Reviewer's report

Title: Levels of activated platelet-derived microvesicles in patients with soft tissue sarcoma correlate with an increased risk of venous thromboembolism

Version: 0 Date: 30 Jan 2017

Reviewer: Nicolaus Friedrichs

Reviewer's report:

The manuscript of Fricke et al. analyses microvesicle counts in peripheral blood of patients with soft tissue sarcoma (n=39 cases) and healthy controls (n=17 cases) using FACS. Microvesicles are small vesicles expressing specific antigens from their cells of origin. This study aims to evaluate the role of microvesicles as biomarkers of soft tissue sarcoma. Results point to an association of circulating microvesicles to malignancy grade of sarcomas and to the presence of vital tumour tissue. Furthermore, high counts of activated platelet-derived microvesicles correlate with the occurrence of venous thromboembolism (VTE). The authors conclude that the detection of these microvesicles might be an interesting new tool for early diagnosis of soft tissue sarcoma patients with increased risk for VTE, possibly facilitating VTE prevention by earlier use of thromboprophylaxis.

As serum parameters for monitoring of sarcomas are needed I think this manuscript contains new and interesting data. I recommend accepting the current paper after the revisions mentioned below:

- Abstract, page 2, line 24: The abbreviation for VTE is explained later (under abstract, conclusion, page 3). Please explain the abbreviation as it first occurs in the text.

- Abstract (and results and discussion): "...we showed that levels of circulating microvesicles correlate with tumor activity and grade of localized soft tissue sarcoma." I think this statement is too strong with regard to grading because for example Annexin V shows higher counts in G1 versus G2 and CD45 and CD61 show no significant difference between G2 and G3 (figure 2,A,B,C). Please formulate differently (weaker or more specific).

- Results, page 8:
o (also in discussion, page 9) "The total amount of Annexin V positive microvesicles as well as levels of endothelium-derived (CD62E-positive) microvesicles in the peripheral blood of patients with soft tissue sarcoma were shown to correlate with tumor activity, decreasing significantly after tumor resection”. What do the authors mean with "tumor activity”? Has this parameter been (statistically) evaluated within the tested tumours? (How?) How do the authors interpret the strong variance of microvesicle-counts among pre-operative tumours (figure 1A,B,C)? In my view figure 1A can only show, that number of microvesicles is decreasing significantly after tumour resection. In my view "tumor activity" would mean something like proliferative index or other parameters of tumour vitality (which have not been determined here). Maybe the authors could consider using another term instead of "tumor activity".

If the authors want to use this term it should be substantiated by further analyses, e.g. by semiquantitative immunohistochemical analysis of single cases analyzing primary tumour tissue, its matched metastasis and non-metastasized primary tumour tissue. In these further experiments "tumour activity" might be visualized by Ki67-immunohistochemistry (proliferation).

"Pre- and post-operative Hb and platelet counts of patients with localized soft tissue sarcoma undergoing resection differed significantly (p=0.0037 and p=0.0054, respectively) (Tbl. 1), with decreased Hb and increased platelet counts after tumor resection." Why is this finding important for the study? Maybe the authors could discuss this and explain more clearly why this "might influence the results" (as mentioned in discussion, page 10)? To me, the information as demonstrated is not substantial for the study.

Are the methods appropriate and well described? 
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls? 
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown? 
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments
which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal