Short Duration of Type 1 Diabetes Does Not Alter Material Properties in Juvenile Mice

Amy Creecy[1], John Damrath[2], Jennifer Hatch[3], Joseph M. Wallace [1,3]
[1]Indiana University School of Medicine, [2]Purdue University,[3]Indiana University Purdue University Indianapolis
Indianapolis, IN

Introduction

Type 1 diabetes (T1D) increases fracture risk throughout a patient's lifetime [1]

T1D decreases bone mass and bone quality, likely through tissue-level changes [2]

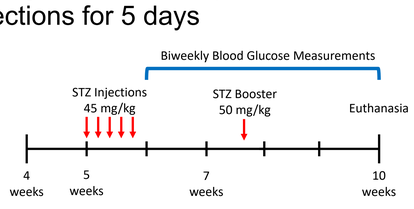
Much of the research in T1D mice has been done in mice starting at 10 weeks of age

We hypothesize that material properties will be lower in both male and female young diabetic mice compared to non-diabetic mice

Study Design

Male and female C57BL/6J were given either streptozotocin (STZ) (45 mg/kg) or PBS IP injections for 5 days

- Males PBS: n = 14
- Males STZ: n = 15
- Females PBS: n = 14
- Females STZ: n = 15



Body weight and non-fasting glucose levels were measured at least once a week

A booster shot of 50 mg/kg of STZ or PBS was given 2 weeks after the initial injections

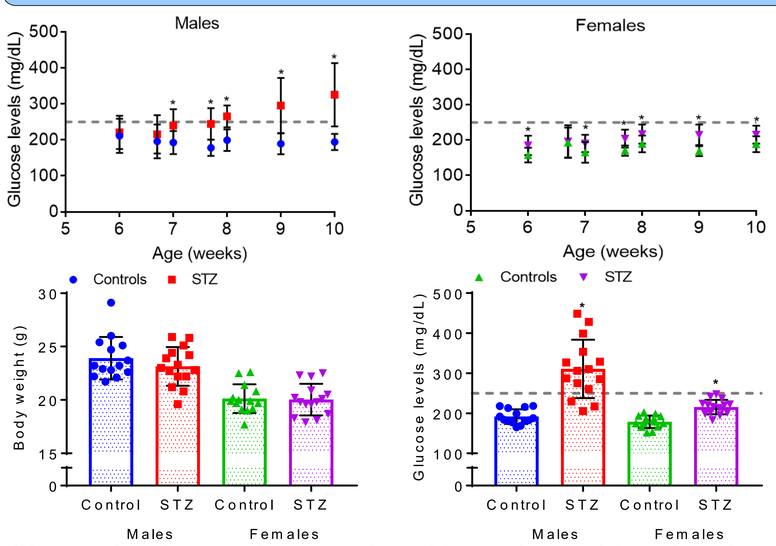
Mice were euthanized at 10 weeks of age and femurs were harvested and stored in PBS-soaked gauze at -20 °C

Left femurs were scanned using μCT at a voxel size of 9.8 μm

Femurs were broken in 3-pt at a displacement rate of 0.025 mm/s

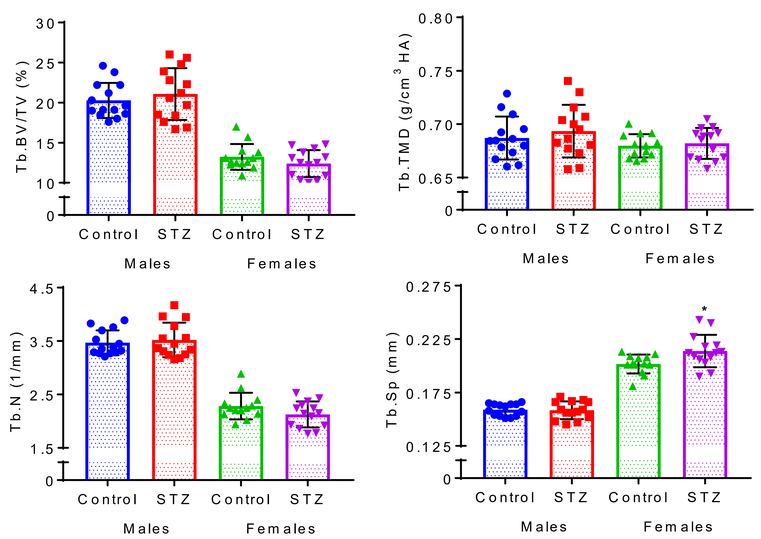
Significance was determined by either student t-tests or Mann Whitney U tests.

Male mice became diabetic with STZ injections but females were resistant to developing diabetes



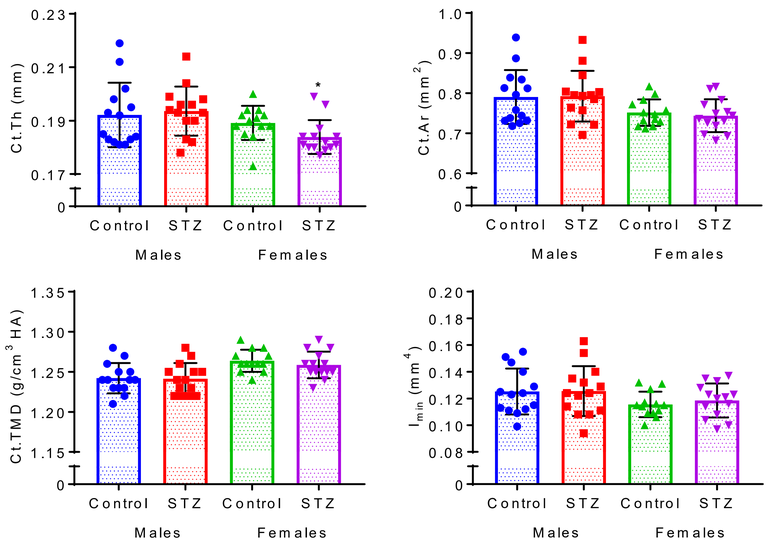
Glucose levels over time are plotted for males and females along with final body weight and the average glucose levels over the last two weeks. Gray line indicates diabetic level of 250 mg/dL. Asterisks indicate statistically significant difference.

Neither males nor females had significant trabecular bone loss with elevated glucose levels

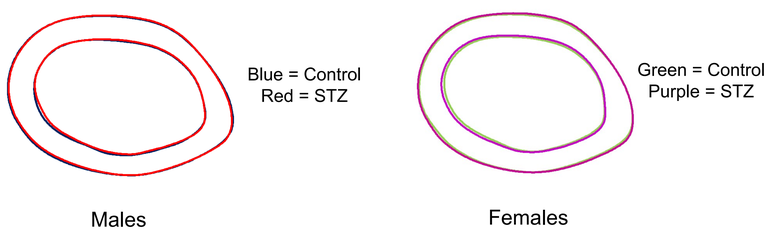


There were no differences in trabecular bone volume (Tb.BV/TV), or tissue mineral density (TMD) with diabetes. Females did have an increase in trabecular spacing (Tb.Sp) with elevated glucose levels. Asterisks indicate statistically significant difference.

Diabetes did not induce changes to cortical bone in males, but elevated glucose levels in females may have resulted in thinner cortices



Average Cortical Bone Distribution



Cortical thickness (Ct.Th) was lower in females that had been given STZ injections compared to controls. There were no differences in cortical area (Ct.Ar) or cortical tissue mineral density (Ct.TMD) in either males or females. Asterisks indicate statistically significant difference.

Diabetes did not alter material properties in male mice, but females had lower yield stress with elevated glucose levels

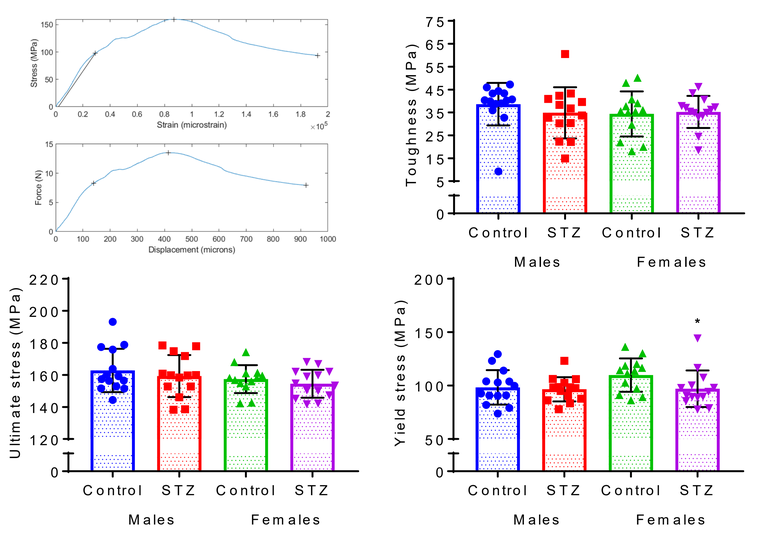


Table 1: Mechanical properties of femurs

		Male			Female		
Property	Unit	STZ	Control	p value	STZ	Control	p value
Yield force	N	8.23 ± 1.16	8.27 ± 1.04	0.938	8.00 ± 1.14	8.91 ± 1.08	**0.044**
Ultimate force	N	13.6 ± 1.3	13.8 ± 2.0	0.672	12.8 ± 1.0	12.8 ± 1.0	0.944
Displacement to yield	μm	126 ± 19	132 ± 31	0.538	135 ± 27	144 ± 23	0.328
Total displacement	μm	1746 ± 709	1929 ± 510	0.137	1952 ± 471	1860 ± 677	0.867
Modulus	GPa	4.1 ± 0.6	4.0 ± 0.7	0.704	4.0 ± 0.6	4.2 ± 0.6	0.293
Strain to yield	mε	26.1 ± 4.1	27.5 ± 6.0	0.482	27.3 ± 5.4	28.7 ± 4.3	0.421
Total strain	ε	0.361 ± 0.141	0.402 ± 0.106	0.227	0.395 ± 0.961	0.370 ± 0.131	0.981

Toughness and ultimate stress were not altered in females or males, but females had lower yield stress with STZ injections. Asterisks indicate statistically significant difference.

Discussion

While females injected with STZ had elevated glucose levels compared to controls, they did not develop overt diabetes (glucose ≥ 250 mg/dL). They may have had impaired glucose tolerance.

Females did not develop diabetes but had some subtle differences in bone structure and mechanical properties

Males did develop diabetes, but the duration of disease may not have been long enough to observe alterations to bone's structure and mechanics

Conclusion

Short duration of diabetes in juvenile mice does not result in a loss of material properties.

References

[1] Weber et al. *Diabetes Care*. 2015. [2] Hamann et al. *Nat. Rev. Endocrinol.* 2012.

Acknowledgements

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