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Original Article

Contemplation of head and neck intensity-modulated radiotherapy

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Abstract

Intensity-modulated radiootherapy (IMRT) is being rapidly embraced as a radiotherapy technique in many cancer centres across the world. This paper aims to highlight the reported problems associated with the use of IMRT for the treatment of head and neck cancer. Specific areas of concern that are mentioned are the identification of tumour volumes, reproducibility of treatment, issues of tumour resistance and tumour recurrence. Radiotherapy departments are advised to make haste slowly when considering the implementation of this technique.

Keywords

Head and neck irradiation; intensity-modulated radiotherapy; reproducibility

INTRODUCTION

Radiotherapy departments, especially in the United States, despite limited data concerning outcome and toxicities, have rapidly embraced intensity-modulated radiotherapy (IMRT). It has been suggested that the popularity of IMRT in the United States is related to financial reimbursements. If renumeration was not a significant priority, then concern for patient care would become a guiding factor in the choice of whether to utilise IMRT or not. Comparing difficulties related to this new technique in the United States and in other countries can eliminate funding and political biases in publications.

The original concept of IMRT was that by partially shielding critical structures with a large number of beam orientations it would be possible to get more radiation dose to treatment target areas whilst sparing sensitive areas, notably the parotid glands to reduce xerostomia. The availability of multileaf collimators (MLCs) that allow multiple segments of irregularly shaped treatment fields to be rapidly delivered to the patient may be a direct cause of the utilisation of IMRT.[1] Additionally, the advent of inverse planning systems which devise treatment plans that can aim to deliver high doses of radiation to the target volume, whilst sparing normal tissue such as the parotid gland, make the IMRT process more viable.

Whilst investigating IMRT of the head and neck some areas of concern begin to emerge. These areas include identification of gross tumour volume (GTV), set-up reproducibility, overcoming tumour resistance and recurrence in the high dose area. These may be valid reasons for radiotherapy departments to consider when evaluating whether to implement IMRT for head and neck cancer and are described in detail below.

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IDENTIFICATION OF GTV, CLINICAL TUMOUR VOLUME AND PLANNING TARGET VOLUME

In the published literature there are some differences of opinion regarding the GTV and the clinical target volumes (CTVs) that should be used for IMRT. It is indisputable that accurate delineation of these areas is necessary to encompass disease, but IMRT is a conformal technique, which introduces the risk of underdosage of tumour if subclinical disease is not adequately covered.

Advances in imaging technologies (computed tomography (CT), magnetic resonance imaging, 18-fluoro-deoxy-glucose positron emission tomography) mean that valuable information regarding the extent of disease in patients with cancer of the head and neck is possible. However, although it is possible to pinpoint where the tumour is located there are inaccuracies related to the extent of disease in the mucosa with these imaging modalities. The clinical experience of the radiation specialists remains as the determining factor for the selection of the GTV to be irradiated.[2]

The CTVs that need to be selected for head and neck cancer are the primary tumour CTV and the lymphatic CTVs. The primary tumour CTV is the GTV plus a margin for perceived microscopic extension of tumour and is identified via imaging and physical examination. A difference of opinion exists in the radiation community surrounding the demarcation of the lymphatic CTVs. In 2003 an international consensus of opinion was published, which recommended guidelines regarding the CT-based delineation of lymph node CTVs in patients with negative neck nodes.[3] This was followed in 2006 by new guidelines for CTV delineation for patients with node positive necks and post-operative necks.[4] However despite these recommended guidelines published studies do deviate from them. For example, Eisbruch et al.[5] noted that although their approach was similar, they differed in their delineation of the extent of targets high in the neck and at the base of skull. Bussels et al.[6] changed the cranial limits of two of the nodal levels from the consensus guidelines. It is apparent that further evidence from practice needs to be acquired regarding the delineation of lymph node levels to ensure adequate treatment margins are uniformly used. A standardized approach would allow accurate comparison of studies.

Due to the advancement of radiation techniques and the introduction of new procedures which conform closely to the target volume the International Commission on Radiation Units and Measures (ICRU) published a supplement to the ICRU Report 50 (*Prescribing, Recording, and Reporting Photon Beam Therapy*).[7] Report 62 suggests guidelines for delineation of a planning target volume (PTV) for radiotherapy treatment and introduces the concept of the planning organ of risk volume (PRV), both of which include margins to compensate for uncertainties in microscopic spread of the tumour, tumour shape and treatment set-up variabilities. Often the PTV and PRV overlap which means that a compromise must be made at some point. The report acknowledges the fact that sometimes the balance between controlling disease whilst minimizing complications from the treatment results, in less likelihood of cure.

There are insufficient published studies that demonstrate a consistent approach to the delineation of planning volumes for head and neck IMRT. As with the identification of the GTV and CTVs, the ultimate decision regarding the delineation of the PTV and PRV depends on experience and judgement of the radiation team.

SET-UP REPRODUCIBILITY

As previously mentioned, the delineation of the PTV takes into account set-up variations. However this margin is generally in the range of 3–5 mm, which means that consistent reproducibility of set-up is essential in order to avoid dose deviations.

Three potential ways that set-up displacements could occur are:

1. Patient movement (interfraction movement).
2. Change in patient contour (interfraction movement).
3. Organ movement (intrafraction movement).

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Patients who undergo radiation to the head and neck area are conventionally immobilised with a shell during treatment. It has been well documented in the literature that there will likely be some deviation from the planned isocentre and this may be due to slight differences in machine parameters, laser alignment and patient positioning. These deviations are described as random or systematic errors and they must not exceed the margin that is included for set-up variation in the PTV. The analysis of random and systematic errors suggests that current recommended treatment margins are sufficient. However, some patients may have more movement than others such that conventional immobilisation with thermoplastic shells may be inadequate. It is recommended that around ten patients should be analysed to ascertain the magnitude of set-up errors when IMRT is implemented as a new technique in order to ensure the correct PTV margin.[8–10]

Anatomical changes in head and neck patients often occur during treatment because the tumour can change size and shape as the treatment starts to have an effect or because of reduction in post-operative swelling. In addition, patients who have treatment for head and neck cancer often lose weight due to treatment side effects, but at the same time there may be swelling from chemotherapy hydration. All these situations will affect the contour of the patient, which is more significant in IMRT than conventional head and neck treatment because of the sharp dose gradients that are employed. With the feasibility of equipment, daily imaging and correction of set-up variations are common practice. However, there is no standard policy concerning when to re-plan an IMRT patient. Standard procedure ought to include at minimum a repeat CT scan a few weeks into treatment with the capability to re-plan the treatment. This is not always practical and patients might have to revert to a conventional treatment plan if an IMRT plan cannot be made readily available to avoid interruption of treatment. Research is underway to try to find a way to rapidly adjust for inter-fraction errors during IMRT using daily CT imaging. This infers that in order to successfully treat patients using IMRT for head and neck cancer the treatment machine needs to have the ability to take daily CT images.[11,12] Even though the patients are immobilised, organ movement (such as swallowing) occurs inside the patient's body (intra-fraction movement), which can result in dose deviations of the treatment plan. Four dimensional (4D) CT imaging and planning take the dimension of time into account and are more relevant for treatment areas such as lung and prostate because it is not possible to immobilise these areas like head and neck treatment sites.[13] However in the future, 4D planning and treatment delivery would be appropriate for all tumour sites. In addition, inverse planning that is used in the design of IMRT plans could be improved if the plan is not based on only a single instance of patient positioning for IMRT. In the future it may be possible to incorporate inter-fraction organ movement into the planning process. However, this would mean that patients would require several CT scans and the research model being used is based only on prostate cancer.[14] Future research is concentrating on intra-fraction motion to deliberate how breathing and swallowing affect set-up reproducibility, but it is not yet available.

RECURRENCE IN HIGH DOSE AREA

The aim of IMRT treatment is to administer high doses of radiation to the target volume whilst sparing normal tissue, notably the parotid gland. There is concern that this highly conformal technique might result in marginal misses of treatment causing the tumour to recur.[5,6,15] It could be possible that in a bid to improve xerostomia, by sparing the parotid gland, the main objective of tumour control is put in jeopardy.[16]

There have been several publications that specifically investigate failure patterns in head and neck IMRT patients.[5,15,17,18] It is difficult to compare results because of the differences in methodology, especially radiotherapy technique and whether IMRT is a primary treatment modality with or without chemotherapy, used post-operatively or as a boost treatment. In addition, different authors have different definitions

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of what they defined as an in-field or out-of-field recurrence. However, it appears regardless of methodology that the majority of recurrences occur in the loco-regional treatment areas, specifically in CTVs that receive planned maximum doses of radiation, which means that the tumour volume was correctly treated but was not eradicated for other reasons such as radioresistance. Table 1 demonstrates that even though the different studies delivered similar doses to tumour targets, all of the studies reported loco-regional recurrences.

One study compared three radiotherapy techniques for the treatment of head and neck cancer after surgery: radiotherapy, IMRT and 3D-conformal radiotherapy. Although there was a difference in outcome in other areas it was concluded that radiotherapy technique did not impact the treatment outcome and similar disease control was maintained by all three techniques.[19] There is some evidence that tumour control using IMRT is at least comparable with conventional head and neck radiotherapy techniques[20] and follow-up reports demonstrate that there is a decrease in xerostomia after treatment with IMRT.[21–23]

OVERCOMING TUMOUR RESISTANCE

Head and neck cancers recur in IMRT patients due to radioresistance by the tumour and this is justified by the fact that recurrences occur predominantly within the CTV that receives the highest radiation dose.[17] The predominance of loco-regional failures within the high radiation dose target areas would mean that dose escalation ought to be a consideration in the future for IMRT patients.[6] It is the clinical and pathological features of tumours that cause loco-regional failures to occur and because of the conformality of IMRT treatment it ought to be possible to deliver a higher dose to the patient. It is likely that concurrent chemotherapy with IMRT improves loco-regional control for patients who had IMRT as a primary treatment or post-surgery. Similarly, patients who presented with extracapsular tumour extension of disease have a worse prognosis and need to be treated more aggressively with concurrent chemotherapy.[17,24] Higher rates of loco-regional tumour control for IMRT patients who have surgery as a primary treatment is achievable even for those patients with significant risk of recurrence. Patients who have had neck dissections should only receive IMRT to avoid recurrences in junction areas in conventional techniques that abut fields.[6,20,25]

CONCLUSION

Studies reported to date indicate that treatment failure rates and patterns for IMRT do not exceed those of conventional techniques, but do improve the patients' quality of life by sparing normal tissue, notably the parotid gland. Good loco-regional control is possible in post-operative patients with the addition of concurrent chemotherapy. Patients must be carefully selected so that the IMRT planning

Table 1. *Reported loco-regional recurrences*

Authors	**Minimum dose to GTV (Gy)**	**Minimum dose to post-op bed CTVs (Gy)**	**Minimum dose to non-dissected neck (Gy)**	**Locoregional recurrences (%)**
Eisbruch et al.	67	60	52	16
Dawson et al.	72 Gy	60 Gy	52 Gy	21
	Mean dose to GTV (Gy)	**Mean dose to post-op CTV (Gy)**	**Mean dose to non-dissected neck (Gy)**	**Recurrence (%)**
Chao et al.	72.6	68.5	64	14
Lee et al.	74	69	66	7

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would not be problematic and the treatment consistently reproducible. The data for the treatment of head and neck cancer infer that loco-regional control rates using IMRT are comparable with conventional treatments with possibly lower toxicities. However, the disadvantages of IMRT include potentially less dose homogeneity due to the sharp dose gradients employed, more chances of a marginal miss of the target volume due to inaccuracies of volume delineation and inter-fraction and intra-fraction errors.

There is no standard IMRT technique or process and because of the difficulties in planning and re-planning during treatment, small radiotherapy departments should think carefully before implementing this technique. An increase in time and money are necessary to implement this technique and treatment machines need to be equipped with up-to-date imaging technology. Also, it may be necessary to purchase or develop a new head and neck immobilisation system. Specialist training of staff should be undertaken as many of the decisions required in the IMRT process depend ultimately on experience and judgement. IMRT is a promising technology whose full indications and utilisation are still being analysed.

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