



<b>National Imaging Associates, Inc.</b>	
<b>Clinical Guideline:</b> <b>NON-HODGKIN'S LYMPHOMA</b>	<b>Original Date:</b> June 2013 <b>Page 1 of 5</b>
<b>Radiation Oncology</b>	<b>Last Review Date:</b> July 2018
<b>Guideline Number: NIA_CG_133</b>	<b>Last Revised Date:</b> July 2018
<b>Responsible Department:</b> <b>Clinical Operations</b>	<b>Implementation Date :</b> January 2019

## **INTRODUCTION:**

The incidence of non-Hodgkin's lymphomas has increased substantially over the past few decades due to age-related disease. The majority of non-Hodgkin's lymphoma originates in B-lymphocytes (80-85%) with T-lymphocytes comprising 15-20%. Natural killer cell lymphomas are very rare. The classification of non-Hodgkin's lymphoma is based on the cell of origin (large B, large T, or large NK), precursor or mature lymphocytes, as well as genetic, immunophenotype, and clinical features. Radiation therapy is typically delivered to the involved field either alone or in consolidation following chemotherapy. CT-based simulation and 3-dimensional planning is typically advised.

The use of intensity modulated radiation therapy, as well as stereotactic body radiotherapy would be unusual. If requested, this would require peer to peer review to determine medical necessity. For nodal sites, radiation therapy alone or consolidation following chemotherapy should treat the involved field in most cases. Regional/ extended fields are typically not recommended.

Initial Clinical Reviewers (ICRs) and Physician Clinical Reviewers (PCRs) must be able to apply criteria based on individual needs and based on an assessment of the local delivery system.

## **INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:**

Three-dimensional conformal radiation therapy (3D-CRT) or two-dimensional (2D) radiation therapy (2D) is the appropriate technique for treatment of Non-Hodgkin's Lymphomas. The following include radiation dose guidelines for the following lymphomas:

- Follicular lymphoma (24-30 Gy, or 36 Gy if bulky) up to 24 fractions (NCCN, 2018a)
- Mantle cell lymphoma (24-36 Gy) up to 24 fractions (NCCN, 2018a)
- MALT lymphoma – Marginal Zone (24-30 Gy) up to 20 fractions (NCCN, 2018a)
- Diffuse large B cell lymphoma (30-55 Gy) up to 37 fractions (NCCN, 2018a)
- Primary cutaneous anaplastic large cell lymphoma: 24-36 Gy up to 24 fractions (NCCN, 2018d)
- NK/T Lymphoma
  - primary treatment: 50-55 Gy up to 31 fractions
  - combined modality: 45-50.4 Gy up to 28 fractions
  - Localized chronic lymphocytic leukemia (CLL) and Small Lymphocytic Lymphoma (SLL): 24-30 Gy up to 17 fractions

- Palliative dose (up to 10 fractions) for symptom control

*Unless otherwise indicated, standard radiation fractionation consists of 1.5 Gy to 2.0 Gy per day. (NCCN, 2018a)*

#### **TREATMENT OPTIONS REQUIRING PHYSICIAN REVIEW:**

##### **Intensity modulated radiation therapy (IMRT)**

IMRT is not indicated as a standard treatment option and should not be used routinely for the delivery of radiation therapy for non Hodgkin's lymphoma. IMRT is strictly defined by the utilization of inverse planning modulation techniques. IMRT may be appropriate for limited circumstances in which radiation therapy is indicated and 3D conformal radiation therapy (3D-CRT) techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance, the delivery is anticipated to contribute to potential late toxicity, or tumor volume dose heterogeneity is such that unacceptable hot or cold spots are created.

Clinical rationale and documentation for performing IMRT rather than 2D or 3D-CRT treatment planning and delivery will need to:

- Demonstrate how 3D-CRT isodose planning cannot produce a satisfactory treatment plan (as stated above) via the use of patient specific dose volume histograms and isodose plans.
- Provide tissue constraints for both the target and affected critical structures.

##### **Stereotactic Body Radiation Therapy**

Stereotactic Body Radiation Therapy (SBRT) is not currently an approved treatment option for the treatment of Non Hodgkin's Lymphoma. Recent studies comparing SBRT conventional radiation therapy are limited.

##### **Proton Beam Radiation Therapy**

Proton beam is not an approved treatment option for non Hodgkin's Lymphoma. Proton beam has not been proven superior treatment to conventional radiation therapy.

#### **THE FOLLOWING APPLIES TO CMS (MEDICARE) MEMBERS ONLY:**

*For Proton Beam and Stereotactic Radiotherapy refer to Local Coverage Determination (LCD), if applicable.*

## REFERENCES

- Advani R, Rosenberg S, Horning S. Stage I and II follicular non-Hodgkin's lymphoma: Long-term follow-up of no initial therapy. *J Clin Oncol*. 2004; 22:1454-1459. doi: 10.1200/JCO.2004.10.086.
- American College of Radiology (ACR). ACR Appropriateness Criteria®. Diffuse Large B Cell Lymphoma. <https://acsearch.acr.org/docs/3091906/Narrative/>. Published 2014. Retrieved July 13, 2015.
- American College of Radiology (ACR). ACR Appropriateness Criteria®. Localized Nodal Indolent Lymphoma. <https://acsearch.acr.org/docs/3082846/Narrative/>. Published 2013. Accessed May 2, 2018.
- Bentzen SM, Constine LS, Deasy JO, et al. Quantitative analyses of normal tissue effects in the clinic QUANTEC: An introduction to the scientific issues. Introductory paper. *Int J Radiat Oncol Biol Phys*. 2010; 76(3):S3-S9.
- Campbell BA, Voss N, Woods R, et al. Long-term outcomes for patients with limited stage follicular lymphoma: involved regional radiotherapy versus involved node radiotherapy. *Cancer*. 2010; 116:3797-3806. doi: 10.1002/cncr.25117.
- De Sanctis V, Finolezzi E, Osti MF, et al. MACOP-B and involved-field radiotherapy is an effective and safe therapy for primary mediastinal large B cell lymphoma. *Int J Radiat Oncol Biol Phys*. 2008; 72:1154-1160. doi: 10.1016/j.ijrobp.2008.02.036.
- Goda JS, Gospodarowicz M, Pintilie M, et al. Long-term outcome in localized extranodal mucosa-associated lymphoid tissue lymphomas treated with radiotherapy. *Cancer*. 2010; 116:3815-3824. doi: 10.1002/cncr.25226.
- Guadagnolo BA, Li S, Neuberg D, et al. Long-term outcome and mortality trends in early-stage, Grade 1-2 follicular lymphoma treated with radiation therapy. *Int J Radiat Oncol Biol Phys*. 2006; 64:928-934. doi:10.1016/j.ijrobp.2005.08.010.
- Haas RL, Poortmans P, De Jong D, et al. High response rates and lasting remissions after low-dose involved field radiotherapy in indolent lymphomas. *J Clin Oncol*. 2003; 21:2474-2480. doi: 10.1200/JCO.2003.09.542.
- Hartford AC, Palisca MG, Eichler TJ. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guidelines for Intensity-Modulated Radiation Therapy (IMRT). *Int J Radiat Oncol Biol Phys*. 2009; 73(1):9-14.
- Horning SJ, Weller E, Kim K, et al. Chemotherapy with or without radiotherapy in limited-stage diffuse aggressive non-Hodgkin's lymphoma: Eastern Cooperative Oncology Group study 1484. *J Clin Oncol*. 2004; 22:3032-3038. doi: 10.1200/JCO.2004.06.088.

Illidge T, Specht L, Yahalom J, et al. Modern radiation therapy for nodal non-Hodgkin lymphoma-target definition and dose guidelines from the International Lymphoma Radiation Oncology Group. *Int J Radiat Oncol Biol Phys*. May 1, 2014; 89(1):49-58. [http://www.redjournal.org/article/S0360-3016\(14\)00064-9/fulltext#sec3](http://www.redjournal.org/article/S0360-3016(14)00064-9/fulltext#sec3). Accessed May 11, 2017.

Miller TP, Dahlberg S, Cassady JR, et al. Chemotherapy alone compared with chemotherapy plus radiotherapy for localized intermediate- and high-grade non-Hodgkin's lymphoma. *N Engl J Med*. 1998; 339:21-26. doi: 10.1056/NEJM199807023390104.

Morschhauser F, Radford J, Van Hoof A, et al. Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma. *J Clin Oncol*. November 10, 2008; 26(32):5156-5164. doi: 10.1200/JCO.2008.17.2015.

National Comprehensive Cancer Network (NCCN). B-cell Lymphomas V3. [https://www.nccn.org/professionals/physician\\_gls/pdf/b-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf). Published 2018a. Retrieved May 2, 2018.

National Comprehensive Cancer Network (NCCN). Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma V5. [https://www.nccn.org/professionals/physician\\_gls/pdf/cll.pdf](https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf). Published 2018b. Accessed May 2, 2018.

National Comprehensive Cancer Network (NCCN). Hairy Cell Leukemia V2. [https://www.nccn.org/professionals/physician\\_gls/pdf/hairy\\_cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf). Published 2018c. Accessed May 2, 2018.

National Comprehensive Cancer Network (NCCN). T-cell Lymphomas V3. [https://www.nccn.org/professionals/physician\\_gls/pdf/t-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf). Published 2018d. Accessed May 2, 2018.


Phan J, Mazloom A, Medeiros LJ, et al. The benefit of consolidative radiation therapy in patients with diffuse large B-cell lymphoma treated with R-CHOP chemotherapy. *J Clin Oncol*. 2010; 28:4170-4176. doi: 10.1200/JCO.2009.27.3441.

Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin*. 2012; 62:10-29. doi: 10.3322/caac.20138.

Wilder RB, Jones D, Tucker SL, et al. Long-term results with radiotherapy for Stage I-II follicular lymphomas. *Int J Radiat Oncol Biol Phys*. 2001; 51:1219-1227. [http://www.redjournal.org/article/S0360-3016\(01\)01747-3/abstract](http://www.redjournal.org/article/S0360-3016(01)01747-3/abstract).

Witzig TE, Gordon LI, Cabanillas F, et al. Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. *J Clin Oncol*. May 15, 2002; 20(10):2453-2463. doi: 10.1200/JCO.2002.11.076.

Zinzani PL, Stefoni V, Finolezzi E, et al. Rituximab combined with MACOP-B or VACOP-B and radiation therapy in primary mediastinal large B-cell lymphoma: a retrospective study. *Clin Lymphoma Myeloma*. 2009; 9:381-385. doi: 10.3816/CLM.2009.n.074.

Reviewed / Approved by  Caroline Carney, MD, Chief Medical Officer