Evidence for the bone structure change and osteocytes' biorhythm during orthodontic tooth movement

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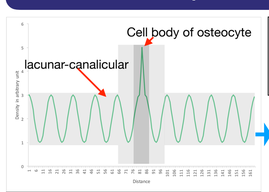
Introduction

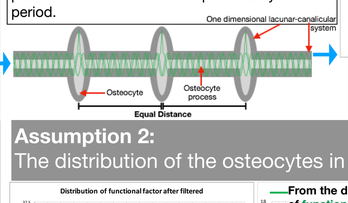
The **objective** of this study is to investigate the relationship between the change of sclerostin spatial distribution and the morphological change of bone structure during orthodontic tooth movement. **Sclerostin** is the key regulator of bone modeling and remodeling, which is almost exclusively formed by osteocytes and has anti-anabolic effects on bone formation. Meanwhile, as the most plenty cell emerged in bone matrix, **osteocytes**, is an appropriate indicator for the property of bone structure. In this study, we used **fast Fourier transform** (**FFT**) and **wavelet transform** to reveal the tiny changes in bone structure and to detect the changes of sclerostin spatial distribution.

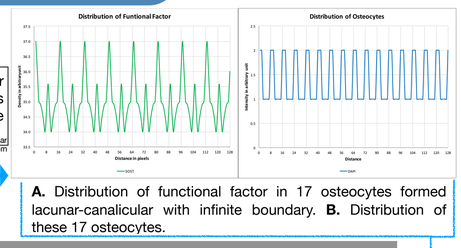
Materials and Methods

Assumptions & Simulation



Simulate an one dimensional lacunar-canalicular system with 17 osteocytes, and all osteocytes produce its functional factor periodically in same period.

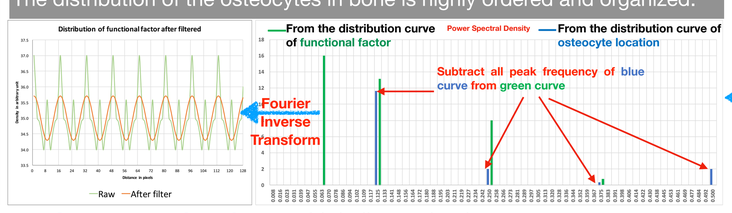




A. Distribution of functional factor in 17 osteocytes formed lacunar-canalicular with infinite boundary. **B.** Distribution of these 17 osteocytes.

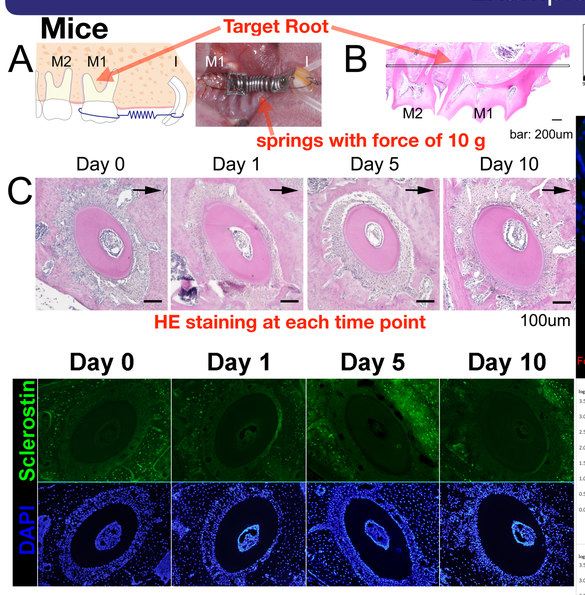
Assumption 1:
If osteocyte performs its function **periodically**, the density distribution of its functional factor in lacunar-canalicular system will follow a periodic function, but high density in cell body.

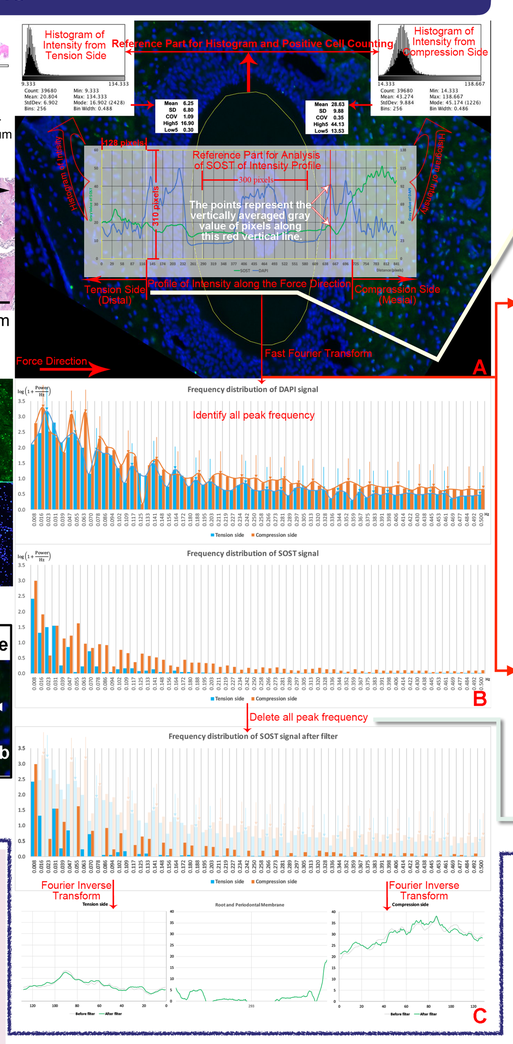
Assumption 2:
The distribution of the osteocytes in bone is highly ordered and organized.

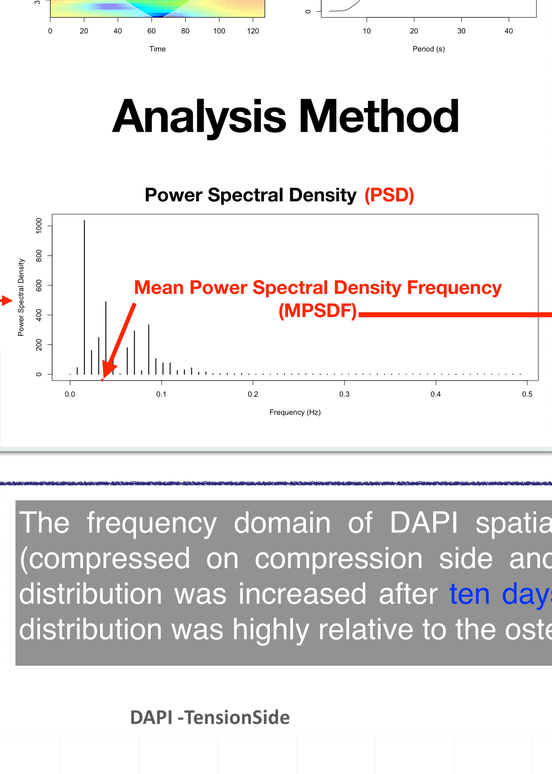


Thus, the **distribution curve of osteocyte location** could indicate the bone structure property, and the **distribution curve of functional factor** after filtered could indicate the functional period of osteocyte.

Example

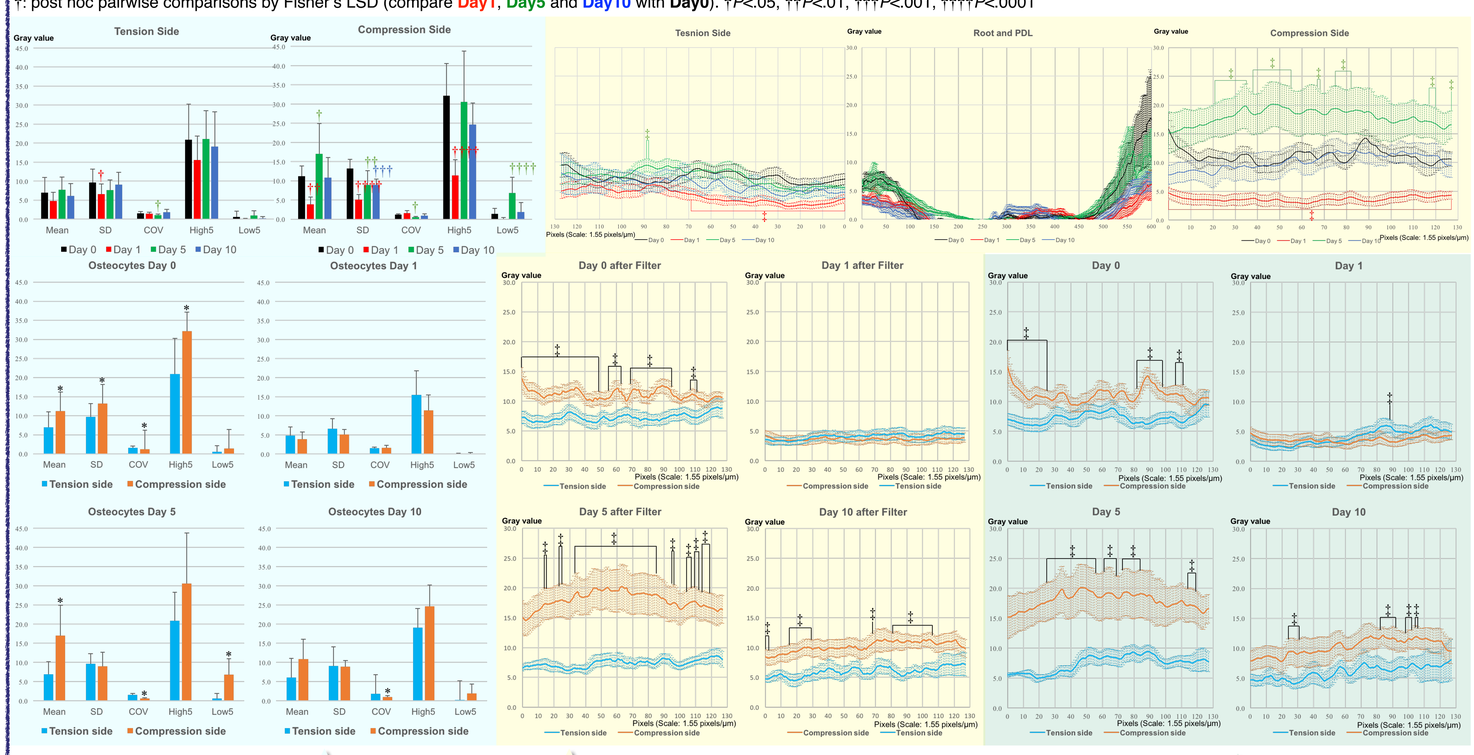






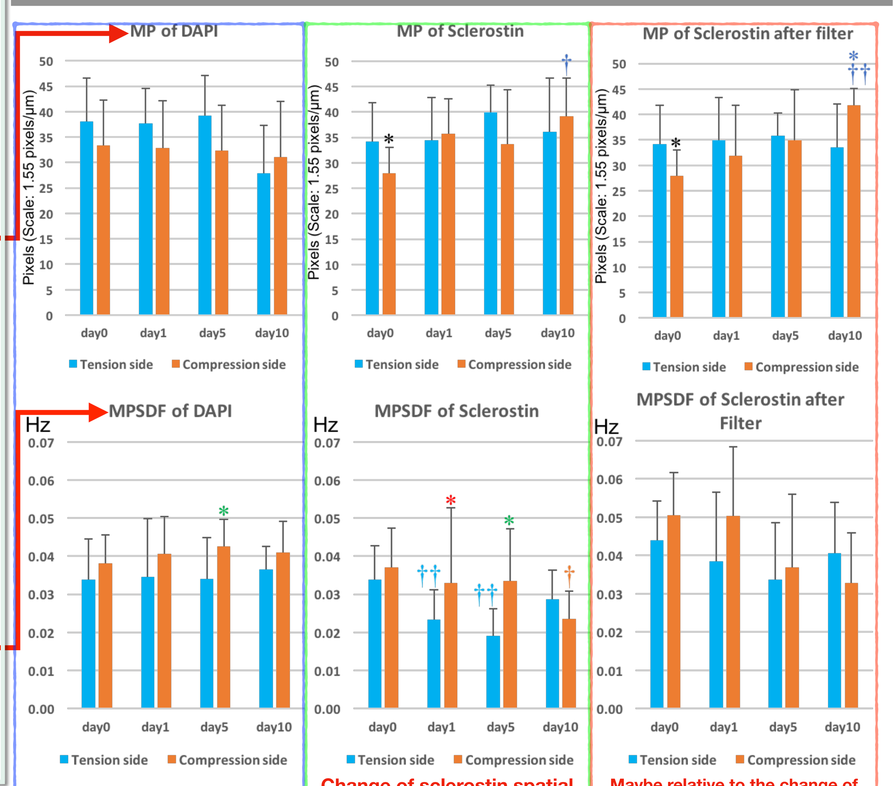
Results

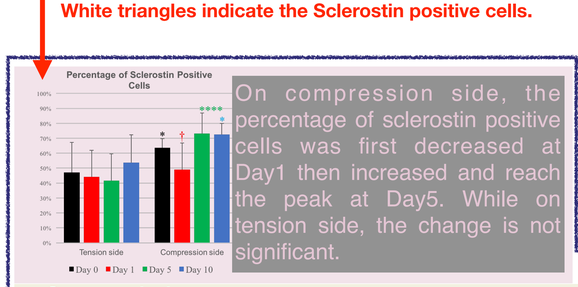
*: paired *t*-test (comparison between **compression** and **tension** side). **P*<.05, ***P*<.01, ****P*<.001, *****P*<.0001
‡: multiple unpaired *t*-test without False Discovery Rate-controlling procedure (compare **Day1**, **Day5** and **Day10** with **Day0**).
†: post hoc pairwise comparisons by Fisher's LSD (compare **Day1**, **Day5** and **Day10** with **Day0**). †*P*<.05, ††*P*<.01, †††*P*<.001, ††††*P*<.0001



After one day force load, the sclerostin expression decreased on both sides. On the tension side, almost no change in five days and ten days force load. While on the compression side, the sclerostin expression dramatically increased after five days force load, then turn back to day0 level after ten days force load.

The results from the histogram analysis were almost consistent with the profile results. One interesting thing is that the COV significantly decreased after five days force load on both sides, which indicated the osteocytes were highly synchronized after five days force load





On compression side, the percentage of sclerostin positive cells was first decreased at Day1 then increased and reach the peak at Day5. While on tension side, the change is not significant.

The frequency domain of DAPI spatial distribution curve obviously showed the bone structure change (compressed on compression side and extended on tension side). The MP of filtered sclerostin spatial distribution was increased after ten days force load on the compression side. The filtered sclerostin spatial distribution was highly relative to the osteocytes' functional period.

Spearman's rho

Table 1. Significant relative factors[a] (34 sections from 18 mice)

	Spearman's correlation coefficient	*P* - Value
Factors relative to the percentage of sclerostin positive cells		
MPSDF of sclerostin signal	0.35	<0.00**
Mean	0.43	<0.00***
SD	0.36	<0.00**
COV	-0.24	<0.05*
High5	0.48	<0.00****
Factors relative to the MPSDF of DAPI signal		
High5	0.25	<0.05*
Factors relative to the MPSDF of sclerostin signal after filter		
Low5	-0.28	<0.03*

a: Mixed compresion, tension side and every time point. MPF: mean power frequency. SOST: sclerostin.
**P* <0.05, ***P* <0.01, ****P* <0.001, *****P* <0.0001

Multiple linear regression

Table 2. The results of multiple linear regression[a] (34 sections from 18 mice)

	R^2	F statistic	*P* - Value (F statistic)	Coefficient estimate ± SE	t value	*P* -Value	Square of semipartial correlations	VIF[b]
The percentage of sclerostin positive cells	0.38	13.067	<0.00****					
Intercept				36.12 ± 5.62	6.43	<0.00***		
The MPSDF of sclerostin signal				373.25 ± 153.92	2.43	<0.02*	0.06	1.06
Mean				1.61 ± 0.31	5.27	<0.00****	0.27	1.22
Low5				-1.66 ± 0.34	-3.43	<0.00**	0.11	1.29

VIF, variance inflation factor; b: VIF higher than 10 suggests a linear relationship between the predictors; SE: standard error.
a: Mixed compresion, tension side and every time point; **P* <0.05, ***P* <0.01, ****P* <0.001, *****P* <0.0001

The High5 have the highest correlation coefficient to the percentage of sclerostin positive cells and have significant correlation to the MPSDF of DAPI signal (represent the bone structure property). This means the High5 cells can response to the bone structure change and impact the sclerostin expression. The MPSDF of sclerostin signal (indicate the period of sclerostin expression) also have correlation with the sclerostin positive cells.

Conclusions

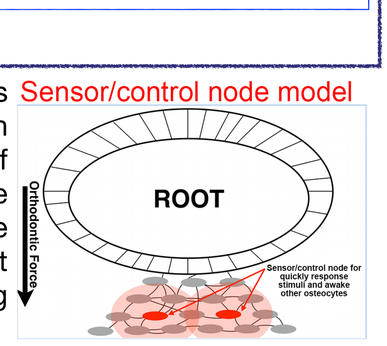
In this study:

1. **We revealed the spatial distribution change of sclerostin expression during the orthodontic tooth movement.**
2. **The spatial distribution change of sclerostin expression have association with bone structure change.**
3. **The spatial distribution change of sclerostin expression maybe mainly induced by the osteocytes' functional period.**

Hypothesis

Our **previous study [1]** showed that not all osteocytes have observable gap junctional intercellular communication (GJIC) in chick calvariae and demonstrated two types of GJICs in the development of mature osteocytes in chicks: passive transduction (low GJIC osteocyte) and active transduction (high GJIC osteocyte). Combination of the findings in this time, we hypothesize a pattern in which high5 osteocytes function as a sensor/control node that maintains a high GJIC to allow a quick response to stimuli, to activate the surrounding osteocytes, and to maintain the coordination of the period of the sclerostin expression.

Sensor/control node model



The Japanese Orthodontic Society COI Disclosure. Ziyi WANG, Yoshihito ISHIHARA, Naoya ODAGAKI, Masahiro NAKAMURA, Ei EI HSU HLAING, Hiroshi KAMIOKA. **The authors have no financial conflicts of interest to disclose concerning the presentation.**

Reference

1. **Wang, Ziyi, et al. "Alternation in the gap-junctional intercellular communication capacity during the maturation of osteocytes in the embryonic chick calvaria." *Bone* 91 (2016): 20-29.**