3D model based documentation with the “Tumor Therapy Manager” (TTM) improves reproducibility of head and neck tumour patient data

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For publication in International Journal of CARS

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Abstract

Purpose
Diagnostics and therapies of head and neck cancer (HNC) have been extensively investigated in the last years, which has led to a complex variety of treatment approaches. Hence, the multidisciplinary medical team is faced by new challenges to match the patient to an appropriate regimen.

At this key point, primary diagnostics and its reliable documentation are indispensable. We therefore investigated whether the reproducibility of this data, especially the TNM classification, could be improved by a three-dimensional (3D) documentation system.

Methods
We aggregated 42 data sets of HNC patients during primary diagnostics including panendoscopy, which was performed and evaluated by a proven head and neck surgeon. In addition to the conventional panendoscopy form and report, we generated a 3D documentation with the software “Tumor Therapy Manager” (TTM).

Afterwards, the cases were randomly re-evaluated by 11 experienced otolaryngologists from 5 hospitals, half with and half without the TTM data. The finding accuracy was assessed in classes by pre-post comparison of the TNM classification.

Results
The tumour classification (T) differed on average by -0.04 ± 0.63 classes with and -0.05 ± 0.86 without 3D from the primary diagnosis (p=0.950). Hence, there was a significant decrease in variance from 0.86 to 0.63 via TTM (p=0.027).

In the re-evaluation without TTM, the lymph nodes (N) were significantly underestimated with -0.39 ± 0.79 classes compared to 0.07 ± 0.69 with TTM (p=0.002). Likewise, the variance was reduced from 0.79 to 0.69 (p=0.032).

There was no influence on the evaluation of distant metastasis (M).

Conclusions
Increases in reproducibility are achieved through 3D documentation of HNC primary data. The more precise assessment of the tumour classification allows a more profound decision-making process concerning the therapy, especially within the interdisciplinary tumor board.

Keywords
Tumor Therapy Manager, head and neck cancer, documentation, three-dimensional, patient data, reproducibility, panendoscopy.
Introduction

The worldwide incidence of head and neck cancer (HNC) in 2008 has been rated 634,760 by the World Health Organization (WHO) and hence represents 5.1% of all cancer diseases [1]. In the mentioned year, there were 47,560 cases counted in the USA [2] and 17,130 in Germany [3]. Current estimations even assume an incidence of 53,640 for 2013 in the United States [4]. While the number of head and neck malignancies attributable to the primarily dominant risk factors alcohol and smoking decreased as a result of lowered consumption, the human papillomavirus (HPV) associated entities came to the fore and are supposed to cause the rising incidence in particular of oropharyngeal head and neck squamous cell carcinoma [5,6].

The epidemiological changes and the enormous developments in diagnostics and therapy of HNC in the recent years have led to a more complex treatment management. Medical imaging with sonography, computer tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) has been broadened by higher resolutions and hybrid systems like PET-MRI. On the other side, there was a diversification of treatment approaches such as organ-preserving surgery, combined radiochemotherapy and targeted therapies with biologicals or intensity-modulated radiation therapy (IMRT) [6-8]. This requires the inclusion of all available information allowing for an intensified decision-making process taking into consideration not only primary staging data like radiological images, pathological and molecular findings but also the clinical and haptic impression. Today, various specialists are involved in the treatment of HNC besides otolaryngologists: radiologists, radiotherapists, oncologists, pathologists and maxillofacial surgeons. Hence, according to several authors, the diagnostic findings and the therapy options for the individual patient should be discussed, agreed and scheduled within multidisciplinary head and neck oncology meetings [9,10]. In addition, Simo et al. claim an integrated media presentation in these conferences [11].

With the “Tumor Therapy Manager” (TTM) developed by our group a three-dimensional (3D) based documentation system is available, that integrates the above mentioned data of the tumour and the patient [12,13]. This computer programme is capable to manage segmented CT scans, anatomic 3D reconstructions, endoscopic photographs or sketches with annotations but also allows spatial distance measuring and 3D volumetry. We could demonstrate that the TTM is operational in the daily routine [14]. However, no investigation so far addressed the question, whether the integrated presentation of information using the TTM indeed increases the reliability of documentation and leads to a better reproducibility of the tumour evaluation. In the here presented study, these aspects were investigated with focus on reproducibility of staging by means of the TNM classification.
Methods

To investigate exactness of tumour staging, decision-making by experts in the field of head and neck oncology based on data sets provided for randomly chosen patients that were otherwise blinded to the otolaryngologist (i.e. without availability of any further information or knowledge about the patient than represented in the electronic files) was judged to be the only appropriate way to detect a potential benefit provided by the TTM. Therefore, the study was conducted in two phases. First, individual HNC patient data was gathered, which in the following served as base for the actual trial with re-evaluation through otolaryngologists.

Data acquisition

In the period from 05/2011 to 09/2012, the primary staging data of 42 HNC patients at the Department of Otolaryngology of the University Hospital Leipzig were acquired considering the following inclusion criteria: first panendoscopy related to the first diagnosis of HNSCC, head and neck CT scan of appropriate quality in regard to the distribution of the contrast agent as well as the slice thickness ≤ 3 mm and an advanced tumour stage (UICC III or IV) to allow further evaluation of the N classification. The sample can be considered representative for mean age, sex ratio and distribution in tumour localisation (Tab. 1).

The CT scans have been segmented with the software “NeckSegmenter” [15] and then 3D models were generated from the segmentation data in the TTM prior to the panendoscopy (Fig. 1). This process takes approximately 90 minutes depending on the number of slices and the quality of the CT scan (e.g. metal artefacts by dentures in the oropharyngeal region) as well as level of detail in 3D structures.

To avoid interobserver variability, a single proven head and neck surgeon solely performed the panendoscopies and primary documentation. Each dataset was pseudonymised and includes a standardised patient’s chart (anamnesis, ENT examination findings, conventional and new 3D panendoscopy form [Fig. 2], panendoscopy report, endoscopic photographs, radiological findings, internistic status) plus the CT data in Digital Imaging and Communications in Medicine (DICOM) format and the 3D documentation in TTM (Fig. 3).
Setting for re-evaluation

We could engage 11 experienced otolaryngologists from 5 hospitals in Cottbus, Erfurt, Leipzig, Potsdam and Riesa (Germany) to re-evaluate the patient data. A detailed test protocol was set up to check for reproducibility of the tumour classification. The 42 patients were randomized to blocks of 5. One physician examined 2 of these blocks, the first one with and the second block without the TTM data. The next physician received the same patients in identical order, but first without and then with the TTM data to prevent a bias through conditioning. Thus, every patient was randomly assigned to the re-evaluating otolaryngologists and re-evaluated in each of both ways, and 10 patients were re-evaluated multiple times.

The patient’s chart as well as the head and neck CT scan was available in both settings. In the TTM cases, the conventional panendoscopy form was replaced with the 3D form and in addition the physicians had access to the 3D documentation in TTM. The assumed diagnosis was recorded on a test sheet. There was no time limit given for the re-evaluation of the TNM classification.

Assessment of finding accuracy

For comparison of the results in both groups, the deviation of the re-evaluation from the primary diagnosis was appraised in classes for each state T, N and M. Since the TNM classification is defined by ordinal parameters, specific intervals had to be determined. Thus, the difference between two adjacent main classes (T0-4; N0-3; M0-1) was defined to the value of one (1). The interval between the subclasses T4a and T4b was set to one half (½) and within N2a-c one third (⅓). If for example a re-evaluator stated the classification of locoregionary lymph nodes N2b instead of the primarily diagnosed N1, the N status was judged to be overvalued +1⅓ classes (Fig. 4). Undefined stages (Tx, Nx, Mx) were not taken into account.

The statistical analysis was performed with IBM SPSS Statistics 20. A p-value below 0.05 was regarded as significant difference. We tested for significances of the means (Student’s t-test) and variance equality (Levene’s test).
Results

The total sample size of 110 re-evaluations is equally allocated to both groups with (n=55) and without TTM (n=55). For the N classification without TTM, 2 dropouts (n=53) were registered due to undefined lymph node stage (Nx). Staging of distant metastasis even showed more uncertainties (Mx) with 12 dropouts (n=43) in conventional and 11 (n=44) in 3D re-evaluation (Tab. 2).

The tumour classification (T) differed on average by -0.04 ± 0.63 classes with and -0.05 ± 0.86 without 3D from the primary diagnosis (p=0.950). However and despite equal means, there was a significant decrease in variance from 0.86 to 0.63 classes by use of the TTM (p=0.027) (Fig. 5, 6, Tab. 2).

In the re-evaluation without TTM, the lymph nodes (N) were significantly underestimated with -0.39 ± 0.79 classes compared to TTM with 0.07 ± 0.69 (p=0.002). Likewise, the variance was reduced from 0.79 to 0.69 classes (p=0.032). Distant metastasis were classified with a deviation of 0.02 ± 0.15 classes in the TTM group and 0.05 ± 0.21 without 3D documentation (p=0.549).

Discussion

The results show a clear superiority of the TTM documentation system regarding the reproducibility of HNC primary staging data, which is naturally based on certain efforts that have to be accomplished.

First, there is the CT segmentation and the generation of the 3D model, which takes about 90 minutes and has to be prepared prior to the panendoscopy. The actual documentation process is performed right after the endoscopic examination and lasts further 10 minutes longer than conventional paper based documentation [14]. To minimize the time exposure, it is necessary to automate the segmentation process as much as possible. Moreover, the documentation system should be implemented in the hospital information system but also into the picture archiving and communication system to avoid recurrent manual user inputs, data disruption and mistaken identities. Bohn et al. describe an integrated IT platform, which addresses these problems [16] and has been successfully established at the University Hospital of Leipzig in March 2013.

The accuracy of the 3D visualisation of the tumour in context to the anatomic structures relies on an appropriate quality of the CT scan. Cancellations on the tumour-associated slices due to metallic foreign material or motion artefacts can make segmentation difficult or
nearly impossible. Another issue could be a vague demarcation of the tumour because of inadequate distribution of the contrast agent or perifocal oedema. MRI scans may overcome such limitations and provide a more reliable segmentation especially of the tumour. A currently ongoing project addresses the development of MRI segmentation and image data fusion.

Despite of these issues, there is much potential, from which the interdisciplinary team as well as the patients can benefit. Difficult surgical approaches could be planned and awareness of risk structures like a kinking arteria carotis might be attracted by means of 3D exploration. Furthermore, the 3D visualisation could be used for better demonstration and explanation of individual findings and therapy for the patient.

Although the effort is already justified by the more precious tumour classification, in our opinion further options should be taken into consideration to raise the overall effectiveness. Hence, a project on transferring segmented CT data for radiotherapy planning is in conception.

With 3D volumetry, a further criterion for reliable response evaluation in neoadjuvant chemotherapy protocols is addressed. Mueller et al. found a higher reliability for volumes estimated by the segmentation-based approach than the widely used diameter-based approach for lymph nodes [17].

Unfortunately there are currently no further comparative studies that address the reproducibility of HNC data, but our results are in full agreement with the aforementioned investigation and, moreover, demonstrate that the use of superior 3D visualization in clinical decision-making should be of high value. Reasons for this are attributable to numerous clinically relevant aspects. It is not only the lowered variance in TNM classification and hence a better reproducibility of initial findings in a second look but rather the transferability of results obtained within the same and also external departments and e.g. in clinical trials.

The most relevant aspect lies in the definition of the appropriate therapy of the individual patients. On the one hand, an underestimation in particular of lymph node metastasis can lead to inappropriate treatment, for instance avoidance of the required neck dissection or adjuvant irradiation, and hence to bad outcome. On the other hand, an overestimation of T, N and M can also harm the patient due to inappropriately intensified treatment regarding irradiation, radiochemotherapy or extended surgery. Therefore, there are good reasons for integration of 3D visualization into clinical routine.
**Conclusion**

The use of a 3D documentation system increases the reproducibility of individual HNC patient data through decreased variance in T and N classification and less deviation of the mean value in lymph node stage. The extra effort needed to aggregate data in the TTM is justified as this method integrates various information, and in particular those which is difficult to imagine if presented singularly or only by means of CT scans, and therefore promises an improved decision-making within the interdisciplinary tumour board.

**Future work**

As our results presented in this article demonstrate and verify advances for the information exchange related to treatment decisions of otolaryngologists in head and neck tumour boards, the investigation must be repeated with physicians from other oncological disciplines and medical experts involved, to prove a common benefit by comprehension of all the clinical data of the particular patient in the TTM.

The intense research on automatic and semiautomatic segmentation algorithms and processes will reduce the preparation time and related costs of 3D model generation.

**Acknowledgements**

We would like to thank all participants and contributors to our study: Prof. Dr. med. Thomas Eichhorn, Dr. med. Eva-Maria Jenzewski, Dr. med. Stefan Koppatz (Cottbus); Prof. Dr. med. Dirk Eßer, Dr. med. Ulrich Kurze (Erfurt); Prof. Dr. med. Markus Jungehülsing, Dr. med. Jörg Berkholz, Dr. med. Christoph Erle (Potsdam); Dr. med. Hans-Joachim Vogel (Riesa); Dr. med. Thomas Berger, Dr. med. Miloš Fischer, Dr. med. Mathias Hofer and Dr. med. Christian Mozet (Leipzig).

**Conflict of interest**

The authors declare that they have no conflict of interest.
Table 1 Mean age, sex ratio, tumour localisation and UICC classification of the 42 HNC patients.

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<tr>
<td><strong>mean age (± SD)</strong></td>
<td>59.8 ± 11.0</td>
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<tr>
<td><strong>sex ratio (m / f)</strong></td>
<td>38 / 4</td>
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<tr>
<td><strong>localisation</strong></td>
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<tr>
<td>larynx</td>
<td>9</td>
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<tr>
<td><strong>UICC classification</strong></td>
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<tr>
<td>0</td>
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<tr>
<td>I</td>
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<td>III</td>
<td>3</td>
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<td>IVA</td>
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<td>IVB</td>
<td>7</td>
</tr>
<tr>
<td>IVC</td>
<td>2</td>
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SD: standard deviation, m: male, f: female

**Fig. 1** Malignant tumour of the oropharynx with infiltration of the vallecula, left tonsil and cervical lymph node metastases leading to a classification as HNC cT3 cN2c cM0. The screenshots show the segmentation process (a) and the 3D model in TTM (b).
Fig. 2 Conventional (a) and 3D panendoscopy form (b) of an oropharynx carcinoma with infiltration of the vallecula, left tonsil and cervical lymph node metastases cT3 cN2c cM0, the same HNC as represented in fig. 1.

Fig. 3 Screenshots of the documentation available in the TTM. a: CT with highlighted structures (yellow: tumour, red: arteries, blue: veins), b: tumour with measurement of volume and distance to the artery as relevant structure at risk, c: panendoscopic photographs with annotations, d: pictograms of tumour spread.
Fig. 4 TNM scoring system for the estimation of deviations in classes.

Fig. 5 Boxplots for the deviation from correct TNM classification with and without TTM.

Table 2 Mean deviation and standard deviation (SD) with related significance level (p) and sample size (n) for the T, N and M classification in both groups with and without TTM.

<table>
<thead>
<tr>
<th></th>
<th>with TTM</th>
<th>without TTM</th>
<th>p</th>
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<tbody>
<tr>
<td>T</td>
<td></td>
<td></td>
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<tr>
<td>mean</td>
<td>-0.04</td>
<td>-0.05</td>
<td>0.950 (Student’s t-test)</td>
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<tr>
<td>SD</td>
<td>0.63</td>
<td>0.86</td>
<td>0.027 (Levene’s test)</td>
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<tr>
<td>n</td>
<td>55</td>
<td>55</td>
<td></td>
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<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>0.07</td>
<td>-0.39</td>
<td>0.002 (Student’s t-test)</td>
</tr>
<tr>
<td>SD</td>
<td>0.69</td>
<td>0.79</td>
<td>0.032 (Levene’s test)</td>
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<td>n</td>
<td>55</td>
<td>53</td>
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<td>M</td>
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<tr>
<td>mean</td>
<td>0.02</td>
<td>0.05</td>
<td>0.549 (Student’s t-test)</td>
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<tr>
<td>SD</td>
<td>0.15</td>
<td>0.21</td>
<td>0.228 (Levene’s test)</td>
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<tr>
<td>n</td>
<td>44</td>
<td>43</td>
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Fig. 6 Relation of the TNM classification in the re-evaluation and the original diagnosis with and without TTM.


14. Boehm A, Wichmann G, Neumuth T, Pankau T, Müller S, Preim B, Dietz A. Documentation and Visualisation with the TTM (Tumor Therapy Manager) for Panendoscopy: Results of Workflow Analysis of the Panendoscopy and the Documentation Process with or without the TTM. In: 8th International Conference on Head and Neck Cancer 2012, Toronto, Canada.

