Reviewer's report

Title: In vivo measurement of tumor estradiol and Vascular Endothelial Growth Factor in breast cancer patients

Version: 2 Date: 28 September 2007

Reviewer: Erik Wiemer

Reviewer's report:

General
The manuscript investigates the applicability of microdialysis to determine VEGF and estradiol levels in breast tumor tissue and normal breast tissue in postmenopausal breast cancer patients. The authors show, and this is the most important message of the manuscript, that this technique enables one to directly compare intratumoral VEGF / estradiol levels with concentrations of these biologically active compounds in normal breast tissue as well as in plasma. VEGF levels are increased in tumor tissue relative to normal tissue. Similarly estradiol levels were found up in the tumors although not in all patients. Estradiol levels in normal breast tissue and plasma correlated well as did VEGF levels in normal breast tissue and plasma. No correlation was found between plasma VEGF levels and intratumoral VEGF or between estradiol levels in tumor and VEGF in tumor. The exact biological significance of these observations, a number of which have been reported before, is not yet completely clear but then again that is not really the scope of this manuscript.

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

1. The authors should incorporate - or at least appropriately refer to - recovery experiments undertaken to determine the level of recovery of the compounds investigated. As it may be difficult, if not impossible, to perform in vivo recovery measurements with these particular compounds, one should provide convincing arguments / experimental data why the authors believe the “raw data” presented to reflect genuine concentration differences between tumor and normal tissue instead of being merely caused by recovery differences.

2. As the variation in plasma VEGF and estradiol levels is not presented in a figure it is informative to give the range.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
1. The fact that IHC staining for VEGF can only be scored as being weakly or strongly positive already indicates that this methodology is far to semi-quantitative (or perhaps not quantitative at all) to be compared to concentration measurements obtained by microdialysis. A far better comparison would be to determine intratumoral VEGF levels / molecular forms by immunoblotting in total protein lysates from tumor biopsies.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**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'