Automatic Sentinel Lymph Node Localization in Head and Neck Cancer Using a Coupled Shape Model Algorithm

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Abstract. The localization and analysis of the sentinel lymph node for patients diagnosed with cancer, has significant influence on the prognosis, outcome and treatment of the disease. We present a fully automatic approach to localize the sentinel lymph node and additional active nodes and determine their lymph node level on SPECT-CT data. This is a crucial prerequisite for the planning of radiation therapy or a surgical neck dissection. Our approach was evaluated on 17 lymph nodes. The detection rate of the lymph nodes was 94%; and 88% of the lymph nodes were correctly assigned to their corresponding lymph node level. The proposed algorithm targets a very important topic in clinical practice. The first results are already very promising. The next step has to be the evaluation on a larger data set.

Keywords: SPECT imaging · Sentinel lymph node detection · Lymph node level classification

1 Introduction

Every year, 600.000 new incidences of head and neck cancer are diagnosed with an annual patient death rate of 300.000 [11]. One of the most significant prognostic factors for the disease is the presence or absence of metastases in sentinel lymph nodes (SLN). Lymph nodes play a crucial role in the human immune system. In case a patient develops cancer, cancerous cells can be transported through the lymphatic system and finally infiltrate lymph nodes. From there the disease can further spread throughout the human body and infiltrate other lymph nodes or organs. These distant metastasis (m-staging) are within the most devastating prognosis for a patient. Any stage of the disease, even an early T1 or

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T2 staged cancer, is upstaged to stage 4, the worst possible classification, when a distant metastatis (M1) is diagnosed [8]. Therefore, the presence or absence of metastases within the SLN and other distant lymph nodes is one of the most significant prognostic factors in (Head and Neck) cancer.

In clinical practice different treatment approaches in head and neck cancer are followed, depending on the location and the stage of the disease. The most extreme forms of treatment are the *active waiting* and the *elective neck dissection* [12]. With the former approach repeated screenings of the patient are done, as long as it is not clear if a metastases has taken place. The idea is, to not expose the patient to a overtreatment. Later is the exact opposite. During an elective neck dissection all lymph nodes in the area around the metastatic lymph node are surgically removed. In many cases this leads to an overtreatment. On the other hand, studies have shown, that the overall survival rate is higher and the reoccurance rate of the tumor is lower [5]. In all cases, where not only the tumor, but the lymphatic system is treated as well, a localisation of the sentinel lymph node is crucial. In cases where a patient is treated with radiation therapy, a selective irradiation of the target volume of the lymph node area containing the SLN is practice by international clinical guidelines [3].

The detection of the sentinel lymph node can be achieved in different ways. One intervention uses blue dye, which is injected during surgery at the tumor site. The flow of the dye is observed and thereby the sentinel lymph node can be determined [4]. Another possible approach is the usage of SPECT-CT imaging to investigate a possible tumor spread. Currently, the common practice in clinical routine is to only visually inspect the SPECT-CT image data, the image data is not used for any further analysis.

In this paper we propose a novel method to fully automatically extract meta information about the patient's lymph nodes from the acquired SPECT and CT image data, which is useful for radiation therapy or a surgical neck dissection. After a short introduction of the methods of our approach (see Sect. 2), we describe the test setup and perform a quantitative evaluation on clinical data sets.

2 Methods

Our approach consists of three steps (although the CT-CT registration is optional). In the first step (Sect. 2.1) the lymph nodes are located within the CT image. The second step is an optional step (Sect. 2.2). If present, the SPECT-CT scan is registered to a planning CT scan with a higher resolution. The idea hereby is to use a higher resolution input for the third step. As the third step (Sect. 2.3), we use our coupled shape model algorithm (CoSMo [6]) to automatically detect the lymph node levels in the head and neck region. The lymph nodes located on the SPECT image data are then mapped to the lymph node levels determined by CoSMo. All of these steps are run without any user interaction and provide the clinician with the lymph node levels of all active nodes and can be used for further clinical procedures (Fig. 1).

Fig. 1. The figure on the left side, shows which input is needed for the algorithm and what output it produces. The figure on the right visualizes the workflow of the lymph node localization process.

2.1 Lymph Node Localisation

Compared to CT image data, where the intensity values are already normalized by protocol, the SPECT image intensity values we observed were in range: [0, 65000]. After further observation it became clear, that no assumptions could be made about the intensity values of active lymph nodes, because there was a noticeable variance between different patients and different lymph nodes. Besides the obvious reason of different machines used for the acquisition of the scans, one of the reasons presumably is the fact that the intensity value of a lymph node depends on the uptake of the radioactive tracer and the time between the injection of the tracer and the image acquisition. But, not only the significant difference in intensity values yields a problem for an analysis, the huge amount of noise is an additional problem. As a result it can be considered that it is completely unfeasible to define a narrow intensity intervall beforehand wherein the lymph nodes reside.

We have designed a top-down approach to iteratively extract the active lymph nodes from the SPECT data. We generate a labelmap [7] of the SPECT image with a lower threshold t_i. Where $i \in [1, 10]$ and s_{max} is the maximum intensity value of the SPECT image data.

$$t_i = 10 * \sqrt{\frac{s_{max}}{i}} \tag{1}$$

Within each iteration all labels are extracted from the label map. The 'hottest' structures always represents the tumor, while the others are considered as lymph nodes. It has been shown, that the monitoring of the 3 or 4 hottest nodes is sufficient for a correct staging [2]. So we are only interested in up to 4 active lymph nodes and for this reason we have added another termination condition, we automatically stop once we have found 4 active nodes,

2.2 Spect-CT - CT Registration

We added an additional optional step to the algorithm. In case a higher resolution planning CT is present (a radiation therapy planning CT), this can be used for

CoSMo adaptation. Since the SPECT-CT and the higher resolution CT are acquired by different machines, these images are not aligned. To transfer the information from the SPECT to the higher resolution CT a registration between the CT of the SPECT and the highres CT is required. The image data we received was taken using a fixation mask, resulting in a negligible amount of deformation between the two different CT image data sets. Therefore, for this scenario a rigid registration method is absolutely sufficient. If a deformation between the CT data sets is present, a more sophisticated approach has to be used. For this task an approach using CoSMo, described in [10], could be used for a deformable image registration. A mean-squared error metric and a gradient descent optimizer were used for the registration process (Fig. 2).

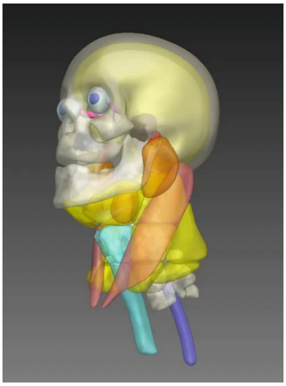

Fig. 2. CoSMo: Visualization of the mean model

2.3 CoSMo Adaptation

CoSMo is a model trained from clinically annotated data sets. Hereby, a statistical representation for every item of interest is obtained. For items with low variance, a rigid model item is trained, which is a probability map plus an average intensity image (for more in depth information see [9]). Structures with high variance are represented as deformable shape models. The model not only trains the possible deformations of the unique items, but how an item deforms, translates and rotates in correspondance to the other items and the complete model.

The adaptation step is divided into several levels. The structures which are best distinguishable within the data set are adapted first, while the structures with the lowest visible contrast, are adapted last. That way first, the model is initialized by locating the skull within the image data. Then, the bone structures are adapted. Next different muscles and glands, the eyes and the brain are adapted. And finally, the adaptation of the lymph node levels is executed. As output, a separate segmentation for each structure of the model is generated. For more in detail information on the process refer to [6].

2.4 Lymph Node Level Determination

The acquired lymph nodes in the CT image data and the segmented lymph node regions from CoSMo are finally combined to extract the lymph node levels of the sentinel lymph node and the active lymph nodes. To determine the lymph node level of a detected lymph node a nearest neighbour search with all lymph node levels retrieved from CoSMo is run. Since the SPECT activity for a lymph node sometimes only occupies one or two voxel within the image data, it might be possible that it does not directly overlap with a lymph node region but resides directly next to one. Therefore, the nearest neighbour algorithm was favored over an overlap metric.

As a result the clinician receives all lymph node levels with active nodes, that should be considered during the radiation therapy planning or surgical neck dissection.

3 Evaluation

The test setup for the evaluation was as follows. Three data sets from patients of Università degli studi di Parma (Italy) and four data sets from Clinique et Maternité Sainte-Elisabeth Namur (Belgium) were used. The data sets from the hospital in Italy consisted of a SPECT-CT and the data sets from the hospital in Belgium SPECT-CT and a radiation therapy planning CT. In addition, we received the information about the number of active nodes and their lymph node level from a clinical expert from each of the centers. This information was used as ground truth and was compared with the output of our algorithm. In total, 17 lymph nodes have been identified by the clinical experts within the 7 patient data sets. The goal was to detect these lymph nodes correctly in the CT data set and match them to their corresponding lymph node level. Table 1 represents the results of the evaluation. The second column contains the found structures. The third column lists how the found structures have been classified (either LN level 1–5 left/right or as an artifact). The last column lists the ground truth lymph node level obtained by a clinical expert. In addition Fig. 3 shows the result of such a detection.

For six out of seven patients all lymph nodes have been detected and located in the image data correctly. For patient 4 only one lymph node in Level II left was detected, although the clinical experts counted two. Visual inspectation of the image data revealed, that the two lymph nodes are located extremly close to each other and the algorithm considers them as one lymph node. Although, this is not the desired output of the algorithm, it is negligible in clinical practice, because an active node has been located in this lymph node level. For radiation therapy or a neck dissection, the complete lymph node level is treated no matter if one or two lymph nodes have been detected. Three times, an activity was detected, that afterwards was correctly classified as an artifact. Only one lymph node was not classified accordingly (Patient 3 lymph node 3). The lymph node was considered as an artifact, although it was a retropharyngeal lymph node.

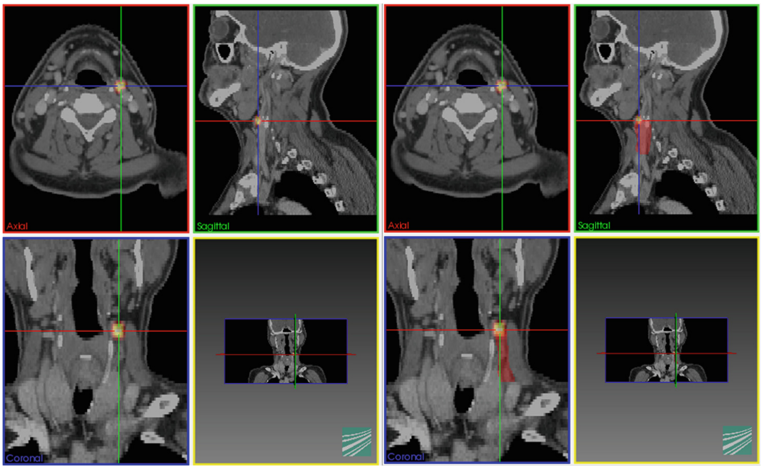

Fig. 3. Visualization of the second lymph node of patient 3 (left) and the overlay with lymph node level III left (right).

Table 1. Comparison of the detected active lymph node levels' with their ground truth

Patient #	Found lymph node #	Classified lymph node Level	Ground truth level
1	1 & 3	Level II left	Level II left (2 SLNs)
	2	Level II right	Level II right
	-	Artifact	-
2	1	Level II right	Level II right (1 SLN)
	2	Level II left	Level II left (1 SLN)
	-	Artifact	-
3	1	Level II left	Level II left (1 SLN)
	2	Level III left	Level III left(1 SLN)
	-	Artifact	Retropharyngeal
4	1	Level II left	Level II left (2 SLNs)
	2	Level II right	Level II right (1 SLN)
5	1	Level III left	Level III left (1 SLN)
	-	Artifact	-
	3	Level III right	Level III right (1 SLN)
6	1 & 3	Level III left	Level III left (2 SLNs)
	2	Level Ib left	Level Ib left (1 SLN)
7	1	Level II left	Level II left (1 SLN)
	2	Level III left	Level III left (1 SLN)

The reason for this misclassification is, that CoSMo only contains the lymph node level I - V left/right and not the Retropharyngeal area.

The runtime for the approach is the following. The duration for the SPECT detection is neglectable, it is around 1 s. CoSMo adaptation takes around 4 min and the SPECT-CT to CT registration takes around 1 min.

4 Conclusion

We have presented a novel approach to automatically extract additional information from SPECT-CT image data. The complete approach does not need any user interaction at all and can be run in background, before the image data is visually inspected by a clinical expert. The additional information obtained by our algorithm can be helpful in clinical practice for the planning of a surgical neck dissection or radiation therapy planning.

The algorithm has been evaluated on seven different patients and 17 lymph nodes have been inspected. 15 out of the 17 have been matched correctly. In one case two lymph nodes have been detected as one. In the other case the lymph node could not be matched properly because CoSMo currently does include the lymph node level (Retropharyngeal) in which the lymph node is located. As future work, additional lymph node levels could be included into CoSMo to match all needed lymph node levels. Finally, the approach has to be evaluated on a larger data set, to improve the statistical relevance of the evaluation result.

Recently, a new tracer has been presented, which primarily focuses on sentinel lymph nodes [1]. It rapidly clears out the tumor but remains in the lymph nodes. A consequence would be a better contrast for the nodes since the images would be free from the ‘shine through effect’. This should greatly enhance the quality of the acquired data and thereby ease the processing by the algorithm. As a future work it would be very interesting, to acquire images with the new tracer and evaluate the approach on these.

In addition, it would be very interesting to evaluate if the proposed approach is suitable for PET imaging as well. Due to its similar nature, it should be feasible to use the algorithm on PET data as well, with some minor modifications.

The proposed algorithm is able to support radiation and surgical oncologists in their daily clinical routine. The approach features a fully automatic, fast and promising robust method to detect SLNs in the head and neck area and determine their corresponding lymph node levels.

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