

## Head and neck cancer

### *Overview*

IMRT (intensity modulated radiotherapy) is the accepted RT (radiotherapy) method for patients undergoing primary and adjuvant radiotherapy for HNSCC (head and neck squamous cell carcinoma), except in T1/2 N0 glottic cancer and for low-dose palliative RT (The Royal College of Radiologists, 2019). A meta-analysis showed a modest overall survival and local control benefit when hyperfractionation was used in oropharynx and larynx cancers, though these schedules can be hard to implement and are not widely used (Bourhis & Overgaard, 2006; The Royal College of Radiologists, 2019). Guidelines suggest no benefit of altered fractionation in those >70yrs (The Royal College of Radiologists, 2019).

### *Stage I/II disease, primary radiotherapy*

For stage I/II disease, patients that are fit for curative surgery may have primary radiotherapy (oropharynx, unknown primary, glottic larynx, supraglottic, hypopharynx), or patients may have primary radiotherapy in nasal cavity/paranasal sinus cancer if they are unsuitable for curative surgery. Currently, the recommendations for stage I/II cancer are 70Gy in 35# (fractions) over 6/7 weeks (for oropharynx, nasal cavity/paranasal sinuses, supraglottic and hypopharynx), 65-66Gy in 30# over 6 weeks (oropharynx, nasal cavity/paranasal sinuses, glottic larynx, supraglottic and hypopharynx cancer) and 66Gy in 33# (oropharynx, nasal cavity/paranasal sinuses, supraglottic, hypopharynx cancer) (Eisbruch & Harris, 2010; The Royal College of Radiologists, 2019; Overgaard & Hansen, 2003; Bourhis & Overgaard, 2006; Lacas, et al., 2017). Additional regimes are used in some local trust policies, including 60Gy/54Gy in 30# over 6 weeks by IMRT for oropharynx, supraglottic and larger T2N0 glottic larynx carcinomas (Benson, et al., 2019). For T1/2N0 glottic carcinoma, 63Gy in 28# over 5.5 weeks, 50Gy in 16# over 3 weeks or 55Gy in 20# over 4 weeks are also recommended (Gowda & Henk, 2003; Ermis & Teo, 2015; The Royal College of Radiologists, 2019). For unknown primary, IMRT can be given at dose 60Gy/53Gy in 30# over 6 weeks, though if p16 is positive primary is assumed to be oropharynx and treated at 60Gy, whereas if EBV positive and p16 negative, 70Gy/60Gy/56Gy in 35# over 7 weeks is recommended (Benson, et al., 2019).

### *Stage I-IV disease, radiotherapy only*

For lip cancer that is unsuitable for surgery, radiotherapy can be used at 55Gy/20# over 4 weeks, 50Gy/15# over 3 weeks or 45Gy/10# over 2-3 weeks (Kerawala, et al., 2016; Benson, et al., 2019). The same doses are used in PORT (post-operative radiotherapy) for larger lip lesions. In oral cavity cancer, patients unfit for curative surgery may only have RT at 65Gy/60Gy/54Gy in 30# over 6 weeks, or if small volume disease/frail patients, 50Gy can be given in 20# over 4 weeks (Benson, et al., 2019). Nasopharyngeal cancer recommendations are 70Gy/60Gy/56Gy in 35# over 7 weeks, 70Gy in 33# over 6.5 weeks and 65Gy in 30# over 6 weeks. (The Royal College of Radiologists, 2019; Benson, et al., 2019; Lee & Lin, 2012; Colaco, et al., 2013; Lee & Harris, 2009)

### *Stage I-IVb – primary surgery, the post-operative radiotherapy (PORT)*

Overall, PORT recommendations for oropharynx, nasal cavity/paranasal sinuses, unknown primary, oral cavity, glottic larynx stage III-IV, salivary gland, supraglottic and hypopharynx are 60Gy in 30# over 6 weeks and a dose of up to 66Gy in 33# over 6.5 weeks to high risk subvolumes (areas surrounding extracapsular spread and/or positive/close margins (Bernier & Dommenege, 2004; Cooper & Zhang, 2012; Bernier & Cooper, 2005; The Royal College of Radiologists, 2019; Lund & Clarke, 2016; Sood & McGurk, 2016). Further possible regimes include 65Gy in 30# (if margins positive or macroscopic

residual disease), 54Gy (to areas at risk of microscopic disease) and 50Gy in 20# (in patients that have reduced performance status or in frail elderly patients that are unlikely to tolerate 6 weeks of treatment, or 55Gy in these patients if there are positive margins, or macroscopic residual disease) (Henderson, et al., 2015). For metastatic neck nodes skin primary, PORT regimes can be used if there is high risk of recurrence, >2 nodes affected or if there is extracapsular spread, including 60Gy in 30# over 6 weeks, 50Gy/20# in frail/elderly patients or those that have reduced performance status, or 55Gy these patients if they have positive margins or macroscopic residual disease (Benson, et al., 2019). In pleomorphic adenomas, an additional regime of 45Gy/25# may be used (Benson, et al., 2019).

#### *Stage III-IVb primary RT + chemotherapy, then surgery*

For patients that are fit for and have disease suitable for surgery and systemic therapy, including in oropharynx, supraglottic and hypopharynx cancer, though excluding nasopharyngeal cancer, the recommendation is 70Gy in 35# over 7 weeks, or 65-66Gy/30# over 6 weeks (Bernier & Domezge, 2004; Cooper & Zhang, 2012; Bernier & Cooper, 2005; The Royal College of Radiologists, 2019; Bourhis & Sire, 2012; Nguyen-Tan & Zhang, 2014; Pracy & Loughran, 2016; Paleri & Roland, 2016).

#### *Stage III-IVb primary RT, no chemotherapy, then surgery*

For patients that are fit for and have disease suitable for curative surgery/therapy, but who are either over 70yrs old, or are <70yrs old, but due to choice or co-morbidities do not have chemotherapy, the recommendations are 70Gy in 35# over 6 or 7 weeks, 66Gy in 33#, 65-66Gy in 30# over 6 weeks (oropharynx, supraglottic, hypopharynx) and also 60Gy/54Gy in 30# over 6 weeks for supraglottic and hypopharynx cancer (The Royal College of Radiologists, 2019) and (Benson, et al., 2019). For unknown primary, the recommended doses are the same as for stage I/II unknown primary, indicated previously (Benson, et al., 2019).

#### *Stage III-IVb, radiotherapy*

If patients are elderly or have multiple co-morbidities making them unsuitable for surgery they may only have radiotherapy. For nasal cavity/paranasal sinus cancer and T3/4 glottic larynx cancer, 65Gy/60Gy/54Gy in 30# over 6 weeks can be given, or if patients are elderly or have a poor performance status, 55Gy in 20# over 4 weeks may be given (Benson, et al., 2019). Conventional fractionation regimes of 70Gy/35# in 6/7 weeks, and 65-66Gy in 30# over 6 weeks can also be used (The Royal College of Radiologists, 2019).

#### *Palliative RT*

Palliative RT may be given for cancer of any stage if the patient is not suitable for curative therapy (including surgery, or systemic treatments) and for stage IVc only if the patient is symptomatic. Current recommendations are broad. For oropharynx, unknown primary, oral cavity, lip, supraglottic, metastatic neck nodes skin primary, glottic, hypopharynx and salivary gland tumours, the current recommendations include 40Gy in 10# over 4 weeks (split course), 21Gy in 3# over 3 weeks, 20Gy in 5# over 1 week and 14Gy in 4# (The Royal College of Radiologists, 2019). Other regimes include 30-36Gy in 6-10 # over 2 weeks in most patients or over 3 weeks if frail, 50Gy in 20# daily and 40Gy in 10# at 3# per week (Benson, et al., 2019). *Total = 905 words, not including in-text citations*

## Bibliography

Benson, R., Barnett, G. & Jadon, R., (2019). *Head and Neck Unit: Radiotherapy and Chemotherapy Protocols (draft)*, Cambridge University Hospitals NHS Foundation Trust: Cancer Division and Haematology Directorate.

Bernier, J. & Cooper, J., (2005). Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (#9501). *Head Neck*, 27, 843-850.

Bernier, J. & Domette, C., (2004). Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med*, 11, 1945-1952.

Bourhis, J. & Overgaard, J., (2006). Hyperfractionated or accelerated radiotherapy in head and neck cancer: a meta-analysis. *Lancet*, 368, 843-854.

Bourhis, J. & Sire, C., (2012). Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised trial. *Lancet Oncol*, 13, 145-153.

Colaco, R. J., Betts, G. & Donne, A., (2013). Nasopharyngeal carcinoma - a retrospective review of demographics, treatment and patient outcome in a single centre. *Clin Oncol*, 25, 171-177.

Cooper, J. & Zhang, Q., (2012). Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. *Int J Radiat Oncol Biol Phys*, 84, 1198-1205.

Eisbruch, A. & Harris, J., (2010). Multi-institutional trial of accelerated hypofractionated intensity-modulated radiation therapy for early-stage oropharyngeal cancer (RTOG 00-22). *Int J Radiat Oncol Biol Phys*, 76, 1333-1338.

Ermis, E. & Teo, M., (2015). Definitive hypofractionated radiotherapy for early glottic carcinoma: experience of 55Gy in 20 fractions. *Radiat Oncol*, 10, 203.

Gowda, R. & Henk, J., (2003). Three weeks radiotherapy for T1 glottic cancer: the Christie and Royal Marsden Hospital Experience. *Radiother Oncol*, 68, 105-111.

Henderson, M. A., Burmeister, B. H., Ainslie, J. & Fisher, R., (2015). Adjuvant Lymph-Node Field Radiotherapy Versus Observation Only in Patients With Melanoma at High Risk of Further Lymph-Node Field Relapse after Lymphadenopathy (ANZMTG 01.02/TROG 02.01):6-year Follow-Up of a Phase 3, Randomised Controlled Trial. *Lancet Oncol*, 16, 1049-1060.

Kerawala, C., Roques, T., Jeannon, J. & Bisase, B., (2016). Oral cavity and lip cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology*, 130, S83-S89.

Lacas, B., Bourhis, J. & Overgaard, J., (2017). Role of radiotherapy fractionation in head and neck cancers (MARCH): An updated Meta-Analysis. *Lancet Oncol*, 18, 1221-1237.

Lee, N. & Harris, J., (2009). Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: radiation therapy oncology group phase II trial 0225. *J Clin Oncol*, 27, 3684-3690.

Lee, A. & Lin, J., (2012). Current management of nasopharyngeal cancer. *Semin Radiat Oncol*, 22, 233-244.

Lund, V. & Clarke , P., (2016). Nose and paranasal sinus tumours: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology* , 130, S111-118.

Nguyen-Tan, P. & Zhang , Q., (2014). Randomized phase III trial to test accelerated versus standard fractionation in combination with concurrent cisplatin for head and neck carcinomas in the Radiation Therapy Oncology Group 0129 trial: long-term report of efficacy and toxicity. *J Clin Oncol* , 32, 3858-3866.

Overgaard, J. & Hansen , H., (2003). Five compared with six fractions per week of conventional radiotherapy of squamous-cell carcinoma of head and neck:DAHANCA 6 and 7 randomised controlled trial. *Lancet* , 362, 933-940.

Paleri, V. & Roland, N., (2016). Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology*, 130.

Pracy, P. & Loughran, S., (2016). Hypopharyngeal cancer: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology*, 130, S104-110.

Sood, S. & McGurk , M., (2016). Management of Salivary Gland Tumours: United Kingdom National Multidisciplinary Guidelines. *The Journal of Laryngology and Otology* , 130, S142-S149.

The Royal College of Radiologists, (2019). *Radiotherapy dose fractionation, third edition*. [Online] Available at:

[https://www.rcr.ac.uk/system/files/publication/field\\_publication\\_files/brfo193\\_radiotherapy\\_dose\\_fractionation\\_third-edition.pdf](https://www.rcr.ac.uk/system/files/publication/field_publication_files/brfo193_radiotherapy_dose_fractionation_third-edition.pdf)

[Accessed 20 December 2019].