The visualization of location and pharmacokinetics of nitroxyl radical using ESRI/MRI fused technique

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INTRODUCTION

EPR imaging technique is very powerful tool to demonstrate the distribution and pharmacokinetics of free radicals in living organisms. However this technique does not provide any anatomical information, because EPR image gives only the free radical distribution. If free radical distribution is fused with the anatomical picture, it is quite easy to clarify the actual distribution and the pharmacokinetics in living animals. In this study, we investigated the localization and pharmacokinetics of nitroxyl radical administered orally or intravenously to living mouse using the EPRI /MRI fused technique.

METHODS

Phantom study: The phantom consisted of seven tubes (4 mm id); the central tube filled with phosphate buffered saline (PBS) and six outer tubes with 2 mM of carbamoyl-PROXYL dissolved in PBS. The individual imaging of the phantom was obtained with EPRI and MRI, respectively, and then both images were fused with image software. **Animal study:** Six position markers containing a 2mM nitroxyl radical/PBS solution were arranged both sides of female c57BL/6 mice. After the anesthetization, either carbamoyl- or carboxy-PROXYL solution was orally or intravenously administered to mice, and then EPRI/MRI measurement were performed.

RESULTS AND DISCUSSION

The EPR image of the phantom gave 6 clear spots, and the picture of MRI gave 7 spots. The position and size were consistent with those of the tubes, and two images by MRI and ESRI co-registered well.

After injection, carbamoyl-PROXYL (po/w: 0.01) was quickly distributed in whole upper abdomen including heart, liver and kidneys area and almost disappeared at 10 min (Fig. 1A). On the other hand, carboxy-PROXYL (po/w: 0.01) was clearly distributed in heart, liver and, kidneys area and the area with strong intensity was relative small compared with that of carbamoyl-PROXYL injected mouse (Fig. 1B). The image intensity of carboxy-PROXYL was still remained in kidneys at 10 min suggesting that the decay of image contrast of carboxy-PROXYL administered to mice is slower than those of carbamoyl-PROXYL in the upper abdomen. Although the decay rate of region of interest (ROI 1-3) was similar, ROI (7-10) was clearly slower than that of carbamoyl-PROXYL injection (Fig. 2). In conclusion, the fused image with ESRI/MRI should be useful technique for determining the pharmacokinetics of spin-labeled compounds in living organism.

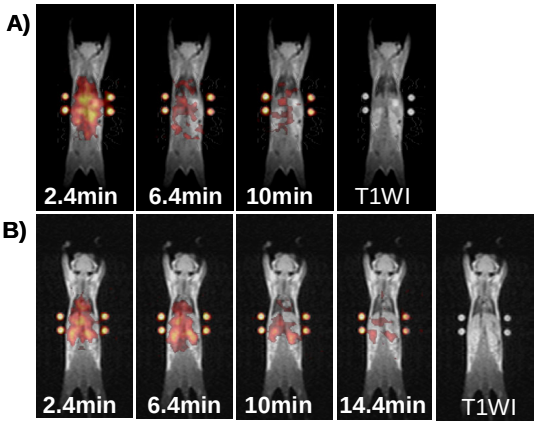

Fig. 1 Sequential EPEI/MRI fused images (A) carbamoyl -PROXYL injection(B) carboxy-PROXYL injection

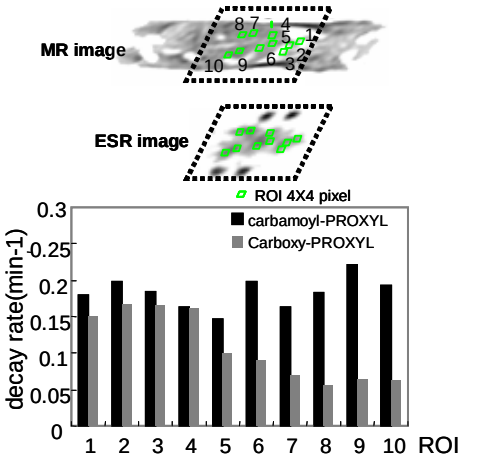

Fig.2 Decaey rate of each ROIs on EPR image