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Guidelines

Recommendations for Radiotherapy Technique and Dose in Extra-nodal Lymphoma

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Abstract

Extra-nodal sites may be involved in around 40% of patients with non-Hodgkin lymphoma. The general principles for target volume delineation in this setting are presented, together with specific examples. In general, the entire organ affected should be encompassed in the clinical target volume with an expansion of at least 10 mm, increased in some instances to account for patterns of potential lymphatic flow. Adjacent lymph nodes may be treated using standard techniques for nodal irradiation. Doses for extra-nodal lymphoma follow the same principles as nodal lymphoma, delivering 30 Gy in 15 fractions for Hodgkin and aggressive non-Hodgkin lymphoma and 24 Gy in 12 fractions for indolent lymphomas, with the exception of certain palliative situations, mycosis fungoides, central nervous system lymphoma and natural killer/T-cell lymphoma.
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Introduction

Extra-nodal lymphoma is a feature of 30–40% of non-Hodgkin lymphoma, although relatively rare in Hodgkin lymphoma. The incidence varies according to histological subtype, ranging from 82% of peripheral T-cell lymphomas to only 9% of follicular lymphomas [1]. The use of radiotherapy in the management of extra-nodal lymphoma is analogous stage for stage to that of nodal lymphoma. The common extra-nodal sites are in the head and neck region, gastrointestinal tract, central nervous system (CNS) and skin, but many other sites may be encountered due to the ubiquitous distribution of lymphoid tissue.

These guidelines, produced with the intention to unify the approach to radiotherapy planning for extra-nodal lymphoma in the UK, reflect extensive discussions at meetings held under the auspices of the UK National Cancer Research Institute Lymphoma Radiotherapy Clinical Studies Groups resulting in the consensus presented in this paper. These may be used to supplement other local and international guidelines [2,3].

Immobilisation and Planning Techniques

Immobilisation and imaging should follow the guidelines proposed for nodal lymphoma [AQ1] [4]. Certain sites

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will need special consideration, for example testicular irradiation will use a shielding lead plate beneath the testis. Departmental techniques used for solid tumours in the same region should be adopted.

Treatment Volumes

Although nodal radiotherapy delineation concepts have evolved from wide field to involved field and more recently involved site and involved node, extra-nodal volumes are primarily defined by the organ involved. In general, they aim for complete inclusion of that organ; where there is adjacent lymph node involvement then this may be integrated into an involved site or an involved node radiotherapy approach, as discussed in our nodal guidelines paper [AQ1] [4]. Computed tomography-based three-dimensional outlining is recommended in all cases and should be based on all clinical information and imaging studies available. Both pre- and post-chemotherapy computed tomography, positron emission tomography (PET) and/or magnetic resonance imaging should be available, especially when volumes are reduced to less than an entire extra-nodal structure.

Although not exhaustive, common sites are discussed below to show these principles. The fundamental principles of defining a clinical target volume (CTV) from which a planning target volume (PTV) will be derived to compensate for set-up variations and organ motion are adhered to.

Clinical Target Volumes

Maxillary Antrum and Paranasal Sinuses

Mucosal spread is of concern in this region. The CTV is defined by the whole ipsilateral antrum or sinus in all cases. If disease extends beyond the sinus walls then this will be included in the CTV, which is based on the pre-chemotherapy gross tumour volume (GTV) + 10 mm. Tissue planes should be respected unless disease invades bone or muscle.

In the case of natural killer cell (NK/T-cell) lymphoma then the nasal cavity and bilateral antra should be included, although a reduction to the involved cavity alone may be considered if there has been a complete or near complete response to chemotherapy.

Waldeyer's Ring

Conventionally, lymphoma arising in any part of Waldeyer's ring has been treated by inclusion of all sites of Waldeyer's ring in the radiation field. However, this is associated with considerable toxicity as it includes most of the salivary gland tissue. It is therefore proposed that only those areas of the ring that are found to be involved with lymphoma are included in the CTV using the principle that CTV = pre-chemotherapy GTV + 10 mm in all directions, except cranio-caudally, when a 15 mm margin is recommended, constrained by bone, air and muscle planes (see the example in Figure 1). If multiple sites are affected and these are contiguous, the whole Waldeyer's ring should be treated; if pre-chemotherapy imaging is not available or suboptimal and if chemotherapy is not given then a wider volume encompassing the entire Waldeyer's ring may be considered. The volume will be constrained to muscle, bone and air with close attention also to adjacent parotid doses.

Orbit

There are three areas in the orbit that may be involved in lymphoma that require different volumes and treatment techniques: the conjunctiva, the orbit itself and the lacrimal gland.

Conjunctival lymphoma is treated by including the whole conjunctiva; formal definition of a CTV is not usual as these tumours will be treated using a direct electron or superficial X-ray beam with a corneal shield [5], the field size being defined by the orbital margins.

Lacrimal gland: the CTV is the entire gland with no margin unless there is extra-capsular disease. In this instance the GTV will be the pre-chemotherapy volume, or for indolent lymphoma the volume at the time of radiotherapy, and the CTV a 10 mm expansion of this in all directions.

Orbit: The CTV will include the whole orbit, constrained to bone (see the example in Figure 2). Well-lateralised disease may be treated using a partial orbit volume.

Brain

Cerebral lymphoma is characteristically multifocal in nature so the CTV should encompass the whole brain and meninges extending down to the C1-C2 junction and including the cribiform plate, posterior orbit and optic canals. A boost to residual macroscopic disease may also be considered when the GTV comprises the post-chemotherapy tumour.

Parotid

This will be treated using a CTV that includes the entire ipsilateral gland unless there is extra-capsular spread pre-chemotherapy (see the example in Figure 3). In this instance the GTV will be the pre-chemotherapy volume and the CTV a 10 mm expansion of this in all directions.

Bone

Conventionally the entire bone would have been irradiated after chemotherapy. However, with modern imaging, which is able to accurately define the site of disease within a bone, this may not be necessary. Pre-treatment magnetic resonance imaging is used to define the pre-chemotherapy volume and this will be the GTV. From our consensus we propose expansion by 15 mm along the bone marrow cavity and 10 mm in all other directions to form the CTV.

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