

Different approaches to volume assessment of lymph nodes in CT Scans of HNSCC in comparison with a real gold standard

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Abstract:

Objectives:

Volume assessment in head and neck squamous cell carcinoma (HNSCC) becomes an increasing important clinical parameter in treatment planning and response control. Various authors showed a significant impact of tumor volume on outcome and local control. In this study we compared the “gold standard”, the diameter based approach, with segmentation based approaches

Methods:

The segmentations were based on CT scans of 4 patients with HNSCC undergoing neck dissection as part of their treatment. These scans were taken during staging and a total of 20 lymph nodes were segmented. They were selected by size and location close to reproducible anatomical structures. The true volumes were measured by water displacement.

Results:

Pearson's correlation index shows a higher correlation of the diameter generated volumes ($r=0.723$) than results generated via segmentation ($r=0.527$) with the true volumes. Nonetheless diameter generated volumes show clearly too high volumes at 146.8% (Confidence Interval: 115.8% – 186.1%). Volumes generated with the segmentation are at 116.5% (Confidence Interval: 93.9% – 144.7%).

Conclusions:

The data show a higher reliability of volumes estimated by the segmentation based approach than the widely used diameter based approach.

Keywords: Tumor Volume, Segmentation, DeLOS, Response, HNSCC

Purpose

The entity of head and neck squamous cell cancer (HNSCC) is showing a worldwide clearly rising incidence [1]. It was shown, that the existence of lymph node metastasis in HNSCC has a significant impact on the survival rate [2]. The 5 year survival rate of patients with HNSCC without nodal metastasis is 73%, dropping to 50% in case of positive nodes without extra capsular spread and even further down to 30% in case of extra capsular spread. The overall survival rate of patients in Europe is 40% and has remained unchanged in the years 1983 until 1994 according to the WHO [1].

In the past years tumor volume investigations have become a subject of increasing interest. The improved quality of radiological images, last but not least due to thin sliced spiral computed tomography (CT) scans, as well as post processing of these pictures have made the volume determination from these sources possible [15]. The general impact of tumor volume on treatment outcome has been shown in various studies [3,4,5,6,7,13]. Some authors also propose a recognition of tumor volume estimations in the TNM staging systems [14,6]. Unfortunately there are no widely used systems or methods with the necessary reliability for tumor volume measurement in HNSCC. Following the lack of such a system there is also no standard in volume assessment.

At the moment it is common practice to follow up lesion extensions as described by the RECIST criteria [8]. Here the largest diameters of initially chosen lesions are being compared along the treatment. Graser et al. could show a higher grade of accuracy for the perimeter based method in comparison to the RECIST criteria [9]. Sorensen et al. [10] could show that the interreader and intrareader variability could be reduced with the perimeter method, hence suggesting that

a higher accuracy in response measurement can be achieved. Based on a performed literature review in pubmed we couldn't find any studies to directly compare the preoperatively determined volume with the real volume of the excised specimen.

The aim of this study therefore is to compare the real volume of a lesion as obtained by using a real gold standard with volume data gained by the diameter based method as well as with perimeter based method. Based on the rising number of studies on primary conservative treatment, like the GermanDeLOS II study, new treatment and outcome monitoring tools should be developed - such focusing on the increasing hardware and software capabilities.

Methods

After completion of the necessary staging examinations and after the histological confirmed tumor diagnosis, the indication for surgical treatment including neck dissection was set by an experienced consultant. This treatment option was discussed, specified and agreed in the tumor board. In all included cases, the surgical procedure applied included at least one neck dissection as part of the overall treatment. Based on the CT scans, two segmentation approaches were performed to facilitate planning of the surgical treatment by selective neck dissection and allowed to make comparison of the data with the real volumes (see below).

After obtaining informed consent from the patient, potential lymph nodes in the CT scans of the neck were selected to perform the investigations. These scans were part of the preliminary staging examinations, so that there was no additional exposure to radiation.

The lymph nodes included in the study have been selected due to their location close to surgical and anatomical landmarks. Such was done to help the surgeon with intra operative recognition of the specific lymph nodes. One criterion for the selected lymph nodes was that they were suspect to be potentially local metastases and that they therefore were part of the anyway removed nodes. This assured avoidance of any unnecessarily performed additional surgical intervention. Another criterion was the size of the nodes included in this study. Taking into account that there is – due to the partial volume effect – an increasing inaccuracy by decreasing size [11], we specifically selected small lymph nodes below 1 cm of maximum diameter. The segmentation was done with the newly developed software “NeckSegmenter”. This software was developed by the visualization group at the University of Magdeburg.

With the assistance of an experienced head and neck radiologist, measurements were obtained by outlining the lymph nodes in each slice. In addition, segmentation of the landmark structures on the neck was performed. The landmark structures segmented included the sternocleidomastoid muscle, the common, internal and external carotid artery, the jugular and facial veins, the hyoid bone, the thyroid cartilage, the cricoids cartilage as well as the major branches of the carotid arteries. For higher accuracy reasons there was no interpolation performed during segmentation. Following the outlining process, the datasets were used to generate a 3D model of the lymph node by the second software called the “Tumor Therapy Manager”. Here the virtual volume could be measured and the structures were visualized.

For comparison with the actual standard in volume assessment, the diameter based method, the three largest orthogonal diameters in every lesion were measured in the same dataset. The volume was then computed by using the formula for standard sphere volume:

$$V = 1/6 \pi (a * b * c) \quad (1)$$

During surgery, the surgeon had access to the 3D reconstruction of the patient neck to identify the selected lymph nodes. After identification and resection, the nodes were put in a transport medium and were brought directly to the laboratory. Any leftover surrounding connective tissue was removed by leaving the node capsule intact. After drying of the nodes we performed a volume measurement by using the water displacement method – according to Archimedes principle. In a previous work it could be shown that this is an accurate method for volume determination especially in irregular shaped and small objects [12].

The displaced volume was assessed using calibrated pipettes (Pipetman; Gilson, Inc., Middleton, WI). Additionally, the displaced water and as well the lymph nodes were weighed by use of Mettler's AJ150 (Mettler-Toledo GmbH, Gießen), an analytical microbalance (d=0.1 mg, e=1.0 mg) calibrated by the *Sächsische Landesamt für Mess- und Eichwesen* (validity until 2013).

Following this process the lymph nodes were further investigated and processed immediately by the department of pathology, and the results were integrated into the final pathological report for the patient.

Results

We analyzed the 20 lymph nodes of four patients with local metastases of their HNSCC. All patients were males, and their mean age was 57 years. Two of the patients underwent surgery because of oropharyngeal cancer of the tonsil, the others suffered from carcinoma of the larynx. After completion of the histological analysis two lymph nodes of the study specimens showed metastasis of the previously diagnosed carcinomas, while the other 18 lymph nodes were his-

tological free of metastasis. We initially selected 27 nodes in the diagnostic CT Scans. Seven of the segmented lymph nodes had to be removed from the final data set, since they could not be reliably detected and exactly localized and hence safely matched between CT scan and the surgical situs without doubt. The 20 remaining lymph nodes that were properly confirmed could be used for further analysis (see table 1).

Table 1 Characteristics of the HNSCC included in the study

Patient	Sex	TNM	Localization	Lymph Nodes analyzed [n]
1	M	pT 2 pN0 cM0	Oropharynx	5
2	M	pT 2 pN1 cM0	Oropharynx	6
3	M	pT4a pN2c cM0	Larynx	5
4	M	ypT1 pN2b cM0	Larynx	4

To compare the obtained results, the Pearson product-moment correlation coefficient (r) was used. This coefficient showed a higher correlation of the diameter generated volumes ($r=0.723$) than perimeter generated results ($r=0.527$) with the true volumes. Further analysis of the data showed a systematic over estimation of true volumes by the diameter generated volumes leading to a mean overestimation of about 50% (mean=146.8%; CI: 115.8%-186.61%). In comparison to that the mean volume difference between the true volumes and the perimeter based volumes was at 116.6% (Confidence Interval: 93.9% – 144.7%).

Conclusion:

The results presented show a higher reliability for the perimeter based volumes, although Pearson's r showed a higher correlation for the diameter based volume. Use of diameter-based volume assessment poses the risk of faulty interpretation of imaging data due to its systematic tendency of overestimation. This makes the diameter-based approach vulnerable and potentially can cause wrong treatment follow up. Contrary, the perimeter based approach shows values closer to the true volumes. However, in interpretation of the presented data one should take into account the relatively small size and therefore the even stronger impact of the partial volume effect. From our point of view, these results show the need for further studies and bigger sample sizes. Thus aiming last but not least to define clear levels of trust for different lesions and their extensions as well as providing new segmentation algorithms with a realistic test setup.

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