[^{18}F]NaF Uptake Spatially Corresponds with Peak Maximum Principal Strains in the Tibia

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Summary

[^{18}F]NaF positron emission tomography (PET) combined with finite element (FE) analysis can be used to interrogate relationships between bone loading and remodeling activity *in vivo*. We assessed spatial relationships between bone strain and [^{18}F]NaF standardized uptake value (SUV) in the tibial diaphysis of 20 participants in response to stair descent. FE models of the tibia and fibula were created from MRI images and used to compute surface strains. Pre-exercise SUV and exercise-induced absolute change in SUV (ΔSUV) were calculated from PET images. Mean SUV and ΔSUV were compared between regions defined by levels of strain. Both SUV parameters were elevated in regions experiencing the highest maximum principal strains, while no relationships were observed at lower levels or with minimum principal strains. These initial results suggest an exponential relationship between peak maximum principal strains and bone metabolic activity.

Introduction

Characterizing relationships between loading and bone remodeling activity is important to better understand bone adaptation and pathophysiologies. [^{18}F] Sodium fluoride ([^{18}F]NaF) is a PET radiotracer that interrogates areas of newly mineralizing bone, an *in vivo* marker of metabolic bone remodeling [1]. When combined with FE analysis, [^{18}F]NaF PET may be used to study the relationship between bone strain and remodeling activity. *This study aimed to evaluate spatial relationships between finite element-predicted strain and [^{18}F]NaF uptake in response to stair climbing exercise.*

Methods

[^{18}F]NaF PET-MRI scans of the lower legs were obtained before and after a stair climbing exercise for 20 volunteers (14 female, 47.5 ± 17.7 years, 77.0 ± 19.7 kg, 1.70 ± 0.10 m).

FE models of the tibia-fibula complex were generated using participant-specific geometry from MRI images [2]. Material properties for cortical bone, trabecular bone, and marrow from literature were assigned. Peak knee contact force and moment during stair descent, obtained from the Orthoload Database [3] and scaled by body mass, were applied.

Pre- and post-exercise SUV and absolute ΔSUV were computed from PET images. Surface points on the tibial diaphysis were binned by strain deciles. The mean pre-exercise SUV and ΔSUV for each strain decile region, both normalized to percentile, were calculated to assess spatial correspondence. This analysis was repeated with finer bin widths (5%) for regions of high strain (70-100th percentile). Kruskal-Wallis and Wilcoxon rank-sum tests with Tukey-Kramer corrections were used to explore differences in SUV parameters between the strain regions.

Results and Discussion

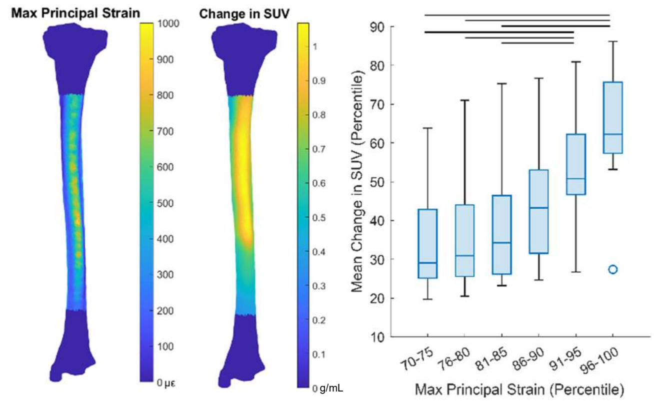

Figure 1: Left: Strain and ΔSUV maps across the tibial diaphysis. Right: Mean ΔSUV is significantly greater in regions experiencing the highest maximum principal strains (91-100th percentile).

Both maximum principal strain and SUV were typically highest along the proximal 2/3 of the anterior crest (Figure 1). On average, pre-exercise SUV and ΔSUV illustrated an exponential relationship with maximum principal strain, where SUV was elevated in regions experiencing the highest (> 90th percentile) maximum principal strains ($p<0.001$, Figure 1) while there were no differences in SUV between lower strain regions. This is consistent with the links between strain magnitude and local changes in perfusion and bone remodeling in preclinical models [1]. Interestingly, there were no directional relationships between SUV parameters and minimum principal strain. This may reflect strength and energy dissipation differences between loading modes [4], and regional differences in cortical thickness where a greater amount of (highly strained) bone led to increased SUV signal.

Conclusions

[^{18}F]NaF PET imaging with FE analysis is a feasible approach to interrogate relationships between bone loading and remodeling *in vivo*. Initial results suggest an exponential relationship between peak maximum principal strains and bone metabolic activity, with no relationship observed at lower strains nor with minimum principal strains.

Acknowledgments

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References

[1] Goyal A et al. (2024). *Osteoarth Imag*, **4**: 100242.
[2] Haider IT et al. (2020). *J Biomech Eng*, 142(2):021010
[3] Bergmann G and Damm P (ed.) (2008). *Orthoload Database*. https://orthoload.com/.
[4] Li S et al. (2013). *J Mech Behav Biomed Mater*, **21**:109-120