Comparison of perfusion parameters in normal and metastatic bone marrow using DCE-MRI and pharmacokinetic modeling: a reference study.

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Introduction

Malignant involvement of bones has significant effects on the blood supply, endothelial permeability and composition of the bone marrow, presumably altering the perfusion of the bone marrow [1]. While dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is increasingly used for the non-invasive assessment of normal [2] or neoplasic marrow [3], quantitative comparative studies of perfusion are missing. Rates of perfusion in normal bone marrow and in bone metastases were assessed based on DCE-MRI and a pharmacokinetic (PK) modeling.

Material and methods

Nineteen patients scheduled for an MR examination of the spine with a normal bone marrow (group 1, normal controls) and nine patients with untreated bone metastases of prostate cancer (group 2) were imaged on a 1.5T scanner (Intera; Philips) with the body coil. A spoiled 2D turbo-FLASH sequence synchronized to the cardiac cycle was used (a non-slice-selective 90° preparation pulse was incorporated). Scan parameters were slice thickness L = 6 mm, in-plane voxel size = 1.56x1.56 after reconstruction, flip angle = 15°, single shot, TE = 1.3 ms, TR = 5.4 ms and a shot duration of 516 ms. 200 dynamics were measured. Patients received 8 mL of Gd-DTPA (Magnevist) followed by 20 mL saline flush injected at a rate of 3 mL/s with an automated injector. Signal intensity versus time curves were obtained after segmentation of regions of interest (ROI) in the abdominal aorta and in bone marrow (large area within the vertebral body in case of normal bone marrow; careful delineation of the metastasis on the basis of sagittal and axial images obtained before contrast agent injection). The percentage increase (PI) in signal intensity was calculated as defined in [2]. To convert the signal intensity into ΔR1 relaxation rate which is proportional to contrast agent concentration, a calibration procedure was used [4]. Then, the data were analyzed with a pharmacokinetic model [5].

Results

Signal intensity versus time curves showed an almost flat profile in group 1 compared to group 2. In group 2, patients exhibited different profiles with as common feature, a fast contrast uptake and either a plateau or a rapid washout, but with PIs always much higher to those observed in group 1. The volume transfer constant K^{trans} (a lumped representation of perfusion and endothelial permeability), the volume of extravascular extracellular space accessible to the contrast agent v_e and the plasmatic volume v_p, were lower in normal bone marrow.

Conclusion

Perfusion is low in normal bone marrow. Perfusion parameters in healthy persons may constitute reference values. DCE-MRI and PK modeling demonstrate significant alterations of the bone marrow perfusion in bone metastases. These techniques may provide useful surrogates for monitoring the response to anticancer therapy.

Figures: Example of bone marrow images acquired with a fast T1-weighted spoiled gradient-echo sequence.

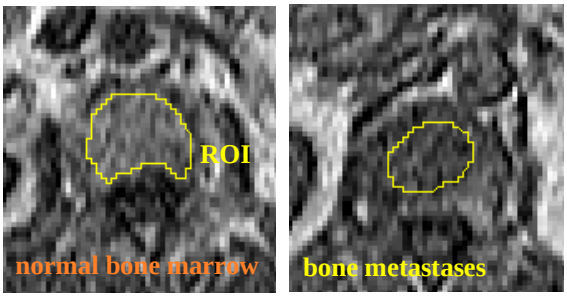


Table: Perfusion parameters (mean ± SD)

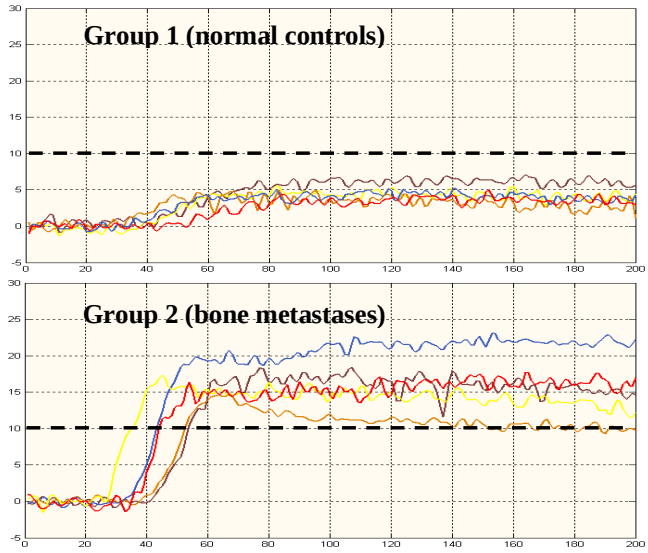
Normal bone marrow (group 1)				Bone metastases (group 2)
PI**	**K^{trans}****	**k_{ep}**	**v_e****	**v_p****
17.2 ± 7.9	6.6 ± 3.1	197 ± 83	3.8 ± 1.5	1.1 ± 0.1
70 ± 20	34.1 ± 13.7	255 ± 109	13.9 ± 4.9	1.6 ± 1.1

PI in %, K^{trans} and k_{ep} in mL/min/100g, v_e and v_p in %
*** Significant differences (Wilcoxon rank sum test, $p < 0.05$)*

Model: The extended Kety model assumes that tissue voxels contain a vascular and an interstitial component. The reflux rate from the interstice to the intravascular space is defined as $k_{ep} = K^{trans}/v_e$ [5].

$$C_{tissue}(t) = K^{trans}.C_{plasma}(t) \otimes e^{-\frac{K^{trans}}{v_e}t} + v_p.C_{plasma}(t)$$

Graphs: Signal intensity versus time curves with a mean signal intensity before the contrast agent injection re-centered on zero.



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