Increased perfusion and venous hypertension is present in regions of bone affected by BMLs in knee OA

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Introduction

- Recently data has emerged that suggest lesions in the bone marrow (BMLs) play an integral if not pivotal role in the symptoms that emanate from knee osteoarthritis, and in structural progression.
- Animal model data suggest that impulsive loading promotes early vascular changes in subchondral bone, which are developed in response to both the magnitude and the rate of loading (1). Similarly BMLs appear to develop in response to mechanical loading, and at sites of loading. Thus the pathogenesis of cartilage breakdown in OA is a biological and a mechanical process in which vascular changes and local bone remodeling play a central role. At this point we are unaware of the vascular changes in BMLs.
- Some authors believe that OA occurs as a result of vascular abnormalities affecting bone in some patients. These conditions are often associated with increased intraosseous pressures, which are thought to be the result of obstruction of venous drainage from the affected bone (2-4). It has been suggested that elevated intraosseous pressure is responsible for the bone-remodeling as well as the necrosis of bone occurring in patients who have these diseases. As yet there is no evidence suggesting that BML's are related to intraosseous hypertension.

Objective

- Our objective was to determine if bone marrow lesions are sites of venous (osseous) hypertension and whether reduced runoff (egress) compared to surrounding normal tissue was observed.

Materials and Methods

- Postmenopausal female subjects with predominantly medial compartment OA, on a waiting list for total knee replacement (TKR) at Boston University Medical Center, were recruited under ethical consent.
- Prior to surgery, subjects had an MRI performed on their study knee using a Philips 3.0T scanner with a dedicated extremity coil. The following dynamic contrast enhanced imaging sequence was acquired before and during GdDTPA administration on each patient: Axial 3D FSPGR flip angle 25 TE min full, RCV BW 42-62, FOV ~12, 3mm slices acquired over 3 minutes interval, 14 loc per slab, 256x128.
- Regions of interest (BMLs) were defined as well as corresponding bone unaffected by BMLs in the same region.

Perfusion Imaging

- Perfusion was assessed using standard post-processing methods by VirtualScopics. These parameters included: the initial area under curve (IAUC), defined as the area under the tissue uptake curve during the first 90 seconds following bolus injection normalized by the area under the AIF over the same period; Ktrans, the volume transfer constant between blood plasma and extra-cellular extra-vascular space (EES); and kep, the rate constant between the extracellular space (Ve) and blood plasma which provides an index of the presence of venous hypertension.

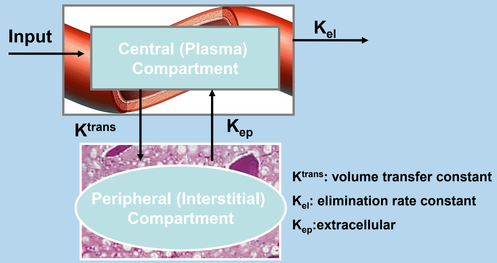


Figure 1. Dynamic Parameters of Bone Perfusion

Statistical Analysis

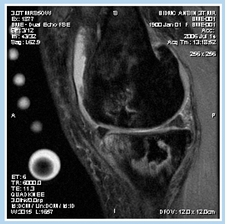
- Statistical comparisons were made within person between regions affected by BML and those that were not affected on both the tibial plateau and femur (for example BML in medial tibia compared to region of medial tibia not affected by BML).

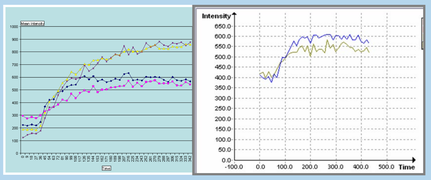
Results

- We recruited 6 postmenopausal female subjects with predominantly medial compartment OA, on a waiting list for total knee replacement (TKR) who ranged in age from 48-90 years of age.

	Medial Tibial BML	Medial Tibia Unaffected by BML	P value for difference	Medial femur BML	Medial femur unaffected by BML	P value for difference
K^{trans} (1/min)	0.03 (0.02)	0.02(0.02)	0.018	0.03 (0.03)	0.02(0.01)	0.188
IAUC	0.14 (0.09)	0.05 (0.03)	0.066	0.13 (0.08)	0.04 (0.02)	0.074
V_e	0.43 (0.39)	0.10 (0.12)	0.274	0.29 (0.25)	0.06 (0.05)	0.080
k_{ep}	12.44 (9.23)	7.13 (7.66)	0.012	10.07 (6.66)	5.68 (5.75)	0.017

Table 1. Mean (SD) values of perfusion obtained from dynamic contrast enhanced imaging in the different regions of the knee affected and unaffected by BML

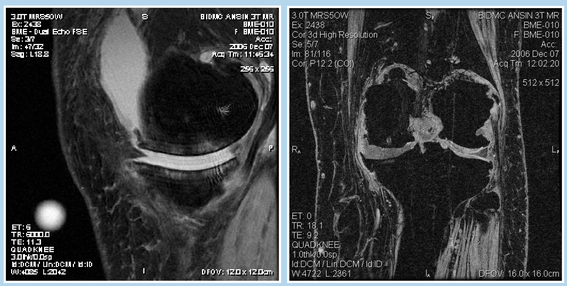


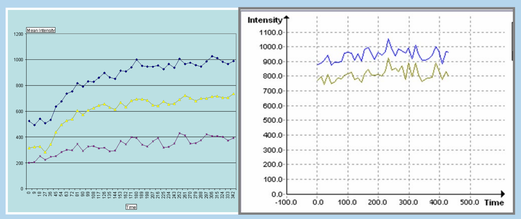


BML Intensity Plot — Non BML Intensity Plot

Non BML Femur (green line)
Non BML Tibia (blue line)

Figure 3. Representative example of BML and time intensity plots of BML and non BML regions depicting ingress and lack of egress from all BML regions (except medial femur) consistent with venous obstruction.





BML Intensity Plot — Non BML Intensity Plot

Non BML Femur (green line)
Non BML Tibia (blue line)

Figure 2. Representative example of BML and time intensity plots of BML and non BML regions depicting ingress and lack of egress from BML region consistent with venous obstruction.

Conclusions

- Areas of bone affected by BMLs in knee OA are associated with altered perfusion and intraosseous venous hypertension (kep) in both the tibial plateau and femur while increased permeability (Ktrans) was observed in the tibial plateau only.
- The increase in kep may be due to the result of obstruction of venous drainage from the affected bone although the causative factor is not yet known.
- These alterations in bone perfusion and hypertension may be responsible for the bone-remodeling as well as the necrosis of bone occurring in patients with knee OA.

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References

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