Single Institute Experience with the Use of ConPaS Technique for the Treatment of Head and Neck Cancer

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Abstract: *Aim*: In the complex therapy of head neck cancers modern 3D based radiotherapy plays an important role. The parotid sparing effect of intensity modulated radiotherapy is proven, but in many patients the conventional 3D based techniques are still being used. Since 2006 the "Conpas" technique has been routinely used in our institution for the treatment of locally advanced head neck tumor patients. The aim of our study was to analyze the dosimetry, survival and side effect profile of this 3D based treatment modality.

Patient and Methods: Between 01.07.2006 and 31.11.2008 a total of 83 patients were treated using this technique. An elective dose of 50,4 Gy was prescribed to the primary tumor and the bilateral neck node regions, followed by a simple two field boost to the primary tumor region (up to 70Gy). We retrospectively analyzed the following factors related to this method: dosimetry profile (PTV and OR doses, focusing on parotid gland doses), clinical responses, local and distant progression free survival profile, acute and late side effects.

Results: The mean dose of primary tumors was 71.98 Gy, the elective region dose of 50.4 Gy was achieved in all cases. Following the treatment in 37 patients complete clinical response in 25 cases partial response in 5 cases stable disease and in 16 cases progressive disease was registered. The mean overall survival was 30,06 months, the mean disease free survival was 25,82 months. When reporting the superficial lobe volumes in "lower" tumor locations good mean parotid doses were achieved (25.3 Gy and 23.4 Gy). Comparing the acute side effect profiles in the "upper" localized group higher rate of Grade III xerostomia (21% *vs*. 2%, p≤0.05) and dermatitis (27% *vs*. 6%, p≤0.05) were observed compared to "lower" localization group. In the "upper" localized group the late xerostomia (grade 2-3) rate was also higher (8% *vs*. 0%, p≤0.05).

Conclusion: Based on our experience Conpas technique is feasible technique for treatment of advanced head neck cancer patients. Our clinical outcome, dosimetry and follow up results show that this technique should be used successfully in patients with "lower" localized primer tumor sites. High attention should be addressed when reporting parotid doses.

Keywords: Head-neck, 3D based radiotherapy, Conpas, parotid sparing, survival, side effect.

INTRODUCTION

Concurrent radio/chemotherapy is considered as a standard of care for locally advanced head and neck cancer (LAHNC). However treatment of the patient group is a complex and difficult clinical challenge. Nowadays, high dose conformal radiotherapy and combined chemo-radiotherapy have an important role in the complex therapy of these diseases [1,2]. The delivery of high doses of conformal radiation to high risk regions while limiting dose to lower risk regions and critical structures is a serious technical problem [3,4]. The need of high dose and big treatment field size result in serious side effects (xerostomia, swallowing problems, dermatitis etc.), especially in case of combined modalities [6,7]. Conformal techniques with different beam directions are needed to reach acceptable coverage of the PTV (planning target volume) and to allow sparing of the parotids and other organs at risk. Even though the use of intensity-modulated radiotherapy (IMRT) in the treatment of the head and neck region has been increasing in popularity over the last decade [8,9,10]. However IMRT is still not available for daily use in many, less economical European and the developing countries.

There are few parotid-sparing techniques without beam-intensity modulation described in the literature [5]. The 3D Conformal Parotid Sparing (Conpas) method, presented by Wiggenraad et al in 2005, could provide a non-IMRT method to spare the parotid glands [13]. In our institution ConPas technique has been used routinely since 2006.

The primary aim of our study was to analyze the clinical efficacy and toxicity achieved with Conpas technique in terms of the loco regional control, clinical response rates and progression free survival. The dosimetry aspects related to this method were analyzed with high attention to parotid gland doses.

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The acute and late side effect profile (xerostomia, swallowing, taste feeling, dermatitis, mucositis) were also studied and reported.

PATIENT AND METHODS

Between 01.07.2006 and 31.11.2008, a total of 83 patients treated with the Conpas technique were enrolled to the study. Based on the tumor localization we have stratified the patients into two groups in function of the localization of the primaries in the head and neck region: ”upper”- and ”lower” situated cancers. The border between “upper” and “lower” localization was defined in accordance with a radiologist specialist the level of tongue base. Patient and tumor characteristics are shown in Table **1**.

Table1: Patient Characteristics

Patient Number	
male	n=72 (86%)
female	n=11 (14%)
Age	
average	61.5
median	56
range	41-76
Primer Tumor Localization	
“upper”	n=38 (46%)
“lower”	n=45 (54%)
Tumor Stage	
Stage IIb	n=13 (15.5%)
Stage III	n=17 (20.5%)
Stage IVa	n=48 (58%)
Stage IVb	n=5 (6%)
Chemotherapy	
Induction CR	n=10 (12%)
CRT	n=22 (26.5%)
Image Fusion	
CT-MR based	n=33
CT-PET based	n=3

Patient Immobilization and CT Scanning

For patient immobilization thermoplastic mask fixation (ORFIT) was used. Tongue wedge was used in oral cavity cases. For planning purposes non-contrast CT scans were performed with a multi slice CT scanner (SIEMENS Somatom Sensation 16), with continuous slice thickness of 5 mm with 2-mm interspaces.

Target Definition

Tumor, target and organ at risk (OAR) volumes were delineated on CT slices. Target volume definition was based on the findings of the clinical examination, fiberoscopy and contrast-injected head and neck CT in all cases. In MR (33 pts.) and/or PET/CT (3pts) were used to help target volume definition. In case of definitive RT, the planning target volume (PTV) encompassed the known primary gross tumor volume (GTV) and positive lymph nodes (GTV nodal) as well as elective volumes without clinical involvement. Clinical target volumes (CTV) for subclinical disease were defined based on the locations of the nodal station as described by Gregoire *et al.* [14]. The high risk treatment volume (PTV boost) encompassed the gross disease (primer tumor & positive nodes). The spinal cord, brainstem, brain, brainstem eyes, optic nerves, salivary glands and oral cavity were defined as organs at risk. For the definition of the parotids two type of delineations were made: superficial lobe only and whole parotid gland [22,25].

Dose Prescription, Planning Process

The ConPas techniques planning procedure is as follows: to begin with, the isocenter is placed in the anterior part of the vertebral body halfway between the upper and lower limits of the PTV. Then, both oblique posterior beams are set up and turned into half-beams by closing the collimators on the side of the spinal cord. These two half-beams are the most important components in ConPas with respect to parotid sparing. Initially beam angles of 220° and 140°, are used respectively. In the beam’s eye view mode the angles may be modified slightly, so that maximal blocking of the parotid glands is possible, while preserving adequate coverage of the PTV. Then, the two oblique anterior beams are set up and turned into half-beams by closing the collimators that are off the side [13].

However some modification was added to improve the quality of the plans. This comprising of a special field distribution in cases when the U-shaped planning target volume (PTV) is localized around the spinal cord. In our further developed 6 (sometimes 5) field technique, two pairs of parallel opposed - complementing fields are combined with two complementing fields from the AP direction. In a few cases, the two complementing fields were substituted with an AP field.

Consequently we performed boost irradiation with a relatively simple two-field oblique, wedged technique maintaining high GTV conformality, yet sparing the spinal cord.

For the definitive treatments 50.4 Gy was prescribed in 28 fractions to PTV elective, followed by 19.8 Gy boost to the primary

Patient Follow Up, Side Effect Analysis

During the treatment patient follow up schedule was made in accordance with our Institutional protocol. Once a week all treated patients were controlled (physical head-neck examination). The acute side effect registration and grading was based on the criteria of the "Common Terminology Criteria for Adverse Events" (CTCAE) v.3.0. [11]. The body weight changes (in kg) were controlled weekly. Following the treatment the first follow up was made on the 4^{th} or 5^{th} week, followed by every 3 months (physical examination and imaging CT-MR). Late side effects were recorded according to the radiation therapy oncology group (RTOG) xerostomia, dental and taste feeling problems were registered [12].

Statistical Analysis

For evaluating the data, unpaired T-test was used (Microsoft Excell 2010). When comparing the data series, the mean values were confronted in all cases and, during evaluation, a significance level of $p \leq 0.05$ was considered to be a significant difference.

RESULTS

The follow up period was closed at 30.11.2013 (follow time was 80 months, mean: 27.17 median: 17, SD: 22.15, range: 2-83). Following the treatment in 37 patients complete clinical response (CR- 40%), in 25 cases partial response (PR-30%), in 5 cases stable disease (SD-7%) and in 16 cases progressive disease (PD-23%) was registered in the six-week control (based on physical examination and CT and results MRI- Table **2**).

The mean OS (overall survival) was 30.06 months (median: 17, SD: 27.65, range: 2-83). The mean DFS (disease free survival) was 25.82 months (median: 13, SD: 29.73, range 0-83). When closing the follow up period 28 patients are tumor free and alive (34%- crude rate), 55 patients died (66%- crude rate). In 46 cases local recurrence, in 22 cases distant metastases were recorded (in 13 patients both).

The mean dose of primary tumors was 71.98 Gy, the elective region dose of 50.4 Gy was achieved in all cases. When reporting parotid doses we compared the volume and dose results of parotid glands according to localizations (upper and lower localized primer tumor) and different contouring methods (superficial lobe only, and the whole volume). The mean left parotid whole volume was 22.7 ccm (median 20.63, SD: 9.41), the mean left parotid superficial volume was 14.43 ccm (median 12.38, SD: 7.33). The mean right parotid whole volume was 22.85 ccm (median 21.38, SD: 9.41), the mean right parotid superficial volume was 15.47 ccm (median 13.75, SD: 7.3).

Table 2: Dose Characteristics, Treatment Data, Clinical Outcomes and Sites of Recurrences. *Clinical Responses Based on the First Post Treatment Follow up Examination (CT/MR/physical Examination).

Radiotherapy doses in Gy (mean, median, SD)	
PTV (elective dose)	52.2 (52.11; 0.79)
PTV2 (primary tumor+involved nodal areas)	71.98 (73.68; 4.31)
Maximum spinal cord dose	41.75 (41.88; 2.34)
Nasal cavity dose	27.57 (26.18; 16.25)
Oral cavity dose	59.65 (59.77; 9.24)
Treatment interruption	n=15
mean/median/range (days)	6/10/2-16
Body weight Changes in kg	
Total (mean, median, SD)	-5.46 (-5, 3.92)
Patients with PEG (mean)	-3.375
Clinical response*	
Complete clinical response (CR)	n=37 (39.8%)
Partial clinical response (PR)	n=25 (30.2%)
Stable disease (SD)	n=6 (7.2%)
Progressive disease (PD)	n=15 (22.8%)
Site of recurrence	
Local failure	n=33 (40%)
Distant metastasis	n=21 (25%)
Both	N=9

When reporting the superficial lobe volumes in "lower" tumor locations good mean parotid doses were achieved (25.3 Gy-mean left and 23.4 Gy-mean right) compared both to superficial lobe volumes in "upper" tumor localizations and whole volume doses in both localization groups (see Table **3**).

Comparing the acute side effect profiles in the "upper" localized group higher rate of Grade III xerostomia (21% *vs*. 2%, $p \leq 0.05$) and dermatitis (27% *vs*. 6%, $p \leq 0.05$) were observed compared to "lower"

Table 3: Detailed Data for Parotid Doses and Volumes. The Grouping was made According Localizations (Mid and Lower Rows) and the Different Contouring Methods (Superficial and Total Volumes)

all regions	mean left parotid dose (total volume)	mean left parotid dose (surface lobe)	mean right parotid dose (total volume)	mean right parotid dose (surface lobe)	left parotid ccm (total volume)	left parotid ccm (superficial lobe)	right parotid ccm (total volume)	right parotid ccm (superficial lobe)
Mean	40.48	36.97	39.10	33.82	22.70	14.43	22.85	15.47
Median	39.31	35.34	38.81	33.90	20.63	12.38	21.38	13.75
SD	11.70	12.34	9.97	10.76	9.41	7.33	9.41	7.30
"upper" localization n = 34	**mean left parotid dose (total volume)**	**mean left parotid dose (surface lobe)**	**mean right parotid dose (total volume)**	**mean right parotid dose (surface lobe)**	**left parotid ccm (total volume)**	**left parotid ccm (superficial lobe)**	**right parotid ccm (total volume)**	**right parotid ccm (superficial lobe)**
Mean	52.08	40.36	49.43	38.27	22.52	15.01	22.04	15.62
Median	51.71	39.73	47.17	37.20	21.38	14.00	21.82	13.88
SD	9.37	10.86	7.59	8.42	7.89	6.71	8.85	7.06
"lower" localization n = 34	**mean left parotid dose (total volume)**	**mean left parotid dose (surface lobe)**	**mean right parotid dose (total volume)**	**mean right parotid dose (surface lobe)**	**left parotid ccm (total volume)**	**left parotid ccm (superficial lobe)**	**right parotid ccm (total volume)**	**right parotid ccm (superficial lobe)**
Mean	30.71	25.34	28.15	23.43	22.86	14.04	23.57	15.36
Median	29.85	26.17	27.00	24.08	19.76	11.63	21.32	13.25
SD	7.24	12.03	6.82	11.61	10.48	7.77	9.71	7.52

Table 4: Acute side effects according to primer tumor sites. Significant differences (at level of p≤0.05) were signed with bold marks. For side effect reporting the "Common Terminology Criteria for Adverse Events" (CTCAE) v.3.0. was used.

Acute Side effects					
"upper" localization n=34	***Grade 0***	***Grade I***	***Grade II***	***Grade III***	***Grade IV***
Mucositis	1 (3%)	10 (29%)	17 (50%)	6 (18%)	0
Dysphagia	8 (24%)	14 (41%)	12 (35%)	0	0
Dermatitis	3 (9%)	11 (32%)	11 (32%)	**9 (27%)**	0
Taste feeling	5 (15%)	17 (50%)	12 (35%)	0	0
xerostomia	5 (15%)	16 (47%)	6 (17%)	**7 (21%)**	0
"lower" localization n=49	***Grade 0***	***Grade I***	***Grade II***	***Grade III***	***Grade IV***
Mucositis	1 (2%)	15 (31%)	27 (55%)	6 (12%)	0
Dysphagia	7 (15%)	21 (42.5%)	20 (40.5%)	1 (2%)	0
Dermatitis	6 (12%)	15 (31%)	25 (51%)	3 (6%)	0
Taste feeling	16 (32%)	21 (44%)	10 (20%)	2 (4%)	0
xerostomia	13 (27%)	20 (40%)	15 (31%)	1 (2%)	0

localization group (Table **4**). In the late side effect profile xerostomia was the leading problem. In the "upper" localized group the late xerosotmia (grade 2-3) rate was also higher (8% *vs*. 0%, p≤0.05) (Table **5**).

DISCUSSION

The complex therapy of locally advanced head and neck cancers is a great challenge for both patients and clinicians. During the radiation therapy serious side effects occur, especially in case of combined therapies (radiotherapy with chemotherapy). Unfortunately, many of the advances in improving the cure rate of head and neck cancer with radiotherapy, such as altered fractionation and the addition of chemotherapy, have resulted in increasing toxicity [1,15,16]. Xerostomia is one of the most common side effects, which may

Table 5: Late side effects according to primer tumor sites. Significant differences (at level of p≤0.05) were signed with bold mark. For side effect reporting the RTOG scoring system was used.

Late side effects					
"upper" localization n=34	***Grade 0***	***Grade I***	***Grade II***	***Grade III***	***Grade IV***
xerostomia	9 (27%)	15 (44%)	7 (21%)	**3 (8%)**	0
Taste feeling	22 (64%)	8 (24%)	4 (12%)	0	0
"lower" localization n=49	***Grade 0***	***Grade I***	***Grade II***	***Grade III***	***Grade IV***
xerostomia	19 (39.5%)	20 (40.5%)	10 (20%)	0	0
Taste feeling	29 (59%)	17 (35%)	3 (6%)	0	0

severely impair the quality of the life of patients with head-and-neck cancer, who have been irradiated [17].

In the available literature, not many 3-D conformal (non-IMRT) techniques for head-and-neck cancer that aim at parotid sparing are described. Sparing of parotid gland is the objective of some conformal techniques which are mostly applied in patients with oropharyngeal cancers [20, 21]. The Conpas technique was published by Wiggenraad *et al.* in 2005. This new parotid sparing technique was designed as an alternative treatment method to IMRT in the treatment of head-neck cancer patients. The use of the conformal parotid-sparing technique Conpas leads to a significant decrease of the mean dose in both parotid glands, when elective radiotherapy of up to 50.4 Gy is given to the neck nodes.

Based on the advantages of the IMRT which are widely discussed in the available literature [19,23,24], IMRT can be ideally used for sparing of the parotid glands. Small phase 2 studies have already shown that low parotid doses achievable with IMRT (24-26 Gy) aids recovery of saliva flow [26]. The real benefits in parotid-sparing effects were reported mostly in the nasopharyngeal region. Pow *et al.* reported their experiences in early stage nasopharyngeal cancer patients. According to their results in terms of parotid sparing and quality of life, significant benefits were achieved using IMRT technique [23]. Kam and colleagues [27] reported a reduction in observer-rated severe xerostomia (RTOG grade 2 or worse) with IMRT (39% *vs*. 82%; p=0.001) in 60 patients with early-stage nasopharyngeal cancer. The study of Nutting *et al*. (PARSPORT study) provided a randomized, controlled data establishing the additional benefit of IMRT *vs*. conventional 3D therapy in head neck tumors other than the nasopharynx [24]. They compared the conventional 3D technique to IMRT in oropharyngeal (n=40) and hypopharyngeal (n=7) localizations. The reported mean parotid doses were 61 *vs*. 25.4 Gy (conventional *vs*. IMRT) in case of contralateral and 60 *vs*. 47.6 Gy in ipsilateral parotid doses.

When comparing our results to this study our Conpas mean parotid doses were higher than the reported IMRT doses. There are several reason for this: first is the difference in the nature of the two techniques, second the majority of our patients were in an more advanced stage (parotid glands involved in the high dose area), thirdly the mean dose to tumor and involved nodes was higher in our patient group (72 *vs*. 65).

The fourth but really important influencing factor is the question of reporting the parotid dose. The “Practical Essentials of Intensity Modulated Radiation Therapy” IMRT handbook [22] recommends to contour just the surface lobe of the gland (see page 146, figure 9-8- [22]), on the other hand the guidelines used for the PARSPORT study recommends to contour the whole volume (figure 1- [25]). As it may be observed on Table **2** major differences appears even in volumes and doses of the parotid glands. In our daily practice we use the whole parotid volumes.

The Conpas technique has been implemented into the daily routine at our institution following a 6-month learning curve. Based on our experience, through precise patient selection and adherence to the optimal immobilization method, the planning process and the treatment result in moderate time consumption for the treatment staff. The acute side effects of the treatments were manageable and comparable to the reported literature results. Treatment interruptions are most likely to occur in the event of swallowing disturbance affecting the daily nutrition of the patients which may compromise the change of securing loco-regional control.

CONCLUSION

Based on our experience Conpas technique is feasible technique for treatment of advanced head-neck cancer patients. Our dosimetry and follow up results shows that this technique may be used successfully in patients with ”lower-neck” located primer tumor sites if there is no access to IMRT. With precise patient selection an acceptable side effect profile can be achieved with comparable survival results as found in the literature. High attention should be addressed when reporting parotid doses.

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