MR Cell tracking in reperfused myocardial infarction with microvascular obstruction and haemorrhage: Fluorine-19 MR could be a better solution

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PURPOSE

Iron oxide nano-particles have been intensively investigated for tracking stem cell transplantation and visualizing inflammatory cell infiltration in vivo in myocardial infarction (MI) animal models and possess the hope for clinical translation [1]. However, accumulating evidences indicate that microvascular obstruction (MVO) is a common phenomenon in acute MI after reperfusion therapy [2]. The magnetic susceptibility effects caused by the degraded hemoglobin products in MVO could interfere the detection of transplanted or recruited cells labeled with iron oxide nano-particles [3]. We hypothesized that 19F cardiac MR could detect cells labeled with perfluorocarbon (PFC) emulsions in MVO/hemorrhagic MI. This was demonstrated on blood monocytes recruited to MI.

METHODS

Six reperfused MI rats (120’ occlusion) were injected i.v. with 900µl of a 30% v/v PFC emulsion 1 day post-MI. Labeling efficiency was examined by flow cytometer on blood samples after injection (fluorescence labeled PFC emulsion). All MR measurements were performed on a 7T small animal scanner. In vivo 1H/19F MR data were acquired using a 1H/19F birdcage coil and ex vivo 1H/19F MR data using a surface coil. Ex vivo imaging was performed on isolated hearts in buffer before deep freezing for later histology and immunohistochemistry studies. 1H-T1WI (FLASH) and 1H-T2WI (multiple Spin Echo) data were both acquired in vivo and ex vivo. In vivo 19F TSE imaging was performed using the following parameters: spatial resolution (SR) = 1.25×1.25×2mm, Turbo Factor (TF) = 40, number of averages (NA) = 256. Ex vivo 19F TSE data were acquired with SR = 0.5×0.5×1mm, TF = 40, NA = 256. 19F images were overlaid on corresponding 1H images to define the origin of 19F signal. In vivo and ex vivo 1H-T2WI were used to appreciate myocardial edema and T2 shortening by paramagnetic components in haemorrhagic MI core. H&E, anti-ED1 and pearl Prussian blue staining were applied to validate myocardial integrity, macrophages and iron contents in MI cores, respectively.

RESULTS

Four of the six rats developed MVO as found by hypointensity zones in the infarct core on ex vivo T2WI (A2) and diffused fair blue/brown on Prussian blue staining (A3). In both in vivo (B1) and ex vivo (B2) 19H/1H MR, 19F signal was present in MI and MVO regions. Corresponding Prussian blue and anti-ED1 staining validated the co-existence of excessive iron (A3) and recruited monocytes/macrophages (B3) in MVO. In vivo T2WI (A1) either underestimated or failed to observe edema areas as estimated by ex vivo T2WI (A2) in these rats. 19F MR also depicted labeled cells in small infarcts without MVO in the other two rats. Flow cytometry revealed that blood CD11b/c+ cells (mainly monocytes/macrophages) were labeled by 19F.

DISCUSSION & CONCLUSION

We show for the first time in a rat model that 19F-MR can detect 19F labeled cells in MI with MVO. Cell tracking with iron oxide in MI with MVO could fail or be interfered using 1H- T2/T2*WI due to magnetic susceptibility effects caused by the degraded hemoglobin products in MVO. Thus, this study demonstrates that 19F cell labeling could be a better approach for MR cell tracking in MI with MVO and other scenarios with strong T2/T2* effect interference. It has been shown that these interferences also alter the 19F signal intensity [4, 5]. Thus, in order to achieve precise interpretation of the 19F signal in MI, further studies are needed to investigate the modulation of 19F signal by local magnetic susceptibility effects.

REFERENCES


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