Reviewer's report

**Title:** Metachronous metastases- and survival-analysis show prognostic importance of lymphadenectomy for colon carcinomas

**Version:** 2  **Date:** 14 January 2012

**Reviewer:** Dieter Hoelzel

**Reviewer's report:**

This is a well written paper with a well defined question and adequately described, sound data. The background is a large, prospective, well documented, patient cohort from a university hospital. A specific feature is the consequent selection with clearly defined criteria, which results in a homogenous cohort. Nonetheless, the conclusion is only partially comprehensible. The lymph node involvement – that is the number of positive lymph nodes – is the most important, classical, prognostic factor. This is shown by the multivariate Cox regression. But a correlation is not causation or “post hoc ergo propter hoc” would be a logical fallacy. Therefore, the prognostic relevance of positive lymph nodes is not a justification for the lymphadenectomy. If positive lymph nodes are not the cause of distant metastases then the reliable identification of a positive lymph node status would be sufficient for the indication of an adjuvant treatment comparable to the sentinel lymph node procedure in other cancers. Therefore, the last sentence in the conclusion and the last chapter of the discussion should be specified, perhaps with an additional paper e.g. Yachida Nature 2010 and PA04.

In addition, the following improvements are recommended:

The term stage is a defined term. Therefore, the term N-stage, T-stage should be replaced by N-category and T-category, also in the figures.

Table 1: A line with the number of deaths in both groups should be added. The differences in the Cox models are in part dependent on the different numbers of each event, metastases or cancer related death or all dependent and in Table 3 all deaths, also the cancer independent cases.

Fig.1: The reduction of the cohort is reasonable but the numbers of the excluded patients are not reproducible. The groups are not disjunctive. Therefore, the sum must be greater then the number of the excluded 645 or 329 patients.

It would be very informative for interested readers, if the selection process would be described with tables with the T-category pT1, pT2, pT3, pT4 and others listed as columns and as lines R1/R2, previous second non-CRC, synchronous metastases, with further grouped criteria such as age <50y, or positive family history. These tables should replace the two boxes.

The exclusion criteria primary surgery is actual unnecessary because Kaplan-Meier curves and Cox models can use cases with shorter follow-up. But a new evaluation would not change the conclusion and is therefore not necessary.
Fig. 2 d should describe the grade dependent survival instead of N-category N0 or N2

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.