Reviewer's report

Title: Clinical Significance of Survivin Expression in Ductal Carcinoma in situ with Microinvasion of the Breast

Version: 2 Date: 15 April 2008

Reviewer: FS Al-Joudi

Reviewer's report:

The article is now generally better, though it still requires a few points to be attended, as outlined in details in the attached report. Other than that, the article cannot be published in its present form.

General remarks: The authors have answered and corrected only a few of the remarks given to them in the early report. This included mostly some language errors. Some points have been completely ignored and were left unattended. As for the major alterations and re-writing requested, they were not done. These are detailed below.

Unanswered or un-met with, questions from the first review:

The title of article.

Abstract: still not good.

Page 14 lines 10-11: the process is more complicated than just bcl-2 and Nax: there is a vast array of molecules which have been uncovered, and still more not known. There are also the pathways for apoptosis, and those activities that prevent apoptosis. There are also the check-points in the cell cycle, and the cyclins ....etc. I mean to say that the matter cannot be simplified in this way, as it becomes more of a weak point in the article.

Specific remarks. These include, in sequence of pages:

Title: The authors refused introducing any alterations in the title, although it reflects only a small part of the truth: the title is required to be concise, but also reflective: let them look at the last paragraph in page 6 starting from “we analyzed: apoptosis related factors, apoptosis index, survivin, bcl-2, Bax, cell proliferation / cycle-related factors (Ki-67, p-53, p21, cyclin D1, Rb, and other factors: OF ALL THOSE FACTORS, THEY SELECTED SURVIVIN ONLY TO DOMINATE THE TITLE!!!!!!!

Page 3:

Abstract:

Background: Still far from satisfactory: the main issue in the title, survivin, and the other issues, biological factors, are barely mentioned. I suggest that the authors remove everything about mammography (here and elsewhere in the text), except
for the correlations of the outcomes of the study with the findings in mammography, which can be made briefly in the discussion section.

To the background, they could add another sentence as an introduction to survivin, along with the biological parameters (factors).

The sentence starting with “TO STUDY UNTIL ADJUVANT SYSTEMIC THERAPY” IS WEAK, GENERALLY, AND CONTAINS A PRE-EMPTIVE IDEA ABOUT THE USE OF WHAT THE AUTHORS CALL, ACTIVE THERAPY. The wording is not correct, and the usefulness of the findings can be discussed later in the discussion, part.

Methods: Proliferative capacity??!! This is meant to say: the actual proliferation, as seen in: mitotic index, cell counts (where relevant), etc.

The only method mentioned here is immunohistochemistry: TUNEL and others: those were not mentioned.

Page 5:

Introduction: again, lines 3-5, these are about mammography, and they MUST be removed: it has nothing to do with the fact that is a DCIS or a DCIS-mi, as these can be detected and confirmed by various methods: before any consideration of the biological factors. Alternatively, the authors are required to put an emphasis on the clinical conversion of DCIS to DCIS-mi, and then they should elaborate more on survivin and other factors, to justify their work, and from there, they can divert gradually to their “OBJECTIVES”: the latter has been done, but still is weakly expressed and requires some re-writing to improve the text.

Line 17: variation: should become “morphology”

Page 6: the last three lines: there is a wild statement here, and it is not well justified: this may be usable in the Discussion.

Materials and methods:

Page 7:

First few lines: strangely, the authors refused in their corrections the idea of removing or even reducing the “mammography” talk: yet in the first description of the methodologies, they contradict themselves by saying that the cases of DCIS and/or DCIS-mi were diagnosed by “post-operative histopathological examinations after surgery. This contradiction of thoughts MUST be alleviated.

Some information is not put in a good-flow pattern: ethical approvals are obtained before the records are approached (to the best of my knowledge).

Another striking remark: Histological diagnosis was made by 2 specialized pathologists, and three clinicians: Since when have clinicians (whose specialties have not been specified) started making up histopathological diagnoses?????!!!!! There is a clear flaw in the information which needs to looked at.
Page 8:
Line 3: “prepared on slides is better be: mounted on slides.
Line 3: slides coated (with what): this needs to be mentioned.
Line 3: sections were must be: The sections were.
Line 5: Retrieval buffer buffer 9 was used for survivin. However, there is no menmtion of the buffers used for other antigens!!!
Line 6: “previously published” better become: previously described”.
Lines 13 and 15: Netherland: it must be :Netherlands” (in the plural form).
Last paragraph: It may be a good idea to specify the following specifications of the primary and secondary antibodies used: polyclonal or monoclonal, source (horse, rabbit, mouse…etc), their titres used. Note that there will be a greta variety of those since many essays have been performed in this work.

Page 9:
Line 2: the authors are required to specify the alcohol used in the dehydration.
Lines 16-17: apoptosis was detected …..: change to: To quantify apoptosis, the mean number of ……….

Page 10:
Paragraph 2: this had better go to the discussion section.
Statistical methods: utilized to exam : examine.
Line before last: statistical analyses.

Results:
Page 11: line 2: frequently: not frequent (unless you say: comedo type tended to be more frequent in…
Page 12: lines 3-5: from “because no cases were detected…..staining was detectable” either remove it or take it somehow to the Materials and methods section. I think it would be better removed, and the negativity of nuclear expression be discussed in “Discussion” especially with reference to relation of intra-cellular location and prognosis. There are a few references that tackled this finding.

Discussion.
Page 13. Line 3: therefore: this is not likely to use: better be : hence, in this study....
The word “Therefore” is used elsewhere, and I tend to think that its use is not likely.
Page 14: end of second paragraph: again, the balance between: I suggest that the authors say "specific interaction" instead of balance.

References:
Ref 24: the reference was mentioned with some missing initials of authors: this means that such imprecision may have appeared, unnoticed in other references: these MUST be revised and rendered fault-free.

Concluding suggestions:
The article is still lacking the state of “near perfection”.
The text is still weak and requires some consolidation, language-wise and science-wise.
It cannot be accepted in its present form.