NCCP advice for medical professionals on acceptable dose fractionation during the novel coronavirus (COVID-19) pandemic

This document relates to patients who do not have COVID-19 or are not suspected of having COVID-19.

Current events surrounding the COVID-19 pandemic are challenging and all public health bodies are placing the safety of patients, staff and communities first in all decisions.

This is an evolving situation. This advice is based on current information, it is additional to the advice of the NPHET, the HSE and the DoH, and will be updated as necessary.

The NCCP acknowledges that each hospital is working under individual constraints, including staff and infrastructure, and as a result will implement this advice based on their own unique circumstances.

The purpose of this advice is to maximise the safety of patients and make the best use of HSE resources, while protecting staff from infection. It will also enable services to match the capacity for cancer care to patient needs if services become limited due to the COVID-19 pandemic.

Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment.

COVID-19 vaccination is now available and is being rolled out to priority groups as agreed nationally. More information on the vaccine and its roll-out is available online from the HSE here: https://www2.hse.ie/screening-and-vaccinations/covid-19-vaccine/getting-covid-19-vaccine.html

Information for cancer healthcare professionals on vaccinations is available on the NCCP website at https://www.hse.ie/eng/services/list/5/cancer/profinfo/covid-19.html

Receipt of the vaccine (by either healthcare workers or their patients) does not eliminate the need to use appropriate PPE and adhere to public health advice in relation to COVID-19.

NPHET, HSE and DoH advice

Hospitals will operate under the overarching advice of the National Public Health Emergency Team (NPHET), the HSE and the DoH. Information is available at:

- HSE HPSC - https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/
- HSE Coronavirus (COVID-19) - https://www2.hse.ie/conditions/coronavirus/coronavirus.html
- DoH Coronavirus (COVID-19) - https://www.gov.ie/en/campaigns/c36c85-covid-19-coronavirus/

The NCCP has defined a number of principles to underpin the delivery of cancer care, where this needs to be delivered outside of cancer centres or the usual designated place of care. These are outlined on the NCCP website at:https://www.hse.ie/eng/services/list/5/cancer/proinfo/covid-19.html

1 Purpose

The purpose of this advice is to provide guidance for medical professionals on acceptable dose fractionation during the COVID-19 pandemic.

2 Acceptable fractionation schedules for cancer patients

These are acceptable fractionation schedules for cancer patients during the COVID-19 pandemic, please refer to the 'NCCP advice on radiation therapy capacity escalation plan in response to the current COVID 19 pandemic' for more information.

Current standard fractionation is acceptable during the pandemic if capacity allows.

Planning meetings are essential during the COVID-19 pandemic. If a planning meeting is not possible the radiotherapy plan should be reviewed by a second Consultant. Any patients with a cancer site not outlined in the below document should be discussed at a peer review meeting or in consultation with another consultant.

3 Recommendations and quality of the evidence

3.1 Breast cancer patients

For advice for medical professionals on the radiation oncology management of breast cancer patients please refer to 'NCCP guidance for Medical Professionals on the management of patients undergoing Breast Cancer Radiotherapy in response to the current novel coronavirus (COVID-19) outbreak'.

3.2 Prostate cancer patients

For advice for medical professionals on the radiation oncology management of prostate cancer patients please refer to 'NCCP advice for Medical Professionals on the management of patients undergoing Prostate Cancer Radiotherapy in response to the current novel coronavirus (COVID-19) outbreak'.

3.3 Lung cancer patients

For advice for medical professionals on the radiation oncology management of lung cancer patients please refer to 'NCCP advice for medical professionals on the management of patients undergoing Lung Cancer Radiotherapy in response to the current novel coronavirus (COVID-19) pandemic'.

3.4 Thyroid cancer patients

For advice for medical professionals on the radiation oncology management of thyroid cancer patients please refer to 'NCCP advice for medical professionals on the management of Thyroid Cancer and Overactive Thyroid Disease in response to the current novel coronavirus (COVID-19) pandemic'.

3.5 Head and Neck cancer patients

For advice for medical professionals on the radiation oncology management of Head and Neck cancer patients please refer to 'NCCP guidance for Medical Professionals on the management of patients with head and neck cancer undergoing radiotherapy in response to the current COVID-19 pandemic'.

3.6 Bladder cancer patients

Recommendations: 52.5 - 55Gy / 20 fractions should be considered.

Quality of the Evidence:

- 55Gy / 20 fractions as was used in the BC2001 (1, 2) and BCON (3) trials. A recent meta-analysis found 55Gy / 20 fractions to be non-inferior to 64Gy / 32 fractions in terms of invasive loco-regional control and late bladder and bowel toxicity (4). Level of evidence: Moderate
- 52.5Gy / 20 fractions has been used in studies (5, 6) and is another option recommended by the Royal College of Radiologists (7). Level of evidence: Low.

3.7 Endometrial cancer patients

Adjuvant radiotherapy

Recommendations

- **Intermediate risk patients:** Observation may be considered.
- **High risk patients:** 46Gy / 23 fractions or vault brachytherapy (21Gy / 3 fractions) alone may be considered.
- **Highly selected stage III or serous carcinomas:** 48.6Gy / 27 fractions may be considered.

Quality of the Evidence:

- **Intermediate risk patients:** The PORTEC 1 trial found the majority of locoregional relapses following surgery for stage 1 endometrial cancer were located in the vaginal vault, with good outcomes following salvage therapy (89% complete response and 65% 5-year survival). There was no survival difference between patients with pelvic relapse and those with distant metastases (8). Level of evidence: Moderate.
- **High risk patients** - 46Gy / 23 fractions was used in the PORTEC 1 (9) study. Vault brachytherapy (21Gy / 3 fractions) alone if available for patients where the benefit of EBRT is uncertain as used in the PORTEC 2 study (10). Level of evidence: Moderate.
- **Highly selected stage III or serous carcinomas** - Chemoradiotherapy 48.6Gy / 27 fractions was used in the PORTEC 3 study (11, 12). Level of evidence: Moderate.

3.8 Cervical cancer patients

Recommendations

In patients with cervical cancer medical professionals may consider the following:

- **Radical cervix:** reducing the number of fractions (e.g. 46 Gy/23 fractions)
- **Brachytherapy:** Use standard 21Gy / 3 if capacity allows. EBRT boost may need to be considered if brachytherapy not available
- **Adjuvant therapy:** reducing the number of fractions (e.g. 46 Gy/23 fractions)

Quality of the Evidence:

- 46 Gy / 23 fractions has been used in several studies (13, 14) Level of evidence: Low.

3.9 Oesophageal cancer patients

Recommendations:

- **Preoperative chemoradiotherapy:** 41.4Gy / 23 fractions should be considered. In case of level 3 capacity, 40Gy/15 fractions may be considered.
- **Definitive chemoradiotherapy:** 50.4Gy / 28 fractions should be considered.

Quality of the Evidence:

- **Preoperative chemoradiotherapy:** CROSS regimen (15). Level of evidence: Moderate. At reduced capacity 40Gy / 15 fractions can be considered with cisplatin/FU (16). Level of evidence: Low.
- **Definitive chemoradiotherapy:** 50.4Gy / 28 fractions has been shown to be effective in several studies (17, 18). Level of evidence: Moderate.

3.10 Rectal cancer patients

Recommendations:

- **Preoperative long course chemoradiotherapy (LCCRT):** 45-50.4 Gy / 25-28 fractions should be considered.
- **Preoperative short course radiotherapy:** 25Gy / 5 fractions should be considered.

Quality of the Evidence:

- **Preoperative long course chemoradiotherapy (LCCRT):** 45-50.4 Gy / 25-28 fractions has been used in several studies (19-22). Level of evidence: Moderate.

- **Preoperative radiotherapy:** 25Gy / 5 fractions (21, 23-26) followed by immediate surgery within a week or surgery delayed for 6-8 weeks if unfit for LCCRT or if LCCRT delivery not an option due to reduced capacity (27, 28). Level of evidence: Moderate.

3.11 Anal cancer patients

Recommendations

- Standard fractionation regimens are recommended due to curative potential of chemoradiotherapy.
- **Definitive chemoradiotherapy:** Early stage: 50.4Gy / 28 fractions should be considered.
- **Advanced stage:** If IMRT available, 53.2Gy / 28 fractions to primary and involved nodes with 40Gy / 28 fractions to uninvolved nodes may be considered.

Quality of the Evidence:

- ACT II trial (29). RTOG 98-11 trial (30). Level of evidence: Moderate.

3.12 Lymphoma patients

- In patients with lymphoma medical professionals may consider the ILROG emergency guidelines for radiation therapy of haematological malignancies during the COVID-19 pandemic (31).

3.13 Palliative Radiotherapy

Recommendations:

In patients receiving palliative care medical professionals may consider the following:

Use as few fractions as possible.

- Bone metastases: Single 8 Gy fraction is recommended where possible (32)
- Spinal cord compression: Single 10 Gy may be considered (ICORG) (33)
- Gynae cancer: Single 8-10 Gy, can be repeated up to three times (34-36) or 21Gy / 3 fractions day 0,7,21 (37)
- Bladder cancer: 21Gy / 3 fractions alternate days over 1 week or single 8 Gy for patients with poor performance status (38). High dose palliative: 30-36 Gy in 5 or 6 weekly fractions (39, 40).
- Lung cancer: 20Gy/5 fractions. For poor PS patients 16Gy in 2 fractions or single fraction of 10Gy (41, 42).
- Brain metastases (multiple): 20Gy in 5 fractions (43, 44), consider single fraction SRS if clinically appropriate and the patient has a good performance status and absent or controlled extracranial disease (45, 46).
- Upper GI:
    - Oesophagus: 30Gy in 10 fractions or 20Gy in 5 fractions (47). Single 12 Gy fraction intraluminal brachytherapy or stent insertion to relieve dysphagia are alternative options, with intraluminal brachytherapy reported to have improved survival and quality of life and fewer requirements for intervention (48-50).
    - Gastric cancer: single 8Gy fraction or 20Gy in 5 fractions for bleeding with more prolonged fractionation schedules not having any clear benefit (51).
    - Lower GI: 20–25 Gy in 5 fractions or 30Gy in 10 fractions (34, 52).
- Palliative Lymphoma: In patients with lymphoma medical professionals may consider the ILROG emergency guidelines for radiation therapy of hematological malignancies during the COVID-19 pandemic (31)

4 Benefit and Harm

The guidance development group agreed that the patients would benefit from reduced attendance in hospital and therefore less risk of contracting COVID-19. Hypofractionation provides the ability to

complete treatment in a rapidly changing environment with reduced capacity. The use of hypofractionation allows each of the centres to treat more patients as it reduces the number of visits per individual patient. It therefore maximises the use of resources.

Some of the alternative treatment and the fractionations schedules recommended are based on lower levels of evidence than that of standard fractionation schedules. There is potential for increased anxiety in patients due to less face to face interaction with healthcare professionals, which may also result in limitations in clinical management. Communication of the justification for changes to a patient's treatment plan is paramount to help reduce a patient's anxiety.

5 Justification for Change

The purpose of this advice is to conserve scarce resources and optimise benefit of treatment whilst reducing harm to patients.

6 Equity, acceptability, preferences and values

Modification of the treatment plan has been found to be acceptable by patients. Patients should be informed prior to commencing treatment of any deviation from standard dose fractionation schedules in their management due to COVID-19 and why these changes are necessary.

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