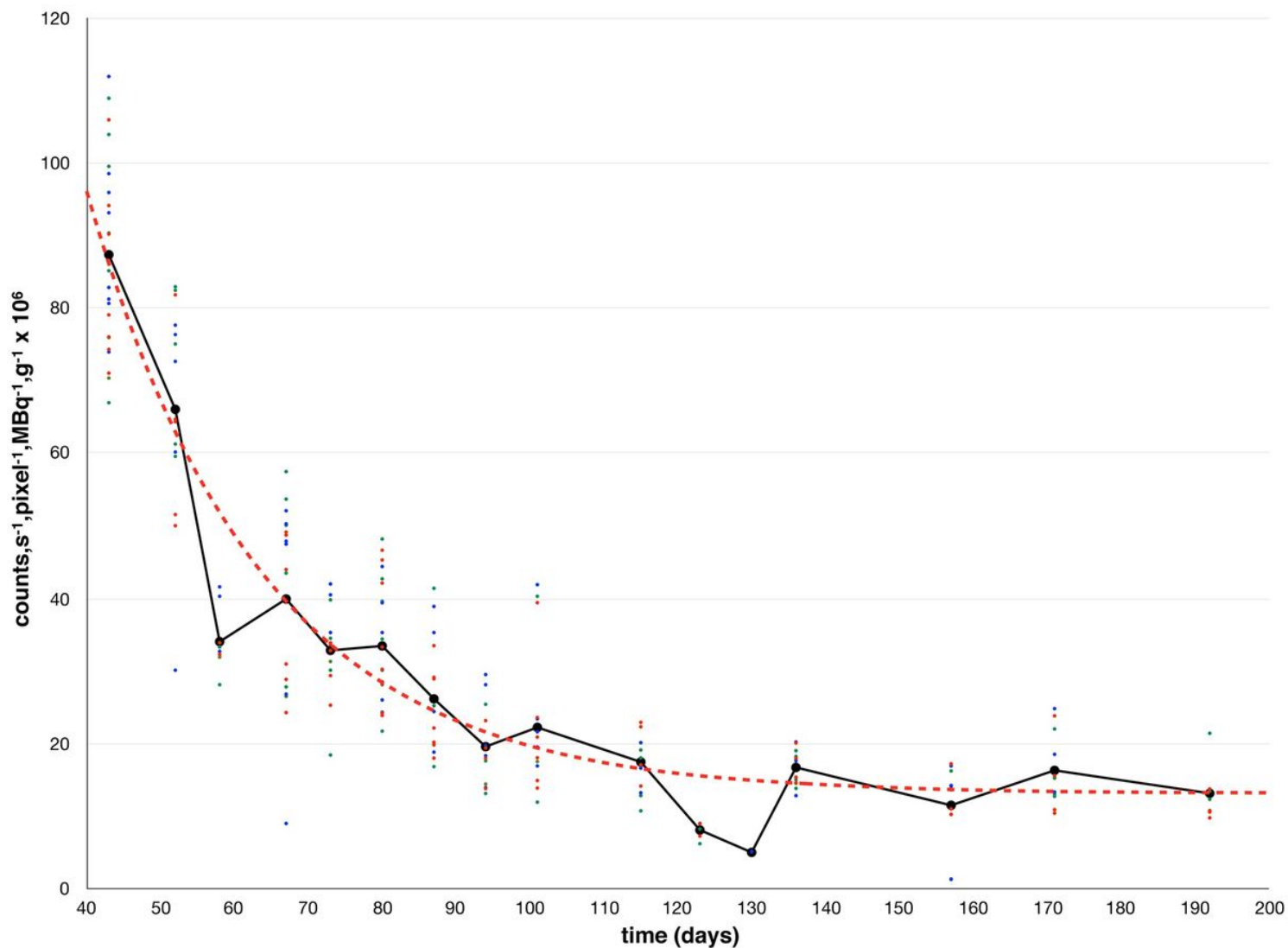


Figure 3

Index reflecting osteoblastic activity as a function of the age of the animals. A color dot (one color per investigator) represents one processed acquisition. In black, the curve connects the dots corresponding to the mean for all investigators at each time of acquisition. The red dotted line represents the exponential formula [1] used to fit scintigraphic data.

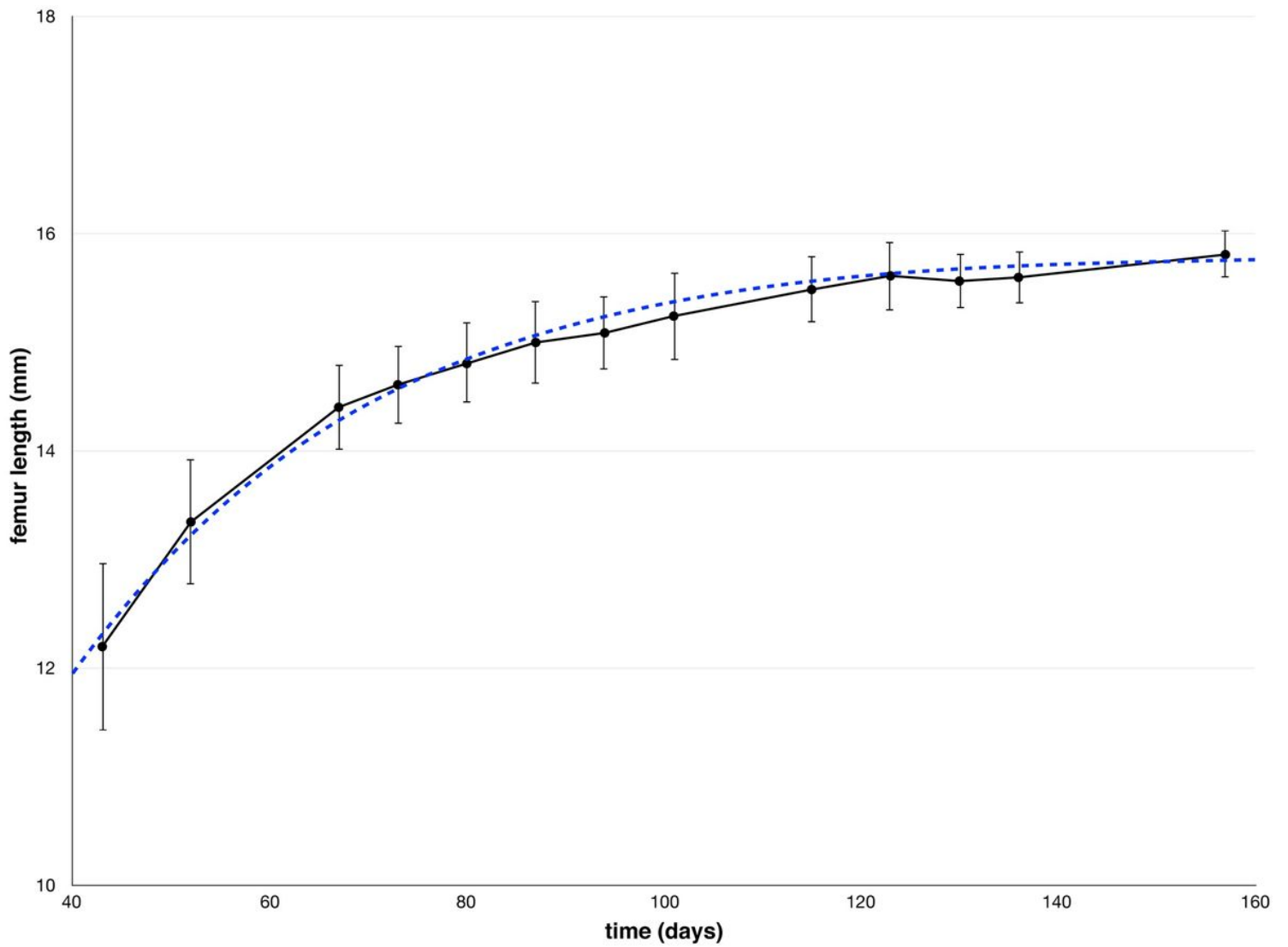


Figure 4

Mean values of femur length measured by μ CT as a function of the age of the animals, along with standard deviations. The blue dotted line represents the Gompertz formula [2] used to fit femur length.