East of England Radiotherapy Network:

Lymphoma Protocol V5.0

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1.0 Indications and patient population

This protocol covers treatment in the following situations:

1.1 Nodal lymphoma

a. Curative radiotherapy for early-stage (clinical stage I-II) low-grade non-Hodgkin lymphoma (NHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL).

b. Curative radiotherapy in combination with systemic therapy for early stage (stage I-II) classical Hodgkin lymphoma (cHL) and high-grade NHL.

c. Curative radiotherapy as part of consolidation radiotherapy for PET positive disease after primary systemic therapy for advanced (stage III-IV) HL and high-grade NHL.

d. Curative salvage radiotherapy for limited stage (stage I-II) chemotherapy-refractory or recurrent lymphoma in patients who are not suitable for high-dose chemotherapy +/- transplantation.

e. Palliative treatment for symptomatic nodal mass(es) in patents with extensive disease and are not candidates for systemic therapy.

f. Palliative treatment for patients with early-stage disease lymphoma, who are not candidates for systemic therapy or who have a WHO performance status of ≥2.

1.2 Extra-nodal lymphoma

a. Curative radiotherapy for early-stage (clinical stage I-II) low-grade non-Hodgkin lymphoma (NHL).

b. Curative radiotherapy in combination with systemic therapy for early-stage (stage I-II) high-grade NHL.

c. Curative radiotherapy as part of consolidation radiotherapy for PET positive disease after primary systemic therapy for advanced high-grade NHL.

1.3 As part of transplant and Chimeric Antigen Receptor T-cell therapy (CAR-T)

a. Curative radiotherapy to selected patients with isolated sites of recurrent refractory lymphoma treated with high-dose chemotherapy followed by transplantation

(radiotherapy may be given before transplant for patients who failed achieve a complete metabolic response after high-dose chemotherapy or after transplant).

b. Radiotherapy as a bridging strategy for patients planning to undergo CAR-T.

1.4 Cutaneous lymphoma

a. Curative definitive radiotherapy for limited stage primary cutaneous marginal zone lymphoma (Primary Cutaneous Marginal Zone Lymphoma (PCMZL)), primary cutaneous follicle centre lymphoma (Primary Cutaneous Follicle Centre Lymphoma (PCFCL)), mycosis fungoides (MF) and primary cutaneous anaplastic large cell lymphoma (C-ALCL).

b. Curative radiotherapy in combination with systemic therapy for limited stage primary cutaneous diffuse large B-cell lymphoma, leg type (Primary Cutaneous Diffuse Large B-cell Lymphoma, L Type (PCDLBCL-LT).

c. Palliative radiotherapy for disseminated cutaneous lymphoma.

1.5 Spleen

a. Curative radiotherapy for primary low-grade splenic lymphoma.

b. Palliative radiotherapy for symptomatic splenomegaly causing pain and/or hypersplenism in myeloproliferative disorders, lymphoma, and hairy cell leukaemia.

c. As part of conditioning regimen for patients with myeloproliferative disorders undergoing transplantation.

1.6 Plasma cell neoplasms

a. Curative radiotherapy solitary bone or soft tissue plasmacytoma

b. Palliative radiotherapy for multiple myeloma

1.1 Nodal lymphoma

a. Limited-stage nodular lymphocyte-predominant Hodgkin lymphoma: definitive curative radiotherapy.

b. Limited-stage classical Hodgkin lymphoma: radiotherapy after systemic therapy according to favourable or unfavourable risk and response.

c. Advanced-stage Hodgkin lymphoma: consolidation radiotherapy for selected PET-positive residual or refractory disease after systemic therapy.

d. Limited-stage indolent non-Hodgkin lymphoma: definitive curative radiotherapy.

e. Limited-stage aggressive non-Hodgkin lymphoma: radiotherapy after systemic therapy where indicated.

f. Advanced aggressive non-Hodgkin lymphoma with bulky disease: consider consolidation radiotherapy.

g. Refractory or recurrent non-Hodgkin lymphoma: consider salvage radiotherapy, including for patients unsuitable for high-dose chemotherapy or transplantation.

h. Symptomatic nodal lymphoma: palliative radiotherapy where appropriate, including when systemic therapy is unsuitable.

1.2 Extra-nodal lymphoma

a. Indolent extranodal lymphoma: definitive curative radiotherapy for selected early-stage disease.

b. Aggressive extranodal B-cell lymphoma after complete response to systemic therapy: consolidation radiotherapy where indicated.

c. Aggressive extranodal B-cell lymphoma without complete response to first-line systemic therapy: radiotherapy where indicated.

d. Residual, relapsed or progressive aggressive extranodal B-cell lymphoma: radiotherapy where indicated.

e. Extranodal NK/T-cell lymphoma, nasal type: radiotherapy with systemic therapy according to disease extent and response.

f. Symptomatic extranodal lymphoma: palliative radiotherapy where appropriate.

1.3 As part of transplant and CAR-T

a. Selected recurrent or refractory lymphoma: radiotherapy as part of high-dose chemotherapy and autologous stem cell transplantation, before or after transplantation according to response.

b. Radiotherapy as bridging treatment before chimeric antigen receptor T-cell (CAR-T) therapy.

1.4 Cutaneous lymphoma

a. Primary cutaneous marginal zone lymphoma, primary cutaneous follicle centre lymphoma and primary cutaneous anaplastic large-cell lymphoma: definitive or palliative radiotherapy according to extent and intent.

b. Primary cutaneous diffuse large B-cell lymphoma, leg type: curative radiotherapy with or without systemic therapy, or palliative radiotherapy.

c. Mycosis fungoides: curative, palliative or repeat radiotherapy according to disease extent and intent.

1.5 Spleen

a. Localised low-grade splenic lymphoma: curative radiotherapy.

b. Symptomatic splenomegaly or hypersplenism in lymphoma, hairy cell leukaemia or myeloproliferative disorders: palliative radiotherapy.

c. Radiotherapy as part of transplantation conditioning for selected patients with myeloproliferative disorders.

1.6 Plasma cell neoplasms

a. Solitary bone or soft tissue plasmacytoma: curative radiotherapy.

b. Multiple myeloma: palliative radiotherapy for symptomatic sites.

2.0 Histological classification, risk group and treatment approach to lymphoma

2.1 Nodal lymphoma

2.1a Limited-stage nodular lymphocyte-predominant Hodgkin lymphoma

Definitive curative radiotherapy; see indications 1.1a and dose row in 5.1. For advanced-stage PET-positive residual disease, consider consolidation radiotherapy after systemic therapy (1.1c; 5.1).

2.1b Limited-stage classical Hodgkin lymphoma

Favourable early-stage disease has no adverse risk factors; unfavourable disease has one or more. Risk factors in this protocol are a large mediastinal mass (>10 cm), extranodal involvement, elevated ESR (>30 mm/h with B symptoms or >50 mm/h without B symptoms), three or more nodal regions, or B symptoms. Radiotherapy after systemic therapy depends on response; it may be omitted in selected complete responders under the HD17 approach. See 1.1b and 5.1.

2.1c Advanced-stage Hodgkin lymphoma

Consider consolidation radiotherapy for PET-positive residual or refractory disease after systemic therapy; see 1.1c and 5.1.

2.1d Limited-stage indolent non-Hodgkin lymphoma

Definitive curative radiotherapy; see 1.1d and 5.1.

2.1e Limited-stage aggressive non-Hodgkin lymphoma
Systemic therapy followed by radiotherapy where indicated; see 1.1e and 5.1.

2.1f Advanced aggressive non-Hodgkin lymphoma with bulky disease
Consider consolidation radiotherapy for selected bulky disease; see 1.1f and 5.1.

2.1g Refractory or recurrent non-Hodgkin lymphoma
Consider salvage radiotherapy in selected patients; see 1.1g and 5.1.

2.1h Palliative nodal lymphoma
Treat symptomatic sites according to clinical need; the 4 Gy option in 5.1 applies only to low-grade lymphoma. See 1.1h and 5.1.

2.2 Extra-nodal lymphoma
2.2a Indolent extranodal lymphoma
Definitive radiotherapy for selected early-stage disease; see 1.2a and 5.2.

2.2b Aggressive extranodal B-cell lymphoma after complete response
Consider radiotherapy after systemic therapy; see 1.2b and 5.2.

2.2c Aggressive extranodal B-cell lymphoma without complete response
Consider radiotherapy for incomplete response after first-line systemic therapy; see 1.2c and 5.2.

2.2d Residual, relapsed or progressive aggressive extranodal B-cell lymphoma
Consider radiotherapy according to disease extent and intent; see 1.2d and 5.2.

2.2e Extranodal NK/T-cell lymphoma, nasal type
Radiotherapy is generally combined with systemic therapy and should start no later than the third cycle where concurrent treatment is planned. Dose depends on disease extent and response; see 1.2e and 5.2.

2.2f Palliative extranodal lymphoma
Treat symptomatic sites according to clinical need; see 1.2f and 5.2.

2.3 Radiotherapy as part of transplant or CAR-T treatment
Selected recurrent or refractory disease may receive radiotherapy before or after autologous stem cell transplantation according to response, or as bridging treatment before CAR-T infusion. See 1.3 and 5.3; the four dose options are not assigned to individual indications in this protocol.

2.4 Cutaneous lymphoma
Primary cutaneous marginal zone, follicle centre and anaplastic large-cell lymphoma; primary cutaneous diffuse large B-cell lymphoma, leg type; and mycosis fungoides have distinct definitive and palliative options. See the same sequence in 1.4 and 5.4.

2.5 Spleen

Distinguish localised low-grade splenic lymphoma from palliative treatment of symptomatic splenomegaly or hypersplenism and transplantation conditioning. See 1.5 and 5.5; section 5.5 does not specify a separate conditioning dose.

2.6 Plasma cell neoplasms

Distinguish curative radiotherapy for solitary plasmacytoma from palliative radiotherapy for symptomatic multiple myeloma. See 1.6 and 5.6.

3.0 Essential Pre-Radiotherapy investigations for curative patients

- Review of histology, diagnostic investigations and any previous lymphoma treatment.
- Review of diagnostic imaging and any response assessment imaging.
- Assessment of performance status

4.0 Localisation

Localisation	Notes	
Position and immobilisation (depends on area of treatment	As per site specific protocol	
Organ pre-requisites	Stomach lymphoma	Patients are asked to fast for 2 hours and then drink 150 ml of liquid 15 minutes prior to CT and treatment Use of 4DCT can be considered.
	Other sites	Site-specific preparation as appropriate e.g., empty bladder for bladder radiotherapy Use of motion management as appropriate
Contrast		IV contrast depends on clinical situation
CT acquisition	Slice thickness:	2-3 mm
	Scanning limits	Based in individual site-specific protocols or 8-10 cm above and below the upper extend of disease on diagnostic scan
	DIBH	Recommended for patients with mediastinal lymphoma
Image co-registration	Combined chemo-radiotherapy for stage I-II	Diagnostic PET/CT scan or diagnostic MRI
	Consolidation radiotherapy	Interim PET /end PET showing PET+ disease/ end of treatment scan
	Refractory disease	PET/CT showing refractory before salvage chemotherapy

5.0 Dose prescription

5.1 Nodal Lymphoma

Indication	Dose (Gy)/#	#/week	Comment
Hodgkin Lymphoma: Limited stage lymphocyte-predominant HL	30Gy/15#	5	
Hodgkin Lymphoma: Limited stage classical HL-favourable group with a complete response after chemotherapy	20Gy/ 10#	5	
Hodgkin Lymphoma: Limited stage classical HL-favourable group without complete response	30Gy/ 15#	5	
Hodgkin Lymphoma: Limited stage classical HL- unfavourable group with a complete response after the chemotherapy	30Gy/15#	5	
Hodgkin Lymphoma: Advanced stage consolidation/ residual/refractory disease after chemotherapy	30 – 36Gy/ 15-18#	5	
Non-Hodgkin lymphoma: Limited stage indolent	24Gy/ 12#	5	
Non-Hodgkin lymphoma: Limited stage aggressive (after chemotherapy)	30Gy/ 15#	5	
Non-Hodgkin lymphoma: Bulky disease (advanced stage)	30Gy/ 15#	5	
Non-Hodgkin lymphoma: Refractory/ recurrent	30 – 40Gy/ 15-20 #	5	
Palliative radiotherapy	4Gy/ 1-2#* 8Gy/ 1# 20Gy/ 5# 30Gy/ 10#	5 1 5 5	*Low dose 4Gy in 1-2 # applies to low-grade lymphoma; ~20% may require re-irradiation within 6 months

5.2 Extra-nodal lymphoma

Indication	Dose (Gy)/#	#/week	Comment
Indolent	24-30Gy/ 12-15#	5	
Aggressive after a complete response to chemotherapy Nasal NK/T cell lymphoma	30Gy/ 15# 45-50Gy / 25#	5 5	
Aggressive no complete response after first-line chemotherapy	30-40Gy/ 15-20#	5	
Aggressive – residual, relapsed or progression after treatment Nasal NK/T cell lymphoma	30-40Gy/ 15-20# 50-60Gy / 25-30#	5 5	
Palliative radiotherapy	8Gy/ 1# 20Gy/ 5# 30Gy/ 10#	1 5 5	

5.3 As part of transplant and CAR-T

Indication	Dose (Gy)/#	#/week	Comment
Commonly used	30Gy/ 10#	5	
	20Gy/ 5#	5	
	12Gy/ 4#	5	
	9Gy/ 3#	5	

5.4 Cutaneous Lymphoma

Indication	Dose (Gy)/#	#/week	Comment
PCMZL/ PCFCL/ PCALCL: Definitive radiotherapy	24-30/ 12-15#	5	
PCMZL/ PCFCL/ PCALCL: Palliative radiotherapy	4Gy/ 1-2#	5	

Indication	Dose (Gy)/#	#/week	Comment
	8Gy/ 1#	1	
PCDLBCL-LT: Curative radiotherapy with chemotherapy	36Gy/ 18#	5	
PCDLBCL-LT: Curative radiotherapy without chemotherapy	40Gy/ 20#	5	
PCDLBCL-LT: Palliative radiotherapy	4Gy/ 2# 8Gy/ 1# 20Gy/ 5#	2 1 5	
Mycosis Fungoides: Curative	24Gy/ 12# 20-30Gy/ 10-15#	5 5	
Mycosis Fungoides: Palliative	4Gy/ 2# 8-12Gy/ 2-3#	2 2-3	Complete response rate <30% Complete response rate >90%
Mycosis Fungoides: Re-irradiation	20Gy/ 5#	5	

5.5 Spleen

Spleen is considered as a node. Unless when it acts as an organ of extramedullary haematopoiesis or with symptomatic hypersplenism, radiotherapy does not cause blood count drop. When spleen is an organ of extramedullary haematopoiesis or there is hypersplenism, FBC should be obtained before each treatment, and treatment should be postponed if there is a significant drop in counts. In patients with hypersplenism up to 90% of total platelets could be sequestrated in the spleen and radiotherapy can cause significant thrombocytopaenia. In chronic myeloproliferative disorders, the spleen may be a site of extramedullary haematopoiesis and even a single dose of radiotherapy can cause significant cytopaenias (reported in 10-30%). Therefore, patients with myeloproliferative disorders and a high-risk of cytopaenia may need individual titration of radiotherapy dose starting at a fraction size of 0.1-0.5 Gy.

Indication	Dose (Gy)/#	#/week	Comment
Localised low grade splenic lymphoma	24Gy/ 12#	5	
Palliative radiotherapy	4-10Gy/ 4-10# (1Gy per #)	5/ 3/1	Use fewer fractions per week for patients with chronic myeloproliferative disorders

5.6 Plasma cell neoplasms

Indication	Dose (Gy)/#	#/week	Comment
Solitary plasmacytoma	40 – 50Gy/ 20 – 25#	5	Use 50Gy if tumour diameter is more than 5cm
Palliative radiotherapy	8Gy/ 1# 20Gy/ 5# 30Gy/ 10#	5 1 5 5	

6.0 Target volumes for lymphoma

- Use standard nomenclature as per Global Harmonization Group consensus guidelines: https://www.thegreenjournal.com/action/showPdf?pii=S0167-8140%2820%2930294-2 PTV ProKnow nomenclature should be used when uploading to NHSE ProKnow Collections.
- The concepts of target volume delineation have significantly evolved in the last two decades and patients are currently treated with small volumes without compromising the chances of cure. Studies have shown that a short course of chemotherapy combined with small-field radiotherapy results in equivalent survival rates to those obtained with extended-field RT (EFRT) but without significant late side effects in early-stage HL and high-grade NHL. This finding led from the use of EFRT to the development of treatment with involved-field (IFRT), involved-node (INRT), and involved-site (ISRT) radiotherapy. The clinical application of ISRT technique depends on the acquisition of the baseline image in the radiotherapy treatment position with the same breathing instructions, and precision of co-registration of the baseline image with the planning CT scan. The CTV for ISRT encompasses the pre-chemotherapy GTV with a margin to account for the uncertainties in transferring the pre-chemotherapy GTV onto the planning CT scan. The margin becomes larger with more uncertainty**. ISRT is the standard technique of choice for all patients treated with curative intent.**
- If optimal diagnostic imaging (e.g., PET/CT) is not available, IFRT or modified IFRT may be considered. The CTV for encompasses the anatomical nodal *regions* with or without first echelon nodes.

6.1 Curative radiotherapy for nodal lymphoma GTV/CTV

Definitive radiotherapy or radiotherapy as part of primary combined modality

- GTV is the radiologically visible enlarged nodes or disease on the diagnostic scan before chemotherapy ('pre-chemotherapy' GTV) or surgery (pre-surgery GTV). For PET avid histological subtypes, it is the PET-positive disease at diagnosis.
- CTV
    - Cranio-caudally, a 15 mm margin is added to the GTV by hand in line with the direction of the nodal compartment (treatment planning expansion tools may overestimate or distort the margin)

- Axially, the CTV stays within/extends up to the boundaries of the nodal compartment in the axial plane (based on published nodal atlases, see references). For radiotherapy after chemotherapy, the CTV should not exclude structures previously displaced by enlarged nodes. However, if lymphoma infiltrates adjacent organs (e.g., the lung) in the prechemotherapy GTV, the initially area infiltrated tissue volume should be included in the CTV. The CTV should not extend beyond uninvolved organs, natural barriers, and air cavities. If there is equivocal disease near GTV at diagnosis (PET-negative nodes of >1 cm in short axis, normal sized nodes with equivocal FDG uptake, increased number of asymmetrically distributed nodes), these should be included in the CTV.
- CTV involving mediastinum: The blood vessels in the mediastinum should not be included in the CTV.

Consolidation radiotherapy after primary chemotherapy

- GTV is residual PET-positive disease or residual enlarged nodes after chemotherapy. If there is an interim PET scan, consider PET-positive disease on an interim scan as GTV, provided it is not too extensive.
- CTV
    - A 15 mm craniocaudal margin is added to the residual disease. In the axial plane, the CTV is edited to stay within/extend up to the boundaries of the nodal compartment. If the site of residual disease is in an area with no clear nodal compartmental boundaries (e.g., mesenteric nodes) a 15 mm isotopic margin is added to the residual disease and edited to exclude uninvolved organs and natural barriers.
    - Primary mediastinal DLBCL and nodular sclerosing HL in the mediastinum may have residual necrotic tumours with low FDG uptake and fibrotic tissue, which often takes time to resolve). The CTV should encompass this mass.

If the CTV is large, treatment may be given using two dose levels: i.e., smaller dose (15-24 Gy) to the entire radiological tumour, and higher dose (30-36Gy) to the PET-positive disease.

Salvage radiotherapy with transplantation or bridging radiotherapy

Timing of radiotherapy in relation to transplant is debatable. Generally, radiotherapy is recommended before Autologous Stem Cell Transplantation (ASCT) for patients who have not achieved a complete metabolic response (CMR) after high-dose chemotherapy (HDCT) and before or after ASCT for patients who have achieved a CMR after HDCT. Bridging RT is given during the interval between harvest and CART infusion.

- GTV for radiotherapy as part of salvage treatment with HDCT and ASCT is the PET-positive refractory/relapsed disease before HDCT. GTV for bridging RT is the PET-positive disease before CAR-T
- CTV - A 15-20mm margin is added to GTV. All adjacent equivocal nodes and sites at risk of relapse should also be included in the CTV. In this situation, tumour control is more important than the potential risk of toxicities. CTV may be edited to exclude uninvolved structures, bones, and air cavities.

Curative radiotherapy for extranodal lymphoma GTV/CTV

Target volume definition for extranodal lymphomas depends on the site of disease. Specific definition of target volume depends on the site of disease. The principles of ISRT for extranodal lymphomas are as follows:

- GTV for definitive radiotherapy, the GTV is visible disease and enlarged nodes on optimal baseline image(s). For radiotherapy after 3-4 cycles of chemotherapy, it is the pre-chemotherapy GTV on the baseline optimal image. For consolidation radiotherapy, it is the residual disease on the optimal image.
- CTV is usually the entire organ (e.g., stomach, salivary glands, thyroid, or brain) or compartment (e.g., orbit for extra-ocular lymphoma). For stage IE disease, elective nodes are not included in the CTV and for IIE disease, nodal CTV is like that for nodal lymphoma. Partial organ CTV may be considered after chemotherapy for extra-nodal lymphomas when disease is unlikely or proven to be multifocal (e.g., bone and breast lymphomas).

Descriptions of CTV for common extranodal lymphomas are as below:

- Primary CNS lymphoma: CTV is the whole brain.
    - If there is no involvement of the eye(s): The whole brain, including first or second cervical vertebrae and the posterior aspect of the eyes.
    - Patients with disease in the eye(s): the whole brain, including first or second cervical vertebrae and the entire globes.
- Primary orbital lymphoma:
    - Conjunctival lymphoma limited to the anterior half of the globe.
        - Anterior direct field (e.g. 300 Kv) usually with a 5 cm diameter circle
        - Alternatively, anterior electron field with bolus
    - Other orbital lymphoma
        - CTV – whole orbit with bolus if disease is anterior
- DLBCL limited to the lacrimal gland.
    - Complete response after chemotherapy – CTV is the entire lacrimal gland.
    - Residual disease after chemotherapy – CTV is the entire orbit.
- Waldeyer's ring (WR)
    - Radiotherapy after chemotherapy for aggressive NHL: While WR is considered as a 'single site,' CTV need not cover the whole WR. The involved sub site is the CTV (e.g., for tonsil, the CTV is the whole tonsillar fossa from the level of the soft palate to the level of vallecula)
- Definitive radiotherapy for indolent NHL: Optimal CTV is not known. CTV is either the involved subsite or the whole of Waldeyer's ring depending upon the accuracy of optimal imaging.
- If cervical nodes are involved, the CTV is based on the principles of ISRT.
- Salivary gland
    - CTV is the whole unilateral salivary gland. If there is any disease at the periphery of the CTV, a 3-5 mm margin is added to the GTV to ensure adequate coverage of microscopic disease. For stage IIE disease, nodal CTV is based on the ISRT approach.

Curative radiotherapy for extranodal NK/T cell lymphoma nasal type

Timing of radiotherapy: Studies have suggested that concurrent chemo-radiotherapy improves survival compared with sequential chemo-radiotherapy. Therefore, radiotherapy should be started along with or before the third cycle of chemotherapy.

Target volume

Small fields as in ISRT may reduce loco-regional control and survival rates. Therefore, 'extended ISRT' is recommended.

- GTV – visible tumour and nodes on pre-chemotherapy disease
- CTV depends on the initial extend of disease:
    - Disease limited to one nasal cavity: Bilateral nasal cavity, ipsilateral maxillary sinus, bilateral anterior ethmoid sinuses, and the hard palate.
    - Disease limited to both nasal cavities: Bilateral nasal cavity, bilateral maxillary sinus, bilateral anterior ethmoid sinuses, and the hard palate.
    - Disease close to or involving the nasopharynx: Bilateral nasal cavity, bilateral maxillary sinus, bilateral anterior ethmoid sinuses, the hard palate, and the nasopharynx.
    - Disease extending to anterior ethmoid sinuses: Bilateral nasal cavity, bilateral maxillary sinus, hard palate, and bilateral anterior and posterior ethmoid sinuses.
        - Nodal CTV: For IE disease without extension to adjacent structures, there is no need to include elective nodes. For stage IE with extension to adjacent structures, the CTV includes bilateral upper cervical nodes, and for Stage IIE disease CTV includes bilateral upper cervical nodes, and the involved nodes.

Thyroid

- GTV is any residual disease or disease on the pre-treatment scan
- CTV encompasses the whole thyroid and pre-chemotherapy or pre-resection GTV

Stomach

- GTV– is the visible disease in the stomach and adjacent enlarged or PET+ nodes.

- CTV – encompasses the GTV and the whole stomach from the oesophago-gastric junction to beyond the duodenal bulb (gastric lymphoma is a multifocal disease) and involved nodes with a margin of 5-8 mm.
- If ITV approach is used, outline stomach in the MIP.

Breast

- GTV – radiological residual tumour or tumour seen on diagnostic imaging
- CTV
    - Stage IE disease: the whole breast is the CTV and there is no need to include any nodes. After chemotherapy, partial breast irradiation is considered appropriate by some experts.
    - Stage IIE CTV: comprises the whole breast and involved nodes as per ISRT.

Bone

- GTV – Pre-chemotherapy GTV and/or residual tumour after chemotherapy
- CTV – pre-chemotherapy GTV with at least 10-15 mm margin in all directions. Residual disease should be included in the CTV with a 5-10 mm margin.

Testis

- CTV: is the entire scrotum with the testes, epididymis, and initial part of the spermatic cord.
- Nodal CTV: If nodes are enlarged, nodal CTV follows the principle of ISRT

Cutaneous lymphoma

PCMZL, PCFCL, PCALCL

A solitary lesion (T1) and some patients with a small number of multiple lesions (T2) can be treated with 'involved lesion' radiotherapy.

- GTV: visible lesion, including erythema and induration superficially and depth assessed.
- CTV: GTV+10-15 mm superficial margin and 5-10 mm deep margin

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Patients considered for chemotherapy followed by radiotherapy should be reviewed before chemotherapy by a clinical oncologist to assess pre-chemotherapy GTV and document with clinical photographs.

- CTV: pre-chemotherapy GTV+10-20 mm

Target volume for solitary plasmacytoma

- GTV: is the radiologically visible soft tissue mass and bone disease. In patients with solitary extramedullary plasmacytoma (SEP), any enlarged lymph nodes should be included in the GTV.
- CTV: GTV +10-15 mm. If there is uncertainty about the extent of bone involvement on imaging, the whole bone should be included in the CTV. Generally, the whole involved vertebra is the CTV.
- Postoperative CTV: should enclose any residual tumour and pre-operative disease shown on the optimal imaging with 5-10 mm margin for microscopic disease. Surgical nails may be included in the CTV if they traverse the tumour, to prevent surgical seeding.

6.2 Curative PTV

Salvage radiotherapy with transplantation or bridging radiotherapy

A margin is added to the CTV depending on the site of disease, immobilisation, and department guideline, for example:

- Head and neck: 3-5mm
- Mediastinum: 7-10 mm axially, 10-15 mm craniocaudally
- Other sites: 10 mm isotopically

PCDLBCL-LT

PTV: A margin is added to CTV depending on the site of tumour, immobilization technique and departmental data.

6.3 Palliative radiotherapy

- GTV is symptomatic nodal or extranodal mass or other symptomatic disease

- PTV: An isotopic margin of 0.5 -2 cm is added

7.0 Organs at risk

Organs at risk depends on treatment area and general principles of OAR outlining should be followed. For description of site-specific OAR refer to the relevant protocols.

7.1 Constraints

Radiotherapy doses are much lower than that used in other curative setting and therefore, it is usually below the tolerance of most organs. Nevertheless, the attempt is to give lowest dose to OARs in keeping with the ALARA principles.

As per the ICRU 83 reporting guidelines when using VMAT/ IMRT we should at minimum be reporting the following PTVs. Additional parameters may also be reported at oncologist request.

Metric	Details	Optimal Dose in%	Mandatory Dose in %
D2% -	Near maximum Absorbed dose	*≤105%*	*≤107%*
D98% -	Dose to near min – dose that covers 98% of the volume	*≥98%*	*≥95%*
D95% -	Minimum absorbed dose that covers 95% of the volume	*≥95%*	*≥90%*
D50% -	Median absorbed dose – normally between +/- 1Gy	-	*+/ - 1 Gy*

8.0 Planning process/ technique

- For curative radiotherapy, depending on the context, all available techniques can be used but the choice of technique depends in individual cases on relative technical advantages and disadvantages.

- 3D conformal, fixed-field IMRT and arc therapy (VMAT or tomotherapy) are increasingly being used. These techniques achieve a more conformal dose to the target volume and lower doses to the neighbouring structures, especially when treating extranodal sites.
- Butterfly VMAT/IMRT (Two coplanar arcs of 60° using gantry starting angles of 150° and 330° and one non-coplanar arc of 60° using gantry starting angles of 330° at a couch angle 90°) often results in lessening the low dose bath to the lung and the breast. It is useful in young women with mediastinal disease to reduce breast dose and thus minimize the risk of a second cancer. Similar benefits are also seen with helical tomotherapy.
- Radiotherapy during deep inspiratory breathhold (DIBH) reduces the dose to the heart and lungs.

- Field-based IFRT uses opposed anterior-posterior beams with appropriate shielding with MLCs.
- Simple field arrangements may be used for palliative RT.

9.0 Peer Review/ Contour QA

- Prospective peer review should ideally be performed prospectively for all patients having curative radiotherapy.
- A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.
- The peer review process and outcomes should be audited.

10.0 Target verification

Treatment verification depends on the site of treatment. For description of site-specific verification refer to the relevant protocols.

11.0 Side effects

Radiotherapy side effects depend on the body area of treatment. Radiotherapy doses used for lymphomas are lower than those used for other malignancies, and therefore short-term side effects are less frequent and often mild. The acute side effects may include fatigue, dermatitis, mucositis, nausea and vomiting, dry cough, diarrhoea etc.

Long-term side effects, even after low-dose radiotherapy, are an issue, especially when irradiating mediastinal disease in young people. These effects may include radiation pneumonitis (<5%) hypothyroidism (20%), cardiac effects, and second malignancies, particularly of the breast and lung. A detailed account of these side effects is beyond the scope of this guideline. Women who had radiotherapy to the chest area involving breast tissue before the age of 36 years should be referred for MRI breast screening. The screening should start 8 years after radiotherapy to breast tissue or at age of 30 years whichever occurs later.

12.0 References

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14.0 Amendment History

A record of changes in this document.

Date	Updated version number	Previous version number	Page Number/ Section	Details
06.01.22	V1.0			New Document
02.02.22	V1.1	V1.0	P21	Peer review section added
14.12.22	V2	V1	5.2	4Gy/ 1-2# removed from dose/# table
			6.0	Target volume nomenclature updated to GHG consensus guidance as per Network Oversight Group request
			6.2	PTV section added
			P19	Salvage RT margin for mediastinum updated to 7-10mm
			9.0	Peer review requirements updated

Date	Updated version number	Previous version number	Page Number/ Section	Details
04.03.24	V3	V2	Pg 7	DIBH added
			Pg 19	Table added
			Pg 21	Reference list updates
26.02.25	V4	V3		No changes made
18.11.26	V5	V4	Throughout	Aligned nodal, extranodal, transplant, CAR-T, cutaneous, spleen and plasma call neoplasms indications throughout
			Section 3	Investigations streamlined to reflect practice
			Section 4	Localisation table updated to refer to site specific protocols
			Section 5.6	4Gy/ 1-2# removed from px table
			Section 6.0	Target volume information updated
			Section 6.3	Target volume margin for palliative updated to 0.5 – 2cm
			Section 13	Membership updated