The evaluation of 3DRT and IMRT techniques in postoperative radiotherapy for thyroid medullary carcinoma

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SUMMARY

BACKGROUND: Radical surgical excision is the treatment of choice in all medullary thyroid carcinomas. External beam radiotherapy for medullary thyroid carcinoma is necessary in advanced cases. Unfortunately, a large volume of the head and neck region which has to be irradiated is close to critical structures such as the spinal cord, larynx, and parotid glands, which creates a challenge during radiotherapy planning.

AIM: The aim of the study is to compare IMRT and 3D plans of patients diagnosed with medullary thyroid carcinoma in terms of CTV coverage and normal tissue sparing.

MATERIALS AND METHODS: A 46-year-old woman with medullary thyroid carcinoma, stage pT4a N1b M0, underwent radical resection, followed by adjuvant radiotherapy to a total dose 60 Gy to the clinical target volume (CTV). Three plans were generated to irradiate the thyroid bed and regional lymph nodes. Two intensity-modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3DRT) plans were compared in terms of CTV coverage and organ at risk sparing.
RESULTS: Using the IMRT plans we achieved more homogeneous dose distribution with higher minimal dose and lower maximal dose in the target volume compared to 3DRT technique. Furthermore, mean and maximal dose to critical structures were lower when IMRT was applied compared to 3DRT.

CONCLUSIONS: IMRT results in improved dose distribution within CTV compared to 3DRT. With the IMRT plan it is also possible to reduce the dose to the organ at risk, especially the larynx, salivary glands and spinal cord.

KEY WORDS: medullary thyroid carcinoma, IMRT, 3DRT, postoperative radiotherapy

BACKGROUND

Five percent of thyroid malignancies are medullary carcinomas, which arise from parafollicular C cells. They are known to have relatively poor prognosis among thyroid cancer patients, and their survival rate is 80% [1–3]. The standard management is surgery, comprising a total thyroidectomy and central node dissection if the lymph nodes are thought to be involved. Selective lymph node dissection might be necessary if further lymph nodes are thought to be involved [4–6]. Radiotherapy is recommended in completely resected disease or as an adjuvant treatment in patients with lymph node metastases, when calcitonin level is high and there is no evidence of distant metastases [7, 8]. Radioisotope therapy, chemotherapy and other pharmacological treatments are delivered only individually in small groups of patients.

In thyroid cancer the dose to a volume at risk for microscopic disease is limited by the tolerance of critical structures such as spinal cord, salivary glands and larynx [3, 9]. It is difficult to deliver high, therapeutic doses of radiation to the thyroid gland or tumour bed and its multiple lymphatic draining (up toward the base of the skull and down to the upper mediastinum) without causing significant toxicity [9].

Recently, intensity-modulated radiation therapy (IMRT) has been implemented in therapy for head and neck patients [10, 11]. Theoretically IMRT creates a possibility to achieve better dose distribution by increasing dose to the target volume and simultaneously decreasing dose to the organ at risk. IMRT has been extensively investigated for many sites within the head and neck, but studies on IMRT in thyroid cancer are scarce. This creates the rationale for the present study [3, 12–16].

AIM

The aim of the study is to compare IMRT and 3D plans of patients diagnosed with medullary thyroid carcinoma in terms of CTV coverage and normal tissue sparing.

MATERIAL AND METHODS

A 46-year-old woman was diagnosed with medullary thyroid carcinoma. Clinical examination and all diagnostic procedures such as computed tomography, X-ray and ultrasound revealed enlarged thyroid with multiple tumours and enlarged bilateral cervical lymph nodes. Radical thyroid excisions with excision of cervical lymph nodes were performed. The histopathological stage was pT4a N1b M0 due to extracapsular and tracheal invasion, size of tumour 6 x 5 x 3 cm, and 5 cervical lymph node metastases. Postoperative calcitonin level was 510.5 pg/ml. There was no evidence of distant metastases. Therefore, the patient was referred to the radiotherapy department for further treatment.

The patient was immobilized with a thermoplastic mask, and planning CT scan of neck and upper thorax was performed. Clinical target volume (CTV) based on CT as well as organs at risk in the head and neck region were delineated. CTV consisted of the tumour bed with margins in all directions and cervical, retropharyngeal and upper mediastinal lymph nodes. Supraclavicular nodes were delineated and denoted as CTV2. A 5 mm margin was added to CTV and CTV2 to create PTV. The target and critical structures were defined and contoured for the CadPlan-Helios treatment planning system.

Two intensity modulated plans (IMRT) were prepared. The first was arranged using 5-field technique and 6-MV photon beam (5-field IMRT), and the second using 9-field technique and 6-MV photon beam (9-field IMRT). A 3-dimensional radiotherapy plan (3DRT) was also created. A 3DRT plan comprised two parts. The first part was arranged using 3-field technique and 6-MV photon beam; the prescribed dose to the CTV and CTV2 was 44 Gy. The second part involved the use of 4-field technique and 6-MV photon beam combined with 2 fields and 9 MeV electron beams; the prescribed dose to the CTV and CTV2 was 16 Gy. For all plans dose volume histograms, minimum, maximum and mean doses were calculated (Table 1). CTV and CTV2 were irradiated to a total dose of 60 Gy in 2 Gy per fraction per day, over 6 weeks using a Varian Clinac 2300 accelerator. Toxicity was monitored weekly during radiotherapy.

RESULTS

In our study better dose distribution in CTV and CTV2 was achieved with IMRT technique than with 3DRT technique. Transversal, median and coronal dose distribution for complete 3DRT technique is shown in Figure 1 a, c, e and for IMRT technique is shown in Figure 1 b, d, f. All mean doses to the CTV, CTV2 and critical structures with minimum and maximum are shown in Table 1.

The mean CTV dose was similar in all techniques (9-field IMRT - 59.8 Gy, 5-field IMRT - 60.2 Gy vs 3DRT - 60.3 Gy). However, using IMRT technique higher minimum and lower maximum dose was delivered compared to 3DRT technique (Table 1). In supraclavicular nodes (CTV2) mean dose distribution was more homogeneous in IMRT (60.3 Gy, 60.8 Gy vs 57.6 Gy); furthermore, higher minimum and lower maximum was achieved with both IMRT techniques compared to 3DRT (Table 1).

Most profitable in terms of critical structures sparing were parotid glands and larynx. The difference between 9-field IMRT and 3DRT in mean dose to the larynx was 6.4 Gy. Also lower minimum (43.1 Gy vs 59.1 Gy) and maximum larynx dose (60.8 Gy vs 63.2 Gy) was achieved with 9-field IMTR compared to 3DRT. The biggest difference in mean dose to the organ at risk between these two techniques was found in the left parotid (13.9 Gy); for the right parotid the difference in mean dose was smaller (9 Gy). Maximum dose to the left and right parotid did not differ between IMRT and 3DRT, since part of the parotids is located close to the CTV. In contrast, both minimum parotid doses were much lower in 9-field IMRT (Table 1).

The spinal cord was irradiated to tolerance by all three techniques. With 9-field IMRT we were able to decrease maximum spinal cord dose by 2.6 Gy. Mean and minimal dose were similar compared to 3DRT.

For the actual treatment the 9-field IMRT plan was chosen. Treatment was well tolerated by the patient, who suffered from a mild skin reaction, dysphagia, with small changes in the diet and pain controlled with local analgesics.

Table 1.

	3DRT	5-field- IMRT	9-field- IMRT
	D mean (min / max)	D mean (min / max)	D mean (min / max)
CTV	60.3 (43.9 / 66.2)	60.2 (55.4 / 64)	59.8 (56.5 / 62,.9)
CTV2	57.6 (40.9 / 65.7)	60.8 (58.6 / 62.4)	60.3 (58.1 / 61.8)
Larynx	61.4 (59.1 / 63.2)	54.0 (46.2 / 61.1)	54.0 (43.1 / 60.8)
Spinal cord	27.0 (0.5 / 46.8)	27.1 (0.3 / 44.9)	28.5 (0.4 / 44.2)
Left parotid	58.6 (32.6 / 66.2)	46 (5.9 / 62.3)	44.2 (5.2 / 61.9)
Right parotid	56.1 (29.7 / 63.8)	49.7 (18.8 / 62.6)	47.1 (11.7 / 62.0)

DISCUSSION

Medullary carcinoma is considered to be rather radioresistant, but doses of 60 Gy or more may eradicate small residual disease [8]. Up to now there is not much evidence concerning IMRT for thyroid carcinoma. In our study more homogeneous dose distribution in the clinical target volume was achieved when IMRT was applied compared to 3DRT. The use of nine- or five-field IMRT produced equivalent results with similar dose distribution in CTVs and in critical structures. 5-field IMRT compared to 9-field IMRT technique led to small increases in dose inhomogeneity, but it is suggested that such small differences in dose distribution are not clinically relevant [14].

Higher minimum and lower maximum dose in the target volume were delivered with IMRT. This is consistent with results published by others on thyroid carcinoma radiotherapy [14, 17]. In a study done by Nutting et al. [14] on patients diagnosed with papillary thyroid carcinoma, IMRT was shown to achieve better dose distribution in the target volume, and reduction of the spinal cord dose when a plan with 5, 7 or 9 fields was applied, compared to 3DRT and conventional techniques. IMRT was also superior in radiotherapy for nasopharyngeal carcinoma due to improving target coverage while sparing the organ at risk [10, 15, 16].

In our study, not only was better dose distribution in CTV found but also better critical structure sparing was achievable with IMRT compared with 3DRT technique. High dose delivered to parotid glands, larynx and spinal cords can lead to acute and late complications in patients irradiated in the head and neck region. Using 3DRT and conventional planning techniques we would not be able to deliver the prescribed dose to the target volume without risking complications related to irradiation of critical structures. In some radiotherapy patients, the dose that can be safely delivered to CTV has to be limited by the tolerance dose of the spinal cord, which is considered to be about 46 Gy in 2 Gy per fraction. In such a situation a clinician must consider a compromise, by reducing the target volume to the area at the highest risk of recurrence, which can contribute to failure of treatment in the lower dose region [14]. The biggest profit from IMRT technique was gained in the parotid glands and larynx. In the spinal cord results obtained with IMRT and 3DRT were comparable.

With improvement of treatment techniques we are able to deliver higher, curative doses to the target volume, which may improve local control. On the other hand, high doses could result in higher incidence of late side effects. Decrease in dose to the organ at risk may decrease the incidence of complications. Using IMRT we are able to spare the organs at risk, and therefore IMRT techniques open the possibility for thyroid cancer patients' curative treatment even when large volumes of the head, neck and mediastinum have to be irradiated.

CONCLUSIONS

IMRT results in improved dose distribution within CTV compared to 3DRT. With the IMRT plan it is also possible to reduce the dose to the organ at risk, especially the larynx, salivary glands and spinal cord. Therefore, we suggest that the IMRT technique should be incorporated into the practice of postoperative radiotherapy of medullary thyroid carcinoma.

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