In vivo measurement of tumor oxygen consumption by 19F-MRI relaxometry

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Introduction

The partial pressure of oxygen (pO_2) is a crucial factor affecting the response of tumors to irradiation and other cytotoxic treatments. It has been predicted that modification of oxygen consumption is much more efficient at alleviating hypoxia than modification of oxygen delivery.

Given the importance of oxygen, many techniques for measuring pO_2 in living animals and humans have been developed, but methods to measure rates of oxygen consumption *in vivo* are more limited. Recently, we developed a new *in vivo* EPR method that can estimate tissue oxygen consumption non-invasively using EPR spectroscopy (1). Because it is crucial to probe heterogeneitiy of response in tumors, the aim of the present study was to develop a method based on ^{19}F-MRI relaxometry for mapping the oxygen consumption in tumors.

Materials and Methods

Hexafluorobenzene was administered in TLT tumors. A SNAP-IR sequence was used to measure ^{19}F-T_1. Oxygen maps were recorded every 90s (2). The protocol used was based on the measurement of pO_2 during a carbogen challenge protocol. The following sequence was used: 1) basal value during air breathing; 2) saturation of tissue with oxygen by carbogen breathing; 3) switch back to air breathing. The assumption was that the kinetics of return to the basal value after oxygen saturation will be mainly governed by the tissue oxygen consumption. The quantitative estimation of the return kinetics was carried out using a monoexponential curve. Kinetics constants (k) were expressed as min^{-1}. This challenge was applied in hyperthyroid mice compared to control mice. This status is known to dramatically affect consumption rate of tumor cells (3).

Results

Typical evolution of pO_2 during the breathing challenge is shown in Fig.1. Kinetics constants from hyperthyroid mice were higher than in tumors control mice. The corresponding histogram of the ^{19}F MRI data was also generated (Fig.3). Compared to control tumors, the kinetics constants display a shift to the right for the hyperthyroid tumors, indicating a higher oxygen consumption in these tumors. For each tumor, we obtained a color map created from the ^{19}F MRI data, reflecting the heterogeneity in oxygen consumption (Fig.4A). The color map shows that each region of the tumor consumes oxygen with different kinetics constants. The kinetics constants of each pixel can also be mapped as illustrated in the figure 4B.

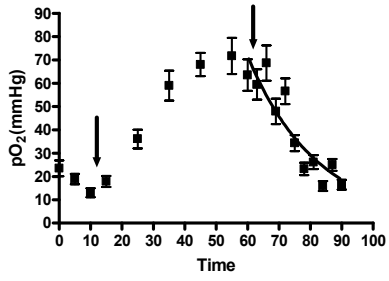

Fig.1: Typical evolution of pO_2 during the breathing challenge. 1st arrow: air switched to carbogen; 2nd arrow: carbogen switched to air.

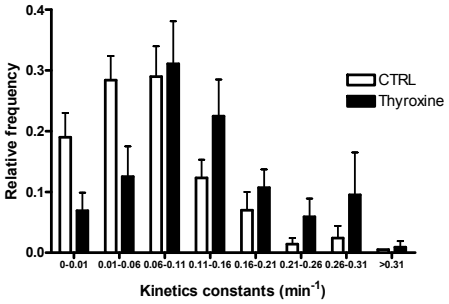

Fig.3: Histogram of the ^{19}F MRI data.

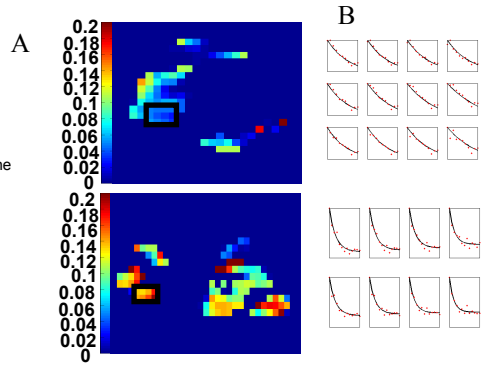

Fig.4: Typical color and kinetics constants map of one CTRL (at the top) and one hyperthyroid (bottom) tumor.

Conclusion

In conclusion, ^{19}F-MRI relaxometry allows the non invasive mapping of the oxygen consumption in tumors. The ability of assessing heterogeneity of tumor response is critical in order to identify potential tumor regions that might be resistant to treatment and lead to a lack of success of the therapy.

References

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