Reviewer’s report

Title: Hyperoxia increases the uptake of 5-fluorouracil in mammary tumors independently of changes in interstitial fluid pressure and tumor stroma

Version: 1 Date: 27 July 2009

Reviewer: Harriet Hopf

Reviewer’s report:

In this study in an animal model, uptake of 5FU in DMBA-induced mammary tumors was increased by hyperoxia. The question posed is well defined and the methods are generally appropriate. The conclusions are well-balanced and adequately supported by the data. The references are appropriate and complete. The title and abstract accurately reflect the findings. The limitations are clearly stated. The writing is strong.

* Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. In clinical hyperbaric medicine, neovascularization in wounded or irradiated tissue is generally considered to require at least 14 hyperbaric treatments. In this study, only 4 were given. Thus, it is not surprising that no effect was seen at 24 hours after the last treatment on increased uptake. It is certainly the case that hyperbaric oxygen acutely increased 5FU uptake, presumably due to a transient increase in tumor oxygen by diffusion. However, the possibility that longer term hyperbaric treatments could increase 5FU by increasing vascularity has not been ruled out by this study. On the other hand, neovascularization in tumors is certainly far different from neovascularization in wounds and previously irradiated tissue, so it would not be surprising to find that a 2 week course of HBO had no impact on 5FU uptake either.

* Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

2. Page 5, Experimental groups and treatment design. How was it decided to give HBO on days 1, 4, 7, and 10?

3. Page 8, Statistics. How was the number of animals per group determined before the start of the study? What attempt was made to estimate the appropriate sample size? Why were there different numbers in each group? Were any animals excluded from treatment? Were those making the measurements blinded as to the treatment group? Were rats randomly allocated to the treatment group? How was the t-test /ANOCA chosen for analysis? Were data normally distributed?

4. Page 9, Hyperoxia and Oxygen Radicals. If the data were not normally distributed, as described, it would have been better to analyze the results with a non-parametric test rather than dropping the aberrant value.
5. Figure legends. Please report data as Mean +/- SD not SEM. Use median / interquartile range when not normally distributed.

6. Figure 1. The data should be presented as a box plot or scatter plot, not a bar graph. SD not SEM should be used.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.