Spatial Correlations in Patellofemoral Joint Osteoarthritis: Analysis of Bone Remodeling and Cartilage Reveals Markers of Early Disease

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INTRODUCTION: Patellofemoral joint osteoarthritis (PFJ-OA) is the most common presentation of knee OA, affecting over 60% of individuals above age 50, and frequently manifests as the earliest site of disease. Disrupted mechanical and biochemical communication between bone and cartilage may trigger the cascade of joint breakdown. While the importance of cartilage-bone cross-talk has been recognized, the spatial patterns linking patellar bone microarchitecture, metabolic bone remodeling, and overlying cartilage quality remain inadequately characterized. This study employed high-resolution, multi-modality imaging and GPU-accelerated spatial correlation analysis to identify markers of early disease progression by examining bone metabolic activity, microstructure, and cartilage composition at thousands of spatially-matched locations.

METHODS: Nineteen patellae from 7 male and 6 female participants (age 38-61 years) were analyzed. Their knees were scanned using high-resolution peripheral quantitative CT (HR-pQCT; XtremeCT II) followed by hybrid [^{18}F]-NaF positron emission tomography-magnetic resonance imaging (Signa 3.0T PET-MR). The patella was segmented into subchondral bone plate (SBP) and trabecular bone (Tb), and metrics of bone structure and density were quantified by applying standardized HR-pQCT image processing methods. Bone remodeling activity was assessed by PET standardized uptake values (SUV). Cartilage thickness (Cart.Th) was quantified from a 3D proton-density-fat-suppressed MRI sequence and cartilage composition was quantified by T1ρ and T2 relaxation time mapping. Conventional ROI-based *mean-value correlations* were computed by averaging all bone and cartilage metrics within each compartment (whole, medial, lateral) for every knee (n=19). Spearman correlations between compartmental means were calculated for the entire cohort. For a detailed analysis of local interactions across bone and cartilage, we computed *local spatial correlations* across tens of thousands of anatomically-matched 5mm probing spheres distributed across SBP, trabecular, and cartilage regions using GPU-acceleration (Figure 1). For each sample, Spearman correlations between neighboring spheres across tissue boundaries were calculated at each spatial location, then averaged to create mean spatial correlation matrices for the whole, medial, and lateral patella compartments. All results were stratified by OA severity using WORMS patella cartilage sub-score grade (0-1: n=6; 2-3: n=9; 4-6: n=4) to assess stage-specific relationships.

RESULTS: *Mean-value correlation analysis* across all knees revealed significant associations between bone metabolic activity and cartilage degeneration: Elevated Tb.SUV correlated with poor cartilage composition (Tb.SUV-T2: r=0.514, p=0.026; Tb.SUV-T1ρ: r=0.505, p=0.029). Further, more robust bone was correlated with thick cartilage thickness (SBP.Th-Cart.Th: r=0.584, p=0.010; Tb.BMD-Cart.th: r=0.688, p=0.002). WORMS stratification revealed contrasting patterns: in healthy knees (WORMS 0-1), strong positive correlations existed between bone quality and cartilage thickness (SBP.Th-Cart.Th: r=0.905, p=0.005; Tb.BMD-Cart.th: r=0.810, p=0.022), while in early and late disease (WORMS 2-3, 4-6) these relationships were absent. *Spatial correlation analysis* revealed local bone-cartilage relationships and allowed the interrogation of how these are altered in OA (Table 1). For example, the strength of the spatial correlation between SBP.BMD and cartilage thickness increased from early to moderate disease (r = 0.180 in WORMS 0-1 → r = 0.526 in WORMS 2-3). In severe disease, correlations between bone quality and cartilage thickness inverted (see Tb.Th, Tb.N, Tb.BMD in WORMS 4-6), potentially reflecting subchondral sclerosis co-located with cartilage thinning. For these spatial correlations, the lateral compartment displayed the most dramatic differences between healthy and OA knees (Table 1).

DISCUSSION: Our analysis suggests that bone-cartilage coupling undergoes stage-specific, compartment-specific reorganization during PFJ-OA cartilage lesion progression. The transition from WORMS 0-1 to 2-3 represents a critical phase, particularly in the lateral compartment where the subchondral BMD-cartilage thickness correlation nearly triples (Δr = +0.346), suggesting establishment of pathological bone-cartilage coupling. Negative correlations in severe disease likely reflect subchondral sclerosis co-located with advanced cartilage loss. The lateral compartment's greater vulnerability may relate to biomechanical factors, as this region experiences higher and more variable shear and compressive stresses. The spatial analysis method reconciles previously variable findings by capturing local heterogeneity missed by traditional ROI approaches. Limitations include cross-sectional design and modest sample sizes in WORMS subgroups.

SIGNIFICANCE/CLINICAL RELEVANCE: This high-resolution, multi-modality, GPU-accelerated spatial correlation methodology provides unprecedented resolution for studying compartment-specific bone-cartilage interactions, identifying the lateral patella as particularly vulnerable during early stages of cartilage disease. These spatial biomarkers could enable earlier OA detection and targeted, compartment-specific interventions during the critical window when pathological coupling first emerges.

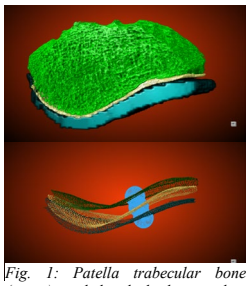

Fig. 1: Patella trabecular bone (green) subchondral bone plate (white) and cartilage (blue) segmentations were created. The processing pipeline created tens of thousands of uniformly distributed points across each ROI, identified nearest neighbor points between adjacent tissue layers, and calculated mean parameter values within 5mm spherical regions centered at each point.

WORMS		SBP. BMD	SBP. Thickness	SBP. SUV	Tb. BMD	Tb. Thickness	Tb. Separation	Tb. Heterogeneity	Tb. Number	Tb.SUV
0-1 Healthy/Early OA	Cart.TH	0.180	0.419	0.590	0.501	0.466	-0.385	-0.128	0.177	0.490
	Cart.T1rho	0.073	0.172	0.370	0.039	0.086	-0.016	-0.077	0.183	0.295
	Cart.T2	0.096	0.212	0.337	0.080	0.113	-0.038	-0.069	0.154	0.283
2-3 Moderate OA	Cart.TH	0.526	0.614	0.573	0.382	0.375	-0.438	-0.342	0.443	0.479
	Cart.T1rho	0.151	0.125	0.334	0.041	0.070	-0.110	-0.071	0.132	0.409
	Cart.T2	0.129	0.140	0.338	0.040	0.058	-0.135	-0.133	0.186	0.399
4-6 Severe OA	Cart.TH	0.222	0.036	-0.037	-0.180	-0.193	-0.022	-0.055	-0.033	0.067
	Cart.T1rho	0.516	0.181	0.374	0.179	0.261	0.101	0.167	-0.358	0.457
	Cart.T2	0.531	0.135	0.461	0.136	0.166	0.135	0.204	-0.380	0.541

Table 1: Spatial correlation matrix across disease stages (lateral compartment). Spatial correlations between bone parameters and cartilage metrics stratified by WORMS grade (0-1: healthy, n=6; 2-3: moderate OA, n=9; 4-6: severe OA, n=4). Blue highlighting indicates positive correlations; red highlighting indicates negative correlations. Correlation coefficients reveal strengthening of bone-cartilage coupling in moderate disease (WORMS 2-3) followed by reversal patterns in severe disease (WORMS 4-6). SBP: subchondral bone plate; Tb: trabecular bone