Reviewer's report

Title: Radiation therapy of anal canal cancer: from conformal therapy to volumetric modulated arc therapy.

Version: 2
Date: 19 May 2014
Reviewer: Marianne Gronlie Guren

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Major Compulsory Revisions

The authors need to give precise definitions for the terms used for radiotherapy techniques, and be consistent in the use. Definitions are needed for the terms such as volumetric modulated arc therapy (VMAT), and Rapid Arc (RA), conformal radiotherapy (CRT), simultaneous integrated boost (SIB), IMRT. The characteristics of these techniques, or how they differ, should be briefly explained. Furthermore, later in the manuscript, a new abbreviation occurs, concurrent CT-RT, which is an unusual abbreviation and should be defined. An abbreviation CT is probably meant to be chemotherapy, but is not defined.

Abstract: It is stated that RA treatments lead to lower incidence of higher grade events. I presume this refers to toxicity, but it should be stated clearly. The toxicity reporting must be rewritten. Since these are two patient series, one can not state that toxicity was "reduced of 20% for GI" etc, one must report the differences in toxicity occurring between the two series. Furthermore, the authors should report how toxicity was graded, whether it was recorded prospectively or retrieved from medical charts, the time-frame, etc.

In general: The manuscript should be edited by an author fluent in English, to reduce the number of grammatical errors in the present manuscript. The first sentence on page 3 "Patients in the CRT cohort, ..." is an example of poor grammar, and difficult to understand.

Methods: The delineation of the GTV, the two CTVs, and the PTV, could be explained more clearly. Also, how were positive lymph nodes handled, and which doses were prescribed to the different volumes.

The chemotherapy regimens used must be described and discussed, in the methods or results section, since this may have impact on the treatment results and the toxicity. Please also define the chemotherapy abbreviations later used (such as MMC, CDDP).

Further details of the scoring of acute and late toxicities should be provided. Was the scoring systematic and prospective, weekly, or retrieved retrospectively as "worst toxicity reported". Was toxicity scored at all follow-up visits?

Results:
In Table 1, there is a large difference in the chemotherapy regimens used. 57% of patients in the CRT group had FU/CDDP, compared to 5.5% of patients in the RA group (where 80.5% had FU/MMC). This must be discussed, since CDDP has been shown in randomised trials to produce more toxicity than MMC.

Please comment the finding of Table 2 in the text. It seems to be favourable for bladder, bowel, femoral heads in the RA group. The same applies to figure 1. Please also provide the statistical significance test and value.

Please provide the number who obtained complete response after chemoradiotherapy, and the number who needed surgery such as APR. These are significant outcomes and should be reported.

Figure 2 can be omitted, as it does not provide necessary information. If this type of figure should be included it should show the different dose distributions obtained by CRT and RA techniques.

The paragraph on survival and local control should be structured better, to improve readability. Details of individual patients should be omitted.

Table 3 should include p-values.

Minor comments:
Discussion: It is stated that the treatment is based on four RCTs; why these four, whereof only 1 (Ajani) is recent, and why is not ACT II referred to (James RD, 2013).

What is Al-Sarraf chemotherapy?
And what is Nigro regimen?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.