In vivo Imaging of Bone Marrow Microstructures

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Introduction

The bone marrow (BM) is a major source of stem- and progenitor cells (1). Inside the BM these cells reside in special microenvironments (ME) called “niches” that maintain and govern these cells fates (1). In efforts to understand and pin-point these niches, researchers have traditionally relied on information from fixed tissue sections. However, since these niches are highly dynamic (1-3), being able to study the BM in real-time is desirable. In order to study stem cell function, lethal irradiation is routinely applied before transplantation of “tagged” cells. Irradiation causes extensive remodeling of the BM during which stem cells home to their niches before normal homeostasis can be restored. Therefore, in-vivo imaging aimed at studying this changing BM ME is highly coveted. Common methods of optical in vivo imaging are not fully capable of penetrating deep through the dense bone that normally surrounds these niches. MRI however has no depth or penetration issues and can provide good resolution and excellent anatomical details. The inherent weakness in MRI of low sensitivity can theoretically be improved by utilizing higher magnetic field strengths to allow for high resolution imaging in vivo.

Experimental

8 week old C57BL6J female mice (n=20) were given 950 Rads of total body irradiation and rescued by transplanting male B6Rosa26 whole BM cells. Transplanted animal tibiae were imaged in vivo over 2 weeks at the AMRIS facility on the 17.6T instrument using a custom built 1H surface coil (Doty) and 3D gradient echo scan sequences.

Results and Discussion

1 day post-irradiation and cell transplantation, the BM is still intact. High cellular density and intact trabecular bone is seen in Fig. 1a-c. 12 days post-irradiation, marked hypo-cellularity as observed on histological sections Fig. 1d, together with increased lipid and iron accumulation (data not shown) are likely responsible for the loss of signal on MR scans Fig. 1e-f. At day12, micro vascular structures are clearly visible throughout the BM while most trabecular bone is absent, as seen in Fig. 1e-f.

Conclusions

BM remodeling following irradiation and transplantation can be visualized by MRI. These high-resolution MR images acquired with a resolution of 22×23×69 µm³ are able to shed light on some of the molecular events that takes place in vivo. Signal loss, likely due to hypocellularity, hypoxia, lipid and iron deposition, can clearly be observed together with vascular structures within the normally inaccessible BM cavity.

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References

Fig 1: In vivo bone marrow remodeling following irradiation. Standard light microscopy (a&d), single axial slice from a 3D gradient echo acquisition (b&e), pseudocolored volume projection of the bone marrow (c&f) prior to (top row) and 12 days following irradiation (bottom row). Note the changes in image contrast and structure of the bone marrow following irradiation (1d,e,f).