Author's response to reviews

Title: Radiation Therapy for Desmoplastic Medulloblastoma - A Retrospective Analysis of Outcome and Prognostic Factors

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Author's response to reviews: see over
Re.: Revision MS 1052173443333246

Dear Ms Neilan, dear Ms. Titmus,

today we are submitting our re-revised original article entitled

**Outcome and Prognostic Factors of Desmoplastic Medulloblastoma treated within a Multidisciplinary Treatment Concept**

We had a native English-speaking colleague read and copyedit our manuscript and hope that the quality of language is now suitable for your journal.

In addition to a statement of ethical approval according to our institutional guidelines in the methods section, we would like to inform you that all patients gave informed consent on the use and publication of their data before inclusion in any treatment. Furthermore, retrieval of any information from our database was legitimized by our institutional data security using a uniform code (“desm. Mb 2009”) for data acquisition. We did not obtain additional ethical approval, as this is not requested in our institution.

Please find below a point-to-point response to the concerns raised by the referees. All corresponding changes in the manuscript are highlighted in red colour.

**Referee 1: Jaques Grill**

We consider it necessary to leave pediatric patients in this analysis, as this tumor entity is very rare and only little data is available on subtype-specific outcome. Furthermore, there were no children under the age of three in our group. For them, distinct treatment regimens with intensified chemotherapy instead of craniospinal irradiation are being established and will probably spare neurological toxicity. Especially with respect to biological features of medulloblastoma, there are major differences between pediatric and adult patients; however, with focus upon clinical approaches, most biological
properties have remained descriptive and only few were translated into clinical treatment stratification. In addition to the introductory statements (pg. 5), we added a comment in the discussion (pg. 14), addressing the differential use of craniospinal irradiation in adult and pediatric patients. We are aware that in children desmoplastic medulloblastoma are located in the vermis more often than in the hemispheres (pg. 4). However, in comparison to classical medulloblastoma (~90% vs. 10%), also in children desmoplastic medulloblastoma are found in lateral location more frequently (~80% vs. 20%; Sarkar, C. et al; Journal of Neurooncology, 2002 Table 2). The sentence was rephrased to avoid misunderstandings.

Referee 2: Christian Senft
As requested, we now provide a suppl. table that provides OS, LPFS, DPFS, initial tumor stage, cerebellar localization, affection of the fourth ventricle, resection state, administration of concomitant and adjuvant chemotherapy, and age at first diagnosis for every single patient. We agree that local or distant relapses cannot be classified as prognostic factors, and rephrased the passages in the conclusion. We still consider it important though to describe the dismal outcome of tumor recurrence, because this description provides a guideline for clinical routine, where recurrent medulloblastomas are seen quite frequently, asking for prognosis and the benefit of salvage therapies.

The extent of surgery was assessed by cross sectional imaging in ten patients (50%; 6 x MRI, 4 x CT). Ten patients were operated before 1995 and did not undergo routine postsurgical imaging. In some cases, neurosurgery was clearly incomplete for sparing of surgical complications, and in these cases no postoperative imaging was performed, as residual tumor was clearly present establishing the need for boost irradiation. The statement of a distinctively better prognosis for desmoplastic medulloblastoma patients in the abstract was overlooked during the first revision and was now deleted. We apologize for any misunderstanding: Comparing treatment results in desmoplastic medulloblastoma with classical medulloblastoma will be addressed in a separate manuscript.

The “Results” section was rephrased and style-adapted: Judgmental phrases were deleted and comments on the findings were moved to the “Discussion” section. We had a native English-speaking colleague read and copyedit our manuscript.

Referee 3: Ira Dunkel
Since a comparison between classical and desmoplastic medulloblastomas will be performed in a separate manuscript, Mr Dunkel is absolutely right in commenting on our abstract conclusion. A statement of distinctively better outcome in desmoplastic medulloblastoma was overlooked during the first revision and has now been deleted.

The extent of surgery was assessed by cross sectional imaging in ten patients (50%; 6 x MRI, 4 x CT), of whom four had residual contract agent-enhanced tumor residues. Ten patients were operated before 1995 and did not undergo routine postsurgical imaging. In these cases, state of resection was defined by the surgical reports. In three cases, neurosurgery remained macroscopically incomplete to spare surgical complications (brainstem infiltration via the fourth ventricle). A detailed description is now included in the methods section.
All authors have read and approved the revised manuscript. We hope that our manuscript is now suitable for publication in BMC Cancer. Please do not hesitate to contact us for any further questions.

Sincerely

Dr. Stephanie Combs and Dr. Stefan Rieken
For all co-authors