Dual-energy x-ray absorptiometry (DXA) differentiates body composition and bone mineral density in different mouse strains

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INTRODUCTION

Dual-energy X-ray Absorptiometry (DXA), peripheral quantitative computed tomography (pQCT) and micro-computed tomography (µCT) are imaging methods in bone research, and DXA and nuclear magnetic resonance (NMR) are imaging methods in metabolic research. These methods have different advantages, and it can be challenging to choose the right methods for a study. DXA technology utilizes variable absorption of X-rays by different body components that allows reliable analysis of body composition and bone mineral density (BMD). DXA is the gold-standard bone analysis method in humans, but its full potential has not been exploited in preclinical studies.

METHODS

DXA is a measurement technology based on variable absorption of X-rays by different body components. DXA uses high and low energy X-ray photons that are differentially absorbed by bone, soft and fat tissues. DXA measurements distinguish bone from soft tissues due to higher number of calcium and phosphorous atoms in bone, as compared to higher number of carbon, nitrogen and oxygen atoms in soft tissues. Fat is largely composed of repeated methylene units ((CH_2)n), whereas X-ray attenuation of lean tissues is similar to water (H_2O). The difference in X-ray attenuation between fat and lean tissues is attributed to the atomic number difference between carbon and oxygen.

Reference image of a small-animal DXA

COMPARISON OF IMAGING METHODS

In bone research, DXA and pQCT can be used for analyzing BMD and bone mineral content (BMC). The analysis is performed from 2D images in DXA and 3D images in pQCT. With pQCT the analysis can be performed separately from cortical and trabecular bone areas of imaged bones. A benefit of DXA is the whole-body imaging and analysis from selected Regions of Interest (ROIs). µCT imaging can be used for analyzing total bone volume from trabecular and cortical bone compartments separately. DXA and pQCT allow repeated measurements in longitudinal studies while µCT is commonly an endpoint measurement, although relatively accurate in vivo µCT equipment are today available. The time from imaging to analysis is lowest with DXA (1 minute per animal) compared to more laborious pQCT (15 minutes) and µCT (30 minutes).

In metabolic research, both DXA and NMR can be used to analyze fat and lean mass. The benefit of DXA is the analysis of specific ROIs from whole-body images whereas NMR only provides results per animal.

Table 1: Comparison of imaging techniques commonly used in bone and metabolic research.

TABLE 1	Bone research			Metabolic research	
Imaging technique	**DXA**	**pQCT**	**µCT**	**DXA**	**NMR**
Measurement readouts	Total or ROI specific BMD and BMC, and bone area	Total or cortial and trabecular BMD and BMC	Bone volume and bone structural paramers separately for cortical and trabecular bone	Total and ROI specific fat and lean mass (g and %), and total mass and tissue area	Total fat and lean mass (g) and free body fluid
Longitudinal studies	Yes	Yes	No (yes with in vivo µCT)	Yes	Yes
Anesthesia	Yes	Yes	No (yes with in vivo µCT)	Yes	No (immobilization during measurement)
Time from imaging to results	Low	Medium	High	Low	Low
Imaging/ analysis time	25 sec/ 30 sec	10 min/ 5min	20 min/ 10 min	25 sec/ 30 sec	1 min/ 0 sec

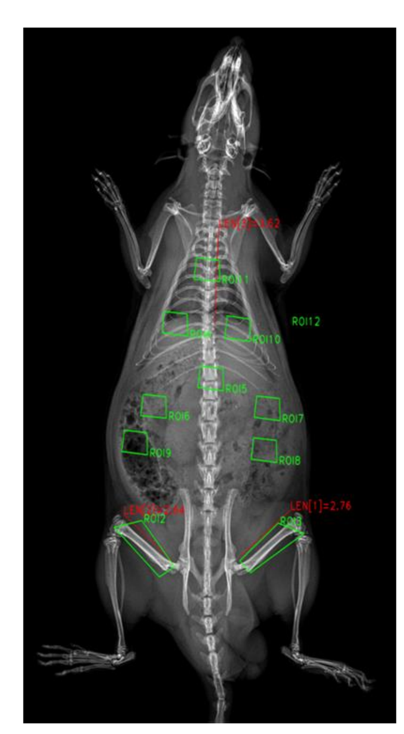

Table 2: Summary of readouts obtained from imaging techniques commonly used in bone and metabolic research. * = less accurate than DXA, ** = provided as an optional setup

Function	DXA	pQCT	µCT	DXA	NMR
3D Image	No	No	Yes	No	No
2D DR Image	Yes	Yes	Yes	Yes	No
BMD (g/㎠)	Yes	Yes	Yes*	Yes	No
BMC (g)	Yes	Yes	Yes*	Yes	No
FAT (g)	Yes	No	Yes**	Yes	Yes
LEAN (g)	Yes	No	Yes**	Yes	Yes
FAT (%)	Yes	No	No	Yes	Yes
Bone Area (㎠)	Yes	Yes	No	Yes	No
Free Body Fluid (Water)	No	No	No	No	Yes
Heavy Animals (~1000 g)	Yes	No	No	Yes	No
Price	Low	Middle	High	Low	Middle

RESULTS

In validation of a small-animal DXA, iNSiGHT, a study was performed to evaluate bone remodelling in three mouse strains, C3H, BALB/c and C57BL6, with different fat and lean masses. C3H mice had the highest body weight together with the highest fat and lean mass as determined by DXA, followed by C57BL6 and BALB/c mice. Bone mineral density (BMD) and bone mineral content (BMC) measured by DXA indicated similar findings, demonstrating that C3H mice with highest body mass had also highest BMD and BMC values, followed by C57BL6 and BALB/c mice. The DXA results correlated with more detailed bone analysis with more extensive methods such as µCT and bone histomorphometry.

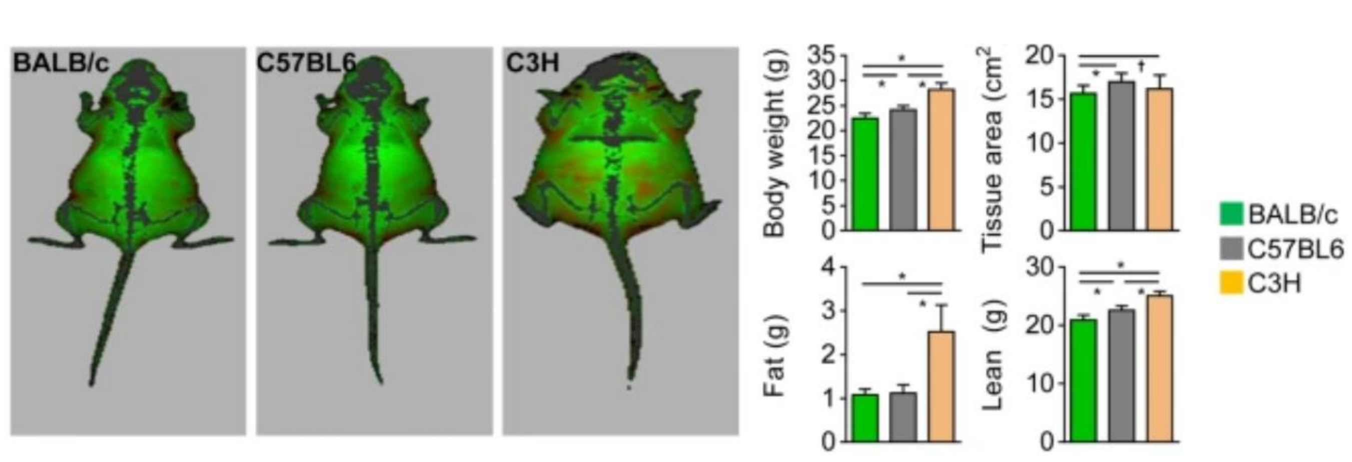

Figure 1. Analysis of body weight (g), tissue area (cm^2), fat (g) and lean mass (g) in different mouse strains by DXA.

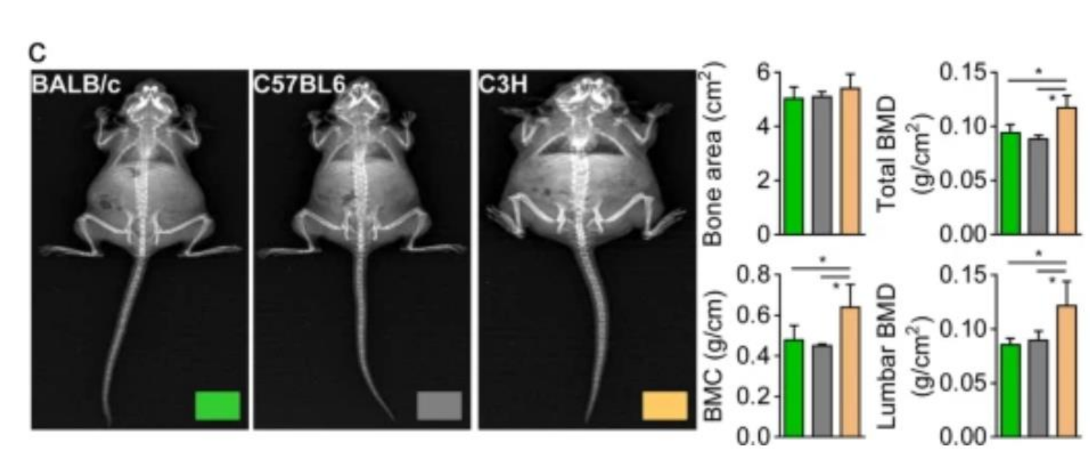

Figure 2. Analysis of body bone area (cm^2), total BMD (g/cm^2), BMC (g/cm), and lumbar BMD (g/cm^2) different mouse strains by DXA.

CONCLUSIONS

Whole-body imaging, ROI analysis and short imaging and analysis time are the main advantages of DXA in both bone and metabolic disease research. Supporting methods such as µCT can be used to access more detailed structural information of bone when needed. Mouse strains have variable body composition and BMD, which can affect the study outcome.

"DXA is a rapid and accurate imaging method that can be utilized in bone and metabolic research. Key advantages over other imaging methods include whole-body imaging capability and analysis of user-selected multiple ROIs during the study."

SELECTED REFERENCES

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OncoBone OsteoSys

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