The Effect Of Solo- Versus Group- Micro-CT Scanning On Detection Of Trabecular And Cortical Disease Phenotype In Mouse Bones

Rachel Kohler[1], Carli Tastad[2], Alexander J. Stacy[2], Elizabeth A. Swallow[3], Corinne E. Metzger[3], Matthew R. Allen[2,3,4,5], and Joseph M. Wallace[2]

[1]Weldon School of Biomedical Engineering, Purdue University, West Lafayette IN, United States; [2]Department of Biomedical Engineering, Indiana University Purdue University of Indianapolis, Indianapolis, IN, United States; [3]Department of Anatomy and Cell Biology, Indiana University School of Medicine, Indianapolis IN, United States; [4]Department of Medicine – Division of Nephrology, Indiana University School of Medicine, Indianapolis IN, United States; [5]Roudebush Veterans Administration Medical Center, Indianapolis, IN, United States.

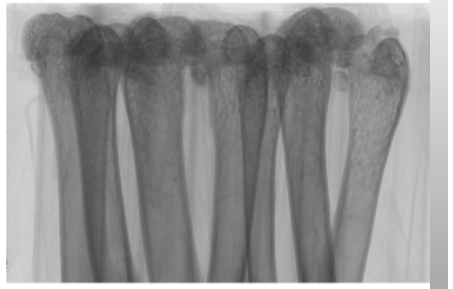
Introduction

Group-scanning bones with micro-computed tomography (µCT)...

- µCT is a critical tool for preclinical bone research
- Can be time-consuming and expensive to use
- Imaging several bones simultaneously reduces costs and scan time

... could affect output data.

- Potential variability in how the bones pass between the source and detector during rotation
- It is unknown if this affects scan quality



µCT scan with 7 femurs

HYPOTHESIS: Scanning methodology will alter the ability to detect differences between experimental groups with known skeletal defects.

Materials and Methods

Materials

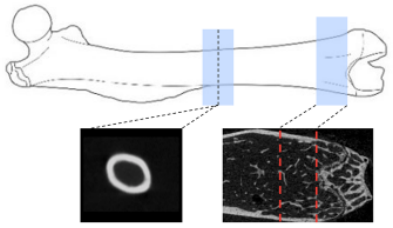
- 2 bone disease groups with controls
  - *Col1a2*$^{G610C/+}$ model of osteogenesis imperfecta (OI)
  - adenine model of chronic kidney disease (CKD)
- Male 16 wk femurs, n=8 per group

Methods

- Scanned at 9 micron resolution, identical settings for all scans on both scan systems (Bruker Skyscan 1176 and 1172)
- Varied group size
  - Groups of 8 and solo on Skyscan 1176
  - Groups of 3 and solo on Skyscan 1172
- 0.1 mm ROI from cortical midshaft and 1 mm ROI from distal trabecular bone

Analysis

- Repeated-measure 2-way ANOVA (main effects of disease, scan-type)
- Secondary analysis: two-tailed t-test and Cohen's d effect size to directly compare ability to detect phenotype

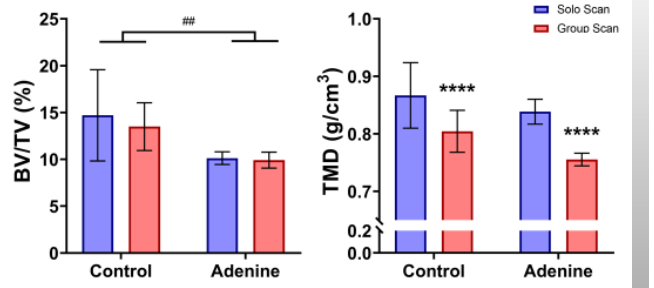


Schematic showing trabecular and cortical ROI selection

Results and Discussion

Trabecular Values

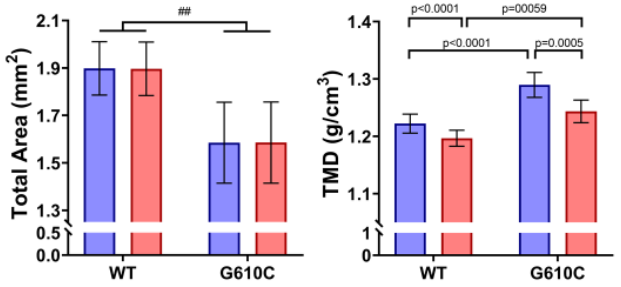
- Sensitive to image quality, with total mineral density (TMD) most affected
- Scan-type did not affect phenotype detection in higher quality scans (1172), as shown by bone volume fraction (BV/TV)



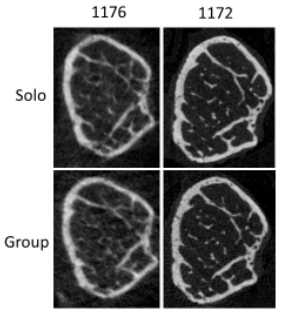
*1172 CKD trabecular properties. Main effects of disease (## p<0.01) and scan-type (****p<0.0001).*

Cortical Values

- Overall little affect of scan-type with many properties being almost identical, as shown by cross-sectional area
- TMD values differed the most but a phenotype was still seen



1172 OI cortical properties. Main effects of disease (## p<0.01), and post-hoc p-values.



Trabecular cross-sections of the same adenine-treated femur

Overall

PRO: Group-scanning affected system output but did not compromise the ability to detect the existence of the severe disease phenotypes, especially in cortical properties.

CON: Group-scanning compounded the limitations of lower quality output images, inhibiting the ability to detect differences in trabecular microarchitecture. Tissue mineral density (TMD) in both trabecular and cortical bone was especially impacted.

CKD t-tests

	1172 Data		1176 Data	
	One	Three	One	Eight
Total CSA	NS	NS	NS	NS
Marrow Area	NS	NS	NS	NS
Bone Area	<0.001	<0.001	<0.001	<0.001
Cortical Thickness	<0.001	<0.001	<0.001	<0.001
Imax	0.039	0.017	<0.001	<0.001
Imin	NS	0.027	0.001	0.001
TMD	0.019	0.002	<0.001	<0.001
BV/TV	0.033	0.009	NS	NS
Tb.Th	0.006	0.003	NS	0.015
Tb.Sp	0.001	<0.001	NS	NS
Tb.N	NS	0.041	NS	NS
TMD	NS	0.010	NS	0.003

OI t-tests

	1172 Data		1176 Data	
	One	Three	One	Eight
Total CSA	0.006	0.004	0.012	0.011
Marrow Area	0.001	0.001	0.001	<0.001
Bone Area	NS	NS	NS	NS
Cortical Thickness	NS	NS	NS	NS
Imax	0.030	0.019	NS	NS
Imin	0.022	0.016	0.045	0.039
TMD	<0.001	0.001	0.013	0.009
BV/TV	NS	NS	NS	NS
Tb.Th	NS	NS	NS	NS
Tb.Sp	0.009	0.016	NS	NS
Tb.N	0.033	0.041	NS	NS
TMD	NS	NS	NS	NS

P-values from two-tailed t-tests comparing phenotypes. Significant values highlighted in red.

For most properties, a significant difference was seen between diseased and control bone, regardless of scan type.

Conclusion

Researchers may be able to use small groupings in micro-CT scans to expedite pre-clinical analyses to decrease costs and increase speed of discoveries; however, the details of scanning (solo or group) should always be reported.

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