Tumor Resistance to Therapy and Sodium-Diffusion MRI

Schepkin, V.D. (NHMFL); Levenson, C.W. (Florida State U., College of Medicine)

Introduction

Ultra-high magnetic fields augment our capability to perform in vivo sodium MRI which is becoming a valuable tool in research and biomedical applications. Chemo-resistance, the ability of cancer cells to repel the treatment, is a common problem that significantly limits our capability to treat cancer and reduce life expectancy in patients with a wide variety of cancers. Tumor progression especially due to unsuccessful therapy can dramatically increase tumor resistance to therapy.

Results and Discussion

Using in vivo sodium/diffusion MRI at the 21.1T magnet, it was found that initial sodium concentration in rat glioma has a large variation, even for the same type of tumor. The analysis of this situation revealed a close relationship of sodium in glioma with glioma chemo-resistance (1).

Sodium concentration in tumors has a unique capability to be an *in vivo* energy biomarker. To maintain low intracellular sodium concentration, cells consume up to 60% of the total energy produced by the cell. Thus, the capability of cells to maintain intracellular sodium gradient could be a natural indicator of the major energy balance in tumor cells.

It is known that excessive glycolysis (Warburg effect) is an essential indicator of cancer metabolism. However, glycolysis is responsible only for a part of the total cellular energy metabolism. In comparison, sodium homeostasis is a more general metabolic energy indicator which can include other sources of energy metabolism, such as lipid metabolism.

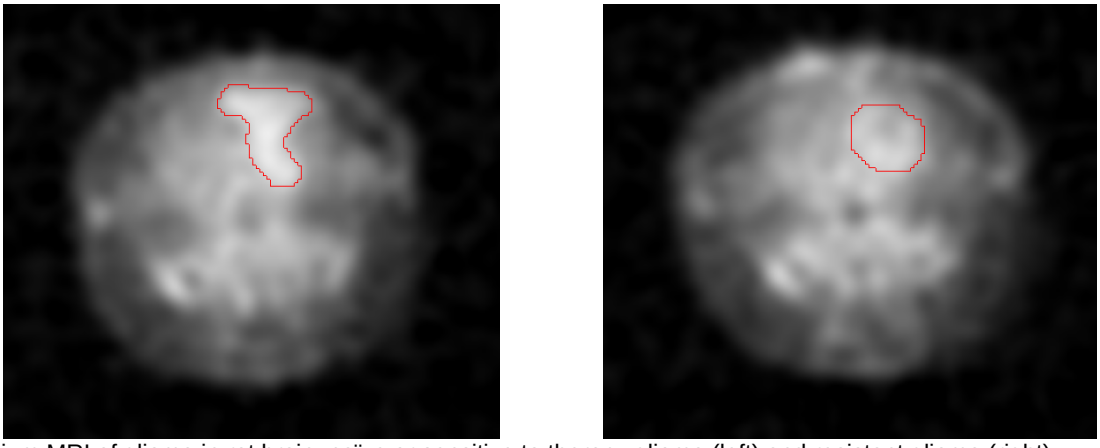

Fig. 1. Sodium MRI of glioma in rat brain: naïve or sensitive to therapy glioma (left) and resistant glioma (right).

Conclusions

Reflecting metabolic energy status, sodium MRI has the potential to reveal tumor chemotherapy resistance both non-invasively and, most importantly, prior to treatment. Application of sodium MRI may lead to individualized cancer treatment strategies, avoiding unsuccessful interventions. Sodium MRI of tumors can also serve as a marker for multidrug resistance and as a valued tool for cancer drug development. While it shares this capability with diffusion MRI, sodium MRI has the advantage of being several times more sensitive. Moreover, it detects the effects of therapy well ahead of diffusion, and, notably, responses to therapy can be seen even when there are no changes in tumor diffusion.

Acknowledgements

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References

[1] Schepkin, V.D., *et al.,* USPN *Patent* 8,880,146 (Nov 4, 2014).