Reviewer's report

Title: Should tumor depth be included in prognostication of soft tissue sarcoma? Minor prognostic value of tumor depth in a population-based series of 490 patients with soft tissue sarcomas of the extremity and trunk wall

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Reviewer: John Healey

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

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Should tumor depth be included in prognostication of soft tissue sarcoma?
Rydholm and Gustafson

This is an enlightened analysis of an important problem, and is a comprehensive review of large number of well-documented cases. The authors have a wealth of experience in the arena and their opinions are important, regardless of the scientific rigor of the work. Consequently, every effort should be made to address the relatively minor criticisms listed below so that the work is published. The problem of soft tissue sarcoma staging is one that has long plagued the field of surgical oncology. Many attempts have been made to clarify the issue. That the AJCC system is on its fifth edition attests to this, as does the number of other systems that have tried to improve on our existing efforts. This paper uses a high quality database that was developed in a population-based system. As such, it is an important addition to the field. It makes a valuable contribution to the debate, but doesn't put it to rest. It fails to use techniques that have been used by other investigators to compare results from different staging systems (e.g. Akike information statistic used by Wunder, et al.) It is sufficiently valuable, however, to publish whether or not more sophisticated analyses are added. Final resolution of the issue waits for another day. It is interesting that the authors have published previously on the importance of more sophisticated pathologic assessment in order to optimize the pathologic grading and prognostication of soft tissue sarcomas. Gustafson has clearly shown that inclusion of features such as tissue necrosis, ploidy, and vascular invasion are important additions to the grading of STS. Why didn't the authors include these factors in their formulation of a better staging system? As a minimum, they must explain their omission. They must give us guidance as to whether they think that better conventional histology, flow cytometry, or even molecular pathology should be included in future systems. I congratulate the authors on a thought-provoking manuscript. Although other authors, as noted, have made many of the points this is the most eloquent statement of these observations.

Specific comments are listed below.

p2 The title should reflect that this study encompasses an unconventional age distribution, including patients 16-20. These patients are not commonly included without specifying that this is a study that includes adolescents. The same applies for the exclusion of neurofibromatosis patients. I therefore
suggest adding the modifier "non-syndromic sarcomas of adults and adolescents."

Results, line 2: The small number of small tumors in the two sites (above and below the fascia) indicates that hater may be insufficient statistical power to support the authors' contention that there is no difference related to tumor depth. In order to state this you must provide the power of the analysis of this specific question, and address the p3 Para 2 line 8 The ages included in the study are somewhat unusual. Most adolescent cases are included in pediatric series. They are rarely included in adult series. This alters the potential for response to chemotherapy, and the distribution of cases in the series. Even a small effect in the outcome for this group of patients may be sufficient to dilute the effects seen in older patients.

P4 Para 1 last line; Consider adding "in adults". the answer may be different for specific diagnoses or for different age groups. this has not been specifically addressed in the existing literature.

P 4 Para 2: Please express the "average" as median values rather than mean results.

P 7 Para 1 line 10: consider using "even though" rather that "although". It is more emphatic and I think it better states your intended meaning.

P 7 Para 2 line 5: Please specify how many of the cases in your series were also part of the series' reported by Trovik. This influences the strength of the statement that "we found the same..."

P 8para 1 Please address the power of your statement that "...is the generally good prognosis for low-grade tumors."

P 9 table 2 etc. Since your hypothesis is that the tumors should be staged by means of a three-part size distribution and grade, not by any of the three existing systems to which you refer in the first paragraph of page 3 (Background), it would be much more educational to present the data addressing this issue in tabular form. Instead, you have presented the data in a mixed fashion that obscures the focus of your paper.

Same: define the abbreviations e.g. RR as relative risk, CI as confidence interval.

Same: Please comment on the major difference in the relative risk based on whether you included the Grade III cancers within the high-grade designation. Why does the risk go down as the histological grade go up?

P 10 How about the group of just grade IV cases? Please analyze and display this subset in the system tricompartmentalized, based on the three part size designations.

Answers to the required additional questions:

Level of interest: findings are important to those with closely related research interests.

Advice on publication: accept after discretionary revisions.

Quality of written English: excellent, acceptable

Competing interests: I have no competing interests.
I have not received any reimbursements that may in any way gain or lose financially from the publication of this paper.
I hold no stocks that are relevant.
I have no other competing interests.  
I have no non-competing interests.  

I agree to have my review posted.  

Sincerely,  
John Healey, M.D.  

**Competing interests:**  

None declared.