Radiotherapy Protocol for the management of HAEMATOLOGICAL TUMOURS

This is radiotherapy protocol for the East Midlands RT Operational Delivery Network (ODN). Tumour sites are: Lymphomas / Myelomas

Document revision History

Version Number	Date	Document History.
0.01	12/23	Initial Draft by Priyesh Mistry
0.02	09/02/24	Reviewed with lymphoma clinicians. In attendance: A.Ramada, C.Esler, L.Speed, P.Das, F.Smith
0.03	05/24	Reviewed and updated with K. Das
0.04	25/06/24	Reviewed and update with trust planning/physics team. In attendance: J.Sutton, V.Ohlendorf, D.Holmes, V.Malysz-Smith, M.Bland, L.Martins
0.05	09/24	Abbreviation changes + glossary added following ECAG feedback. Ratified and agreed
1.0	09/24	Final version uploaded following NOG
1.1	January 2025	KD/PM- References improved as per Dec 2024 NOG action

1. Indications for Radical treatment

- Histologically confirmed disease and agreement for treatment following discussion at MDT
- Post chemotherapy consolidation or residual disease
- Radical Radiotherapy Only
- Bridging radiotherapy CAR-T
- Salvage Radiotherapy (Consider for relapsed disease)
- Concurrent with chemotherapy for Radical NK/T cell lymphoma

Disease sites[1]					
	High Grade NHL	**Low Grade NHL**	**Hodgkins Disease**	**Myeloma**	**Cutaneous lymphoma**
Inclusion	**-DLBCL** **-Mediastinal** **-NK/T cell lymphoma**	**-Follicular** **-MALT** **-Marginal zone lymphoma** **-NOS**	**-(NSHL) Nodular sclerosing hodgkins lymphoma** **- (MCHL) Mixed cellularity hodgkins lymphoma** **-(LDHL) Lymphocyte depleted hodgkins lymphoma** **-(LRHL) Lymphocyte rich hodgkins lymphoma**	**-Plasmacytoma**	**-Mycosis fungodies** **-Cutaneous B cell**
Treatment options	**Stage I & II –** o Radiotherapy is given for consolidation treatment following systemic therapy o Radiotherapy can be considered as a single modality treatment if patient is not fit for systemic therapy o **Advanced disease-** Following systemic therapy, patient can be considered for radiotherapy as discussed at MDT o **Natural Killer (NK) /T cell** -Primary Chemo radiotherapy for	**Stage I & II -** o Radiotherapy is considered as single modality treatment	**Stage I / II -** o Radiotherapy to involved sites. o Extended field radiotherapy in rare cases may be considered for chemotherapy resistant disease or when high dose chemotherapy is not appropriate o **Advanced disease-** Treatment as agreed by MDT o Single modality for LDHL	o Radical radiotherapy	**o (TSET) Total skin electron therapy** **o Radical radiotherapy for limited cutaneous disease**

Spleen Irradiation[2]	
Inclusion	**Treatment options**
• **Lymphoma** • **CLL** • **Hairy cell leukaemia** • **Hypersplenism** • **Splenomegally symptoms** • **Myelofibrosis**	• Depending on disease, indication, performance status and platelet/Hb)

2. Investigations Required

- Histological confirmation of malignancy
- Dental assessment (where appropriate)
- Bone marrow evaluation (where appropriate)
- Consideration of fertility preservation
- Diagnostic/staging imaging may include:
  -CT head, neck, chest, abdomen, pelvis
  -FDG PET-CT. Pre and post treatment as required
  -MRI as per requirements and clinician request

3. Information given to patients

- General radiotherapy booklet
- Site specific treatment leaflet including long term side effects

4. Consent

- By IR(ME)R Practitioner at new patient / planning clinic
- By Entitled IR(ME)R Operator under delegated authority at new patient / planning clinic

5. Trials Open

- Consider current trials open in any of the radiotherapy centres in the East Midlands.
- [EMRTN TRIALS TRACKER LINK]
- If a patient is being treated in a clinical trial then the Trial Protocol overrides the departmental protocol.

6. Position and immobilisation

All patients will be CT scanned as per local protocol and should consider including the following:

- Patients should be scanned in accordance with the area being treated
- Head/Neck: Recommended to create a thermoplastic head and neck shell with arms down. Consider **open** thermoplastic shells for areas of head and neck, where the adequate verification systems are in place
- Thorax: Arms up, wingboard or equivalent
- Abdomen/Pelvis: Head support, pelvic immobilisation including knee and feet indexes
- Other sites: Discuss with local Radiotherapy team
- Additional patient immobilisation as required such as vacuum cushions, knee rest, custom neck rest, hand poles
- Patients to ideally be scanned supine
- Consider intravenous contrast where appropriate (providing adequate renal function and no other contraindications).
- 3DCT CT scan
- 4DCT scans for thoracic patients should be discussed with local teams if this is to be considered
- DIBH for thoracic/abdominal patients should be discussed with local teams if this is to be considered
- Appropriate scan levels covering the area to be treated

7. Planning

Technique

- IMRT/VMAT is the primary choice of planning technique for radical patients. Conformal Radiotherapy can be considered on a cases by case basis
- The GTV/CTV to be outlined by an entitled Clinical Oncologist/Registrar/other entitled practitioner.
- All available information should be used including diagnostic imaging and histology
- MRI/PET fusion may be utilised where available

- If a patient is being treated in a clinical trial, then the trial protocol overrides the departmental protocol.
- If the treatment is off protocol, this should be noted and the correct local procedure for recording/authorising off protocol treatments should be followed.
- Contouring will conform to the Principles of ICRU 50 and 62[10] generally
- The Practitioner is required to exercise their clinical judgement, to clearly indicate the clinical priorities and acceptable compromises to the treatment planning team
- Complex cases should be discussed with other centres for a second opinion and/or peer reviewed once planned.

- Dose constraints

Organs at risk

- **Follow nationally recognised, peer reviewed or trial protocols for constraints.**
- Dose escalation is acceptable within a national/trial protocol scope

- It may not be necessary to include all OAR constraints during optimisation but this will provide dosimetry data and highlight unexpected high dose regions.
- All neural tissue constraints should be respected with high priority unless specified otherwise by the clinician. OAR particularly neural structures should be kept to as low as reasonably possible
- If the OAR dose constraints cannot be met then the Practitioner may opt to accept slightly higher doses to the OARs. In exceptional cases the total dose prescribed may be reduced by the Practitioner

- ICRU 83[10] recommends the use of 'near-max' tolerances, suggested below as 0.01cc or 0.1cc, though centres may use other values if justified.

- For all radical cases, if the mean radiation dose to the spleen >10Gy, consider a vaccination programme and prophylactic antibiotic regimen as laid out in RCR- 'Incidental irradiation of the spleen' [9]

- **The following OAR constraints are adapted from ILROG[8] and site specific network wide local protocols. They are recommended to be used as a guide only and should be adapted depending on lymphoma type and treatment indication.**
- **Additional OAR may also be included depending on treatment site and should follow local protocols**

		Dose Constraints		
OAR	**Parameter**	**Mandatory constraint**	**Optimal constraint**	**Comment**
Head and Neck				
Parotid_(L/R)	Mean dose	<35Gy	<24Gy	
Parotid_CL	Mean dose	-	<14Gy	
Lens_(L/R)	D1%	-	<6Gy	
Lacrimal Gland_(L/R)	D1%	<30Gy	<22Gy	
Thyroid	V25Gy	<62.5%	-	Whole thyroid
Brain				
Lens_(L/R)	D1%	-	<6Gy	
Brain	D0.1cc	-		Record
Parotid_(L/R)	Mean dose	<35Gy	<24Gy	
Above Diaphragm				
Spinal Cord	**D0.1cc**	<45Gy	-	
	D1cc	-	<35Gy	
Lungs	**V20Gy**	-	<30%	
	Mean dose	-	<10Gy	
	V5Gy	<55%	-	
Heart	**Mean dose**	<15 Gy	<5 Gy	
Breast_(L/R)	**Mean dose**	<15 Gy	<4 Gy	For women <30y
Below Diaphragm				
Spinal Cord	D0.1cc	<45 Gy	-	
	D1cc	-	<35 Gy	
Liver	Mean dose	<30 Gy	<28 Gy	
Kidneys (combined)	V20Gy	<35%	<30%	
Kidney_CL	V5.5Gy	<30%	-	If mean to one kidney is >18Gy
Ovary	Dmax	-	<10 Gy	where appropriate
Testis	Dmax	-	<2 Gy	where appropriate
Spleen	Mean dose	-	<10 Gy	
Bladder	V50Gy	<50%	-	
Rectum	V30Gy	<80%	-	
	V40Gy	<65%	-	
Small Bowel	V45Gy	<78 cc	-	
Femur_(L/R)	V50Gy	50%	-	

8. Target VOIs[1]

ISRT-CTV	• **CTV for Involved Site radiotherapy (IS-CTV) includes all initially involved site**
	• **Pre-chemotherapy imaging is used to define the superior and inferior extent of the original disease. This is expanded cranio-caudally by 1.5cm in the direction of lymphatic spread to form the superior and inferior levels of the IS-CTV**
	• **In transverse plane, the IS-CTV includes the nodal chain (or organ) and any residual disease. It is not necessary to encompass entire nodal regions (or adjacent ones)**
	• **CTV is modified by hand to not extend into air, muscle planes or bones unless evidence of direct invasion.**

	IFRT can be considered in circumstances as agreed by MDT
IFRT-CTV	• **Involved field CTV (IF-CTV) will include the anatomical nodal region affected by lymphoma defined by the clinician as that which should be treated by radiotherapy.**
	• **IF-CTV will be outlined to include the involved nodal region, the margins of any tumour mass (primary or residual) in all dimensions and contiguous nodal regions.**
	• **For patients who have had prior chemotherapy, the post chemotherapy volume is used in all directions except cranio-caudal direction where the pre-chemotherapy volume is used**
	• **There may be instances where it will be desirable to modify the IF–CTV to limit toxicity. This will be performed under the clinician's discretion considering site of involvement**

- For **extra nodal disease**: Follow ILROG guidelines[8]

9. Dose prescriptions[1]

Tumour	Treatment inclusion	Fractionations
Hodgkin Lymphoma	Early disease (favourable) (Grade A)	• 20Gy in 10#
	Early disease (unfavourable) (Grade A)	• 30Gy in 15#
	Early disease RT omission (Grade A)	For patients treated with escalated BEACOPP×2 + ABVD ×2, radiotherapy can be omitted if there is CMR on PET scanning after chemotherapy
	Advanced disease Chemotherapy 1st (Grade B)	• 30-36Gy in 15-20#
	Relapsed/Refractory disease Consolidation following chemotherapy (Grade D)	• 30Gy in 15# • 36-40Gy in 18-20# (persistent disease)
	Sole modality treatment	• 30-40Gy in 15-20#
Nodular Lymphocyte predominant Hodgkin lymphoma	ISRT – Early disease (Grade D)	• 30Gy in 15#
Non-Hodgkin Lymphoma	Early stage DLBCL -As part of combined modality treatment (Grade B)	• 30Gy in 15#
	DLBCL Consolidation radiotherapy - CMR following systemic treatment (Grade B)	• 30Gy in 15#
	DLBCL Incomplete response to systemic treatment (Grade C)	• 36-40Gy in 18-20#
	Bridging to CAR-T (Grade C)	• 30Gy in 10-15# • 20Gy in 5#
	Extrapolation of these dose recommendations to other less common subtypes of aggressive NHL is reasonable (with the exception of NK/T-cell)	
Mantle Cell Lymphoma	Radiotherapy alone / Local control with systemic treatment [3] [4]	• 4–30Gy in 2 –15#
Natural Killer (NK) / T-cell Lymphoma	Chemoradiation (Grade C)	• 45-50Gy in 25#
Central nervous system (CNS) Lymphoma	Patients not fit for ASCT or responding to chemotherapy – Consider WBRT (Grade B)	• 23.4-36Gy in 13-20#
Indolent Lymphoma (Follicular, marginal zone, MALT, Lymphoplasmacytic)	Radical Stage I / Durable palliation for advance stage (Grade A)	• 24Gy in 12# • 4Gy in 2# (palliation)
Cutaneous Lymphoma	Mycosis Fungodies	• 8Gy in 2# • 12Gy in 3#
	B-Cell	• 4Gy in 2# • 24Gy in 12#
Solitary Plasmacytoma		• 40-50Gy in 1.8-2Gy #

10. Palliative Intent

- Patients with limited disease and good PS may be considered for definitive Chemo-Radiotherapy to maximise disease control. Patients with advanced disease, but are unfit for Chemo-Radiotherapy, may be considered for standard palliative radiotherapy.
- Conformal Radiotherapy is the primary choice of planning technique for palliative patients. However, IMRT/VMAT Radiotherapy will be considered where it is justifiable, patient appropriate and in circumstances where constraints/targets cannot be achieved through conformal Radiotherapy.

Palliative Dose Fractionations[1]

- **30Gy in 10#**
- **20Gy in 5#**
- **8-10Gy in 1#**
- **4Gy in 2#**

11. Treatment

- Final pre-treatment, Physics and 1st day checks should be carried out as per local protocol.
- These should ideally cover or take into account the following:
  -Monitoring and managing Radiotherapy delays to ensure patients start treatment according to national guidelines
  -Checking plan approval status and parameters as per local protocol
  -All prior preparatory and required patient information is available
  -Imaging requirements for the planned treatment are adequate according to patient plan and local protocol
  -Any prior In vivo dosimetry has been performed as per local protocol.

12. During treatment

- Any monitoring as specified in the local protocol should be performed e.g. dietician review, weight checks, weekly blood counts.
- On treatment imaging as per local protocol. CBCT is strongly recommended.
- For gaps in treatment follow local policy
- On treatment and follow up reviews as per local protocols.
- SGRT / Motion management as per local protocol

13. Late Effects

- Late effects will have been discussed as part of the initial discussions and counselling by the treating clinician and is dependent on the radiotherapy target volumes
- If available, details of the local department's late effects clinic should be provided at the appropriate interval following completion of Radiotherapy.

14. Peer Review

- Peer Review will enable clinicians to provide high quality treatments despite potentially limited referrals. Documenting peer review is essential as per RCR Recommendation 10 + 11.

- In order to meet the RCR standards the review will cover patient selection, prescription and target / OAR delineation. For some cases it may be necessary to review the final treatment plan also.

- The reviewee must provide the reviewer with all relevant clinical information to peer review, which may include demographics, diagnosis and details of proposed treatment. Any relevant clinical tests or images must also be provided (see Table 1 above).
- Responsibility for the patient will remain with the clinician under whom the patient receives their care. If a peer review does not occur, whatever the reason may be, it is that clinician's responsibility to address this.

15. Glossary

Abbreviation	Definition
#	Fraction (i.e. Fractions of treatment)
3DCT	Three dimensional computed tomography (standard CT scan)
CBCT	Cone Beam computed tomography
4DCT	Four dimensional computed tomography
ChemoRT	Chemotherapy with Radiotherapy
CT	Computed tomography
CTV	Clinical target volume
EMRTN	East Midlands Radiotherapy Network
GTV	Gross tumour volume
Gy	Gray (unit of measure for radiation dose)
ICRU	International commission on radiation units and measurements
IMRT	Intensity modulated radiotherapy
ITV	Internal target volume
IR(ME)R	Ionising Radiation (Medical Exposure) Regulations
CAR-T	Chimeric Antigen Receptor T cells
MDT	Multi-disciplinary team
MRI	Magnetic resonance imaging
MALT	Mucosa associated lymphoid tissue
NOG	Network oversight group
FDG	Fluorodeoxyglucose
TSET	Total skin electron therapy
OAR	Organs at risk
PSA	Prostate specific antigen
PET (PET-CT)	Positron emission tomography (Positron emission tomography – computed tomography)
NHL	Non-Hodgkin's Lymphoma
NSHL	Nodular sclerosing Hodgkin lymphoma
PRV	Planning organ at risk volume
PS	Performance status
PTV	Planning target volume
RCR	Royal college of radiologists
RT	Radiotherapy
SABR	Stereotactic ablative Radiotherapy
LDHL	Lymphocyte-depleted Hodgkin lymphoma
NOS	Not otherwise specified
U+E	Urea and electrolytes
VMAT	Volumetric modulated arc therapy
NK	Natural Killer
CLL	Chronic lymphocytic leukemia
DIBH	Deep Inspiration Breath hold
ISRT	Involved site Radiotherapy
IFRT	Involved field Radiotherapy
ILROG	International Lymphoma Radiation Oncology Group
CNS	Central Nervous system

16. References

[1]
- https://www.rcr.ac.uk/media/zckd42lh/10-lymphoma-radiotherapy-dose-fractionation-fourth-edition.pdf

[2]
- Ionising Radiation (Medical Exposures) Regulations (2017).

[3]
- Ning MS, Pinnix CC, Chapman BV et al. Low-dose radiation (4 Gy) with/without concurrent chemotherapy is highly effective for relapsed, refractory mantle cell lymphoma. Blood Adv 2019; 3(13): 2035–2039

[4]
- Dabaja BS, Zelenetz AD, Ng AK et al. Early-stage mantle cell lymphoma: a retrospective analysis from the International Lymphoma Radiation Oncology Group (ILROG). Ann Oncol 2017; 28(9): 2185–2190.

[4]
- Mir et al, Radiother Oncol 2020;150:30-39

[5]
- ICRU Report 83: Prescribing, Recording and Reporting Photon-Beam IntensityModulated Radiation Therapy (IMRT); (2010)

[6]
- ICRU Report 50: Prescribing, Recording and Reporting Photon Beam Therapy; (1993)

[7]
- ICRU Report 62: (Supplement to Report 50); (1997)

[8]
- https://www.ilrog.org/guidelines

[9]
- RCR Incidental irradiation of the spleen- BFCO(21)9 Date: 2021 (https://www.rcr.ac.uk/system/files/publication/field_publication_files/bfco219-incidental-irradiation-spleen.pdf)

- [10]
https://www.icru.org/reports/