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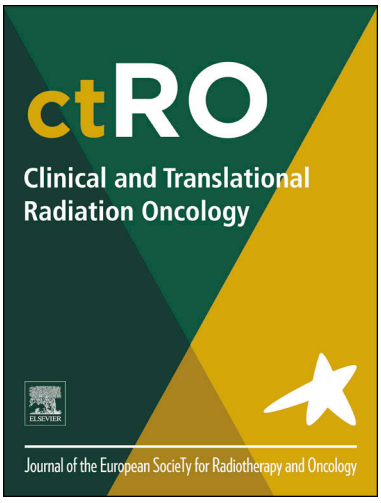


# COVID-19: Global Radiation Oncology's Targeted Response for Pandemic Preparedness

Richard Simcock, Toms Vengaloor Thomas, Christopher Estes Mercy, Andrea R. Filippi, Matthew A Katz, Ian J Pereira, Hina Saeed

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**COVID-19: Global Radiation Oncology's Targeted Response for Pandemic Preparedness**

Richard Simcock, Sussex Cancer Centre, UK
Toms Vengaloor Thomas, University of Mississippi Medical Center, USA
Christopher Estes, Mercy Hospital, Springfield, MO , USA
Andrea R. Filippi, Radiation Oncology, Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy
Matthew A Katz, Lowell, MA, USA
Ian J Pereira, Ontario, Canada
Hina Saeed, Medical College of Wisconsin, USA

**Abstract**

As the global COVID-19 pandemic escalates there is a need within radiation oncology to work to support our patients in the best way possible. Measures are required to reduce infection spread between patients and within the workforce. Departments need contingency planning to create capacity and continue essential treatments despite a reduced workforce.
The #radonc community held an urgent online journal club in March 2020 to discuss these issues and create some consensus on urgent next steps. There were 121 global contributors. This document summarises these discussions around themes of infection prevention, rationalisation of workload and working practice in the presence of infection

**Introduction**

On 11th March, 2020 WHO Director-General Tedros Adhanom Ghebreyesus declared that the novel coronavirus (COVID-19) outbreak a pandemic with over 118,000 cases, more than 4,000 deaths. The virus has found a foothold on every continent except for Antarctica. Exponential growth in those figures is sadly expected.

Global response to this crisis is required in all aspects of healthcare to mitigate the effects of COVID-19 both on patients directly affected by the disease but also on healthcare services that will struggle to support the health of others in a system under stress. The pandemic has

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already necessitated massive healthcare reorganisation in China and Italy. Similar effects are now being observed across the globe. Coping with the crisis requires strong leadership, prior preparation, resources, and clear communication. Champions are required to guide best practices in this fight.

There are specific issues that are pertinent to the practice of radiation oncology in these circumstances related to staffing, patient population, equipment and treatment types (See Table 1). Radiation oncology departments treat a mixed population (unwell palliative patients alongside relatively fit patients receiving preoperative, adjuvant and definitive treatments). Treatment courses may be long with efficacy affected by interruptions, gaps or delays and the ability to use systemic treatments. The treatment equipment is static and used by different patients in constant sequence raising the possibility of cross contamination.

COVID-19 is already impacting providers due to a shrinking oncology workforce. Drivers include cautionary isolation, infection and providers pulled to other services. It is also impacting cancer patients directly. Patients already facing the hardship of cancer, many are likely more susceptible to this infection and are cancelling appointments due to fear of infecting others or being exposed to infection themselves. The current trajectory will see poor outcomes for providers and patients.

Radiation oncologists have had to support their patients and teams through previous disease outbreaks and natural disasters and there are important lessons to be learned. The documented responses to SARS epidemic in Singapore and Hurricane Maria in Puerto Rico are relevant recent examples [1, 2]. One important message from these experiences was the need to **P**repare, **C**ommunicate, **O**perate and **C**ompensate (PCOC). However, the COVID-19 situation is different. Unlike SARS, its scale is much larger (25x cases at the time of writing – 200k vs. 8k; 8x deaths – 8k vs 800; ) making outbreak measures less effective. Unlike natural disasters, its impact is entirely biologic.

**Methods**

Over the weekend of 13-15$^{th}$ March 2020 an online Twitter discussion was held as part of the Radiation Oncology Journal Club (#RadOnc #jc) and moderated by the authors. Members of the global radiation oncology community were invited to comment on issues relevant to the delivery of most effective care during the time of a global pandemic. The conversation was based around the themes of how to reduce transmission, mitigate consequences of reduced workforce and how to continue treatment in the presence of infection. Wakelet, a social media content organization platform, was used in real-time to summarize key insights to help guide the discussion and provide faster knowledge-sharing. Tweets were then reviewed and grouped into themes that formed the basis for these guidelines. A literature review supplemented data where available to expand on issues raised. Results were summarized into consensus-based guidelines.

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**Results**

During the weekend over 121 individuals from 17 countries and 6 continents contributed to the online discussion. Contributions from those listed (see Appendix 1) have been collated online [3] . Content was guided by previous frameworks (Table 1 below) and summarized into three themes (minimizing transmission for maximal social distancing, triaging limited resources equitably, and treating patients with infection) and forms the basis for this document which expands on the issues raised and supplements with data where possible

Synchronous to our online conversation both ESTRO and ASTRO produced statements which also support the key messages of this document [4, 5]

**1. Minimising the risk of COVID transmission during radiotherapy treatment**

Current evidence suggests COVID-19 is spread by droplets and has an incubation period of 1-14 days. The most common symptoms of confirmed cases are fever, cough, and shortness of breath. However, some cases have been found to be asymptomatic or mildly symptomatic, leading to higher than expected transmission rates.

The most effective way to protect staff and patients from COVID-19 is to reduce infection rates. Governments and International health organisations have regularly updated their guidance on self-isolation, social distancing and quarantine rules and these will continue to evolve during the pandemic. Cities and regions are now moving to intense suppressive measures that maximize social distancing for all populations to "flatten the curve" enough to meet available resources and avoid significant deaths. For healthcare workers, this means reducing the need for patients to attend a clinical environment to the lowest possible levels.

Initial assessments are likely to still require face to face visits, but a large amount of follow-up activity can be conducted as telephone or telemedicine where technology allows. Telephone follow up is shown to be possible in multiple cancer settings including. Endometrial [6] prostate [7] lung [8] and colorectal cancer [9]. It has been used in successfully in patients with advanced cancer [10]. It is highly suitable for patients with comorbidities and difficulties with travel and is associated with high patient satisfaction [11, 12]. We recommend that wherever possible consultations are moved to a remote monitoring or telephone alternative as quickly as possible to reduce unnecessary patient traffic through departments. Financial disincentives to telephone consultation should be removed from systems wherever possible. In the USA the CMS (Centre for Medicare and Medicaid) have expanded the benefits to include telemedicine services for Medicare patients.

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Video consultations are a helpful adjunct to telemedicine and may be very valuable during the COVID-19 pandemic but lack of this technology should not delay moves to remote monitoring by telephone [13]

The online group alongside authors helped develop an online tool with key prompts to help with telephone consultations and remote monitoring available at http://bit.ly/COVID_OncFU

Where patient attendance is considered essential it is recommended that the number of additional visitors, family members or carers is kept to a minimum.

**2. Prioritising treatments**

We make treatment decisions supported by evidence. Different circumstances may also call for different approaches to evidence. While in normal circumstances practitioners will favour Level I evidence for treatment recommendations, under situations of externally elevated risks, one may have a higher consideration for regimens that are less common such as those supported by phase II, prospective evidence, or possibly even retrospective series.

Making appropriate treatment decisions with patients requires a careful balance of risks and benefits. When our treatments are accompanied by good quality evidence, we have good estimates of benefit and can consent with access to data on likely acute and long-term harms. The risk benefit ratio of treatment changes in the context of a pandemic. If the likelihood of serious infection increases or the likelihood of the outcome of that infection being more serious increases, then the risk may start to outweigh the benefit. Estimating the harms of COVID infection for cancer patients is currently difficult because there have been too few reported events for modelling. A simple model could use the risk of COVID infection multiplied by risk of serious morbidity/mortality. If a patient has a 5% risk of infection and 10% risk of death from infection there may be a 0.5% mortality through exposure and attendance for radiotherapy. If the patient is young and healthy with a 5% risk of infection and 1% risk of death, then there is 0.05% mortality from COVID-19. The use of chemotherapy in combination with radiotherapy is likely to very significantly increase the risk of morbidity and mortality from synchronous COVID-19 infection.

A further need for prioritisation arises due to the expected shortfall in staffing levels. This may make it difficult for a department with reduced capacity to deliver all planned fractions. Creating capacity by reducing fraction numbers is an important part of preparation for high infection numbers

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**2.1 Radical Treatments**

Where radiotherapy is being delivered for cure there may be no reasonable alternative to proceeding with treatment at the earliest opportunity. If disease biology allows for a delay in treatment (e.g. in the cases of hormonally responsive breast and prostate cancers) then deferring treatment until an expected fall in COVID-19 cases is sensible. Whilst deferral may seem immediately preferable it may have unintended consequence in creating a further unmanageable surge in activity when the crisis has passed.

**2.2 Adjuvant Treatments**

If a patient is being offered radiotherapy as an adjunct to prior surgery, then a careful estimation of risk benefit is required to continue to justify the treatment. Patients who may only gain modest benefit in terms of long-term survival gains may wish to avoid radiotherapy during pandemic. Treatments which reduce loco-regional recurrence rates but do not improve survival might also have reduced priority during a pandemic and it may be appropriate to avoid.

**2.3 Palliative Treatments**

If radiotherapy is delivered for symptom relief then it is best to ensure that all other options have been fully explored e.g. maximising analgesia or bisphosphonates in the case of bone pain [14].

Patients receiving radiotherapy for palliation are best served already by the smallest number of hospital visits necessary to gain a therapeutic outcome. If these trips further risk shortening life through infection, then careful thought should be given to whether or not their symptoms may be palliated medically in preference. If radiotherapy is given to painful bone metastases then multiple studies have demonstrated a single 8Gy fraction to be as efficacious as multiple-fraction courses [15]. Sadly audit data show that the regimen is underused however it should become the default during the pandemic[16] [17]. Recent trial data also reassures that this is an appropriate fractionation for those with malignant spinal cord compression[18].

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The palliation of brain metastases with whole brain radiotherapy is controversial and these patients may maintain equivalent quality of life at the end of life by the use of steroids alone and avoid the risks of hospital attendance [19]. Stereotactic radiosurgery may still be appropriate but needs individualised discussion with patients.

**2.4 Specific Disease Recommendations**

In considering appropriate treatment changes there are multiple lines of evidence that are available to us in choosing regimens that are favourable in terms of fractionation or give us confidence to advise patents not to proceed with radiotherapy. Therapies that have been considered standard of care based on evidence should be reconsidered in the context of the current situation. Some of these are documented in Table 2. It is important to consider that risk-benefit is unique to each patient, disease, and the impact of the pandemic on workforce and risk all of which will change over time. A balance must be struck at each institution. We have sought to provide fair guidelines for specific situations below. Evidence links and brief dose constraint guidance are given for situations where palliative treatment (Table 3) and radical treatment (Table 4) may be altered. Table 5 lists therapies that may be delayed.

**2.4.1 Breast Cancer**

*Hypofractionation*

Adjuvant breast radiotherapy is a significant proportion of fractions delivered for radiotherapy worldwide and are an established part of standard treatment. It has been recognised that hypofractionation is possible in breast radiotherapy and this has been the subject of very major trial efforts in the last two decades. There are very strong data supporting modest hypofractionation in nearly all patients [20] and there a good data to suggest more extreme hypofractionation over 5 sessions in suitable patients either in whole breast or partial breast irradiation [21, 22].

*Breathing Control*

Many radiation centres use deep inspiration breath hold techniques for left-sided breast radiotherapy. We would recommend avoiding the use of active breathing control for radiotherapy due to the risk of aerosol contamination and minimisation of devices requiring decontamination. Deep inspiratory breath hold techniques with voluntary breath hold will help avoid cardiac dose without the need for additional equipment and the attendant infection risks [23].

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Where the technology is available the use of intraoperative radiotherapy may obviate the need for any further outpatient treatment and should be considered an option[24]. Although controversies have surrounded some of the long term data for the intraoperative breast radiation these considerations may be outweighed pressures of a service in crisis [25].

*Avoiding Treatment*

Although a radiotherapy boost may reduce locoregional recurrence in breast cancer the effect on survival is negligible and the possibility of omission should be considered[26]. Patients with non-invasive disease who gain no survival benefit from breast radiotherapy should discuss omitting radiotherapy altogether [27]. Older patients with low risk disease who have minimal survival benefit from breast radiotherapy and much greater risk of mortality from COVID-19 should also consider omitting radiotherapy altogether[28] [29].
Patients with estrogen receptor positive breast cancer may also delay their radiotherapy treatment for up to 5 months with relative confidence if they are established on endocrine therapy and have received prior chemotherapy [30].

**2.4.2 Prostate cancer**

Early prostate cancer may be managed with active surveillance, radiotherapy or surgery. During a pandemic, overall strategies foprostate cancer management include hypofractionation and treatment delays where necessary.

For low risk we would recommend at this time that these patients are put on active surveillance and return in 6 months for a PSA testing. Patients with favourable intermediate risk should be offered active surveillance and return in 3-6 months for a repeat PSA. This is a safe approach with good data to support it in this patient group [31]. A delay of 3-6 months to start radiotherapy if eventually necessary is well supported by the active surveillance literature in this population.

For patients requiring radiotherapy there is an option to either delay the initiation of androgen deprivation therapy (ADT) before starting 2-3 months ADT or else extending the ADT – in either case delaying the start of radiotherapy for at least 4-5 months and with safety data showing that extending ADT out to 8 months is reasonable [32].
For patients with high risk disease shorter delays of 2-4 months but with ADT are recommended as a safe and pragmatic approach. Data also appears to support the use of ADT to delay radiotherapy in a post-prostatectomy salvage situation [33]

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Dose escalation studies in the definitive treatment of prostate cancer have failed to show overall survival benefit which in this scenario provides further comfort in using lower dose schedules [34]. When radiotherapy is required then, just as with breast, there is data to support both modest hypofractionation over 20 fractions (60Gy) or ultra hypo-fractionated regimens (42·7Gy in seven fractions, 3 days per week for 2·5 weeks) [35]
or 36Gy in 6weeks [36]. Ultrahypofractionation (5 fraction) stereotactic body radiotherapy may be most preferred if staff are available to support planning and delivery [37].

***Oligometastatic Prostate Cancer***

Although we have randomized trials for oligometastatic disease weighted heavily towards prostate cancer, these are limited. No survival benefit has been demonstrated with high-level evidence. Observation is reasonable. If PSA-DT is rapid ADT is an option. For low-volume metastatic disease where higher quality evidence suggests treatment of the primary [38] delaying for 4-6 months while on ADT if newly diagnosed is reasonable.

**2.4.3 Lung Cancer**

Patients with lung cancer may be doubly disadvantaged by COVID-19 infection due to the respiratory changes which seems the predominant mode of death in people infected with the virus [39]. Many lung cancer patients will already have compromised lung function and the pneumonitis cause by therapeutic radiation may conceivably increase risk for patients. In this context patient selection for treatment, particularly with respect to fitness and frailty is crucial.

Although modest hypofractionation is possible in non-small cell lung cancer dose constraints with acceptable lung V20 of less than 30% may be challenging if the PTV is large.

In patients suitable for stereotactic radiosurgery with local access then a single fraction regimen may be possible and preferable to a 3 fraction regimen [40, 41].

Sequential regimens might be preferred for stage III unresectable disease over concurrent RT-CT for reducing the risk of lymphopenia; no data are currently available on the incidence and severity of COVID-19 in patients undergoing maintenance immunotherapy with anti PD-L1 inhibitors after chemoradiation, so caution is advised.

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### 2.4.4 Brachytherapy

Whilst brachytherapy can be hugely effective as a treatment and often save patients significant hospital time receiving equivalent external beam radiotherapy it may prove challenging to deliver. Early reports from Italy during a peak of COVID-19 were that all operating theatre capacity had been reduced to critical emergencies due to lack of anaesthetists and ventilator equipment. Brachytherapy may also increase risk of transmission during intubations or upper endoscopic procedures and necessitate increased PPE when they are in short supply. The National Health Service in England announced that from mid-April 2020 all elective surgery would be suspended as an indication of the likely pressures on anaesthetic staff and capacity. Whilst brachytherapy may be a preferred oncological option it may prove impossible to deliver and in certain cancers e.g. vaginal vault boost or prostate cancer brachytherapy it may be prudent to plan for external beam alternatives if necessary.

## 3. Reducing infection risk in the department

Radiation oncology departments will need to take adequate precautions to reduce the likelihood of COVID-19 transmission within their units. These policies will be influenced by national directives and local infection control procedures as well as access and availability of Personal Protection Equipment (PPE).
For indications on the correct use pf PPE, WHO guidelines are available [42].
Inviting the local Infection Control department to critically inspect processes in your own department is likely to be instructive and useful. Nonetheless basic principles apply. Staff should wash hands between each patient contact and patients themselves should be instructed to wash hands or use alcohol hand rub on entering the department. Some departments may choose to do temperature screening of staff, patients and any other visitors on entering the department as was employed during SARS [1]. When patients arrive for treatment and before they leave the department, they should be invited to wash their hands and provided with facilities to do so.

Patient contact should be rationalised as much as possible and departments may wish to map the patient flow through their department and see what proactive steps can be made to reduce the number of staff members a patient may need to have contact with. Equally staff movement around multiple areas of the department should be restricted as far as is practicable to avoid an infected member of staff passing that infection widely thorough all staff groups. If treatments are zoned within different buildings or satellite units it may be preferable to keep staff within these units rather than rotate them to reduce cross-infection risks. Bringing together small autonomous functional teams will help with this. Staff should be included in discussions around changes in practice such as the fractionation policies described in this paper. Regular

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communications should be sent, preferably in an electronic bulletin. All staff should be aware of their responsibilities to report infective symptoms and self-isolate if symptomatic. The teams in Singapore stressed that there should be “no heroes” and that all of those with symptoms no matter their role should self-quarantine.

Suppressive social distancing should be practices wherever possible including remote working [43] In anticipation of self-isolation discuss what working roles could be conducted from home and review what may be required in local governance and information technology to allow home working e.g. can laptops be provided which offer access to hospital data or to treatment planning systems. If working from home is possible then consider allowing staff to do this even when not medically recommended (self-isolation) as this reduces infection risk and the risks of workforce depletion. The NHS in England have reduced guidance that allows for some relaxation of normal data governance to facilitate this sort of working during the crisis and other jurisdictions should follow suit[44].

Physical preparation of the department should involve removing any extraneous materials from treatment areas. This process will mean that if decontamination is required the process should be more straightforward. Wherever possible staff should be trained in the use of PPE and be fit tested for the appropriate masks. If time and staffing allow the team should rehearse treating a patient whilst wearing PPE so they can be accustomed to this in a non-urgent care setting.

It may benefit to request that patients with high mucosal or aerosol output (lung cancer patients with cough or head and neck cancer patients with high mucoid sputum output) wear a paper mask to reduce risks of contamination. Initial indications from Italy suggest requesting patients to wear protective masks during their stay in the radiotherapy department even if asymptomatic (no cough), in all cases, according to WHO guidelines.
The number of positive patients without symptoms is probably higher than initially estimated, and the risk of spread should be kept at minimum [45]

As the pandemic progresses it is inevitable that departments will have to deal with the issue of patients who have symptoms of COVID-19 or are confirmed to have the disease. In this scenario different healthcare systems will have different approaches to confirmatory testing. In the absence of a universal policy for testing and the lack of an instant test we should assume a patient with suspicious symptoms is an infectious carrier of the disease.
For patients with slow growing or low risk disease it may be oncologically safe to either prematurely or temporarily stop the patient’s treatment until they have recovered from infection. In this case any gap should be compensated using an appropriately robust policy using

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agreed radiobiological parameters [46]. Long gaps may require replanning or reassessment of the CTV as described by teams after Hurricane Maria [2].

If it is not oncologically reasonable to pause or stop a patient's radiotherapy treatment (e.g. radical treatment of a squamous cell cancer of the head and neck) then staff and other patients must be protected against the risk of cross infection. If department size allows then plan for a 'hot' bunker – a treatment machine where all potential COVID-19 infected or suspected infected cases are treated. Preferentially route these patients through the department by separate entrance and exit (consider using emergency or rear exits as separate doorways for this group). These treatments should be concentrated at the end of the day so that adequate decontamination and cleaning procedures can take place overnight before treatments resume the next day. The patients should be asked to wear mask to avoid spreading infection by droplet and staff should be all be fitted with appropriate PPE. Store fixation devices (breast boards, thermoplastic masks etc) used by infected patients separately from all other equipment.

Through all of this change and adaptability will be required. Leaders should communicate regularly and agree a regular communication channel. Be prepared to offer proactive emotional and psychological support to both patient and staff who are both dealing with very significant additional stresses in their roles. Work and life balance is critical, especially during times of pandemics when intense social distancing measures severely limit supports outside in addition to inside the hospital (childcare, food, etc.) [2] Emotional fatigue can be as debilitating as physical exhaustion, and both will likely contribute to errors, burnout, and increased infection.

**Conclusion**

Although colleagues around the world have dealt with enormous service pressures in the face of natural disaster or infections previously the global scale and challenge of COVID-19 is unprecedented. Extraordinary times require extraordinary measures that may be guided by the best available evidence. For radiation oncology, this includes best practices from frameworks used successfully in other crises, published evidence, and international input.
Action should follow the program of **P**repare, **C**ommunicate, **O**perate and **C**ompensate (PCOC) outlined in Table 6.

In line with previous recommendations we urge units to proactively prepare their departments with training and PPE and consider their infection control procedures. Departmental agreements on adapting remote working practices and reduced fraction regimes (or even not treating) are likely to reduce the burden of this disease on our cancer population.

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The use of social media, and in particular the #radonc tag, has proven a very effective method of colleagues globally networking and sharing insight and experience. In this setting Twitter has proven to be highly useful and we would encourage colleagues to use the platform in this way.

At the time of writing some areas still have the potential to prepare whilst others are now having to mitigate the effects of widespread infection. We hope that this document will provide some useful guidance.

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Table 1

**Challenges for Radiation Oncology during an outbreak of infectious disease**

| Domain | Problems |
|---|---|
| Patient Groups | Cancer patients may include vulnerable individuals due to use of chemotherapy or frailty due to advanced disease.<br><br>These patients may be co-located with relatively fit patients receiving adjuvant therapies |
| Staffing | Delivery of radiotherapy requires very specific skill sets which are not generic within an acute hospital. Treatment units are therefore very vulnerable to changes in staff levels due to sickness.<br>Radiation therapists in particular have very regular close contact with a large number of patients and are at high risk of exposure |
| Environment | Although most radiation oncology units are have physical separation from other hospital departments there may still be a mixing of a number of patient groups in a waiting area. Some services may share waiting areas between patients on active treatment and those in follow up.<br>Treatment bunkers may contain a large amount of equipment which in cases of |

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| | |
|---|---|
| | potential contamination may be time consuming and difficult to clean |
| Equipment | Treatment relies on highly specialist equipment which will usually treat high volumes of patients in sequence. |
| Treatments | Treatment courses are delivered in fractions and efficacy is influenced by interruptions and gaps.<br><br>Extended treatments over many weeks are more vulnerable to interruption due to patient sickness or workforce shortage.<br><br>Chemoradiotherapy treatments also increase likelihood of serious infection.<br><br>Some treatments given for palliation or as adjuvant therapy may have altered risk benefit in the context of pandemic infections. |

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**Table 2**

**Radiotherapy Treatments that may be omitted**

*These therapies have (mainly) been established by randomised controlled evidence and have are frequently considered a standard of care. In the context of a pandemic the risk benefit of these treatments is altered. General criteria for omission may include more time-sensitive need for treatment decision-making (go vs. no go) and availability of non-emergency/urgency, lower-risk alternatives, etc. that make the additional risk of treating the patient during the pandemic greater than the risk of omitting radiation taking alternatives into account*

| Disaese Site | Subsite or classification | Modality | Comments and Evidence |
|---|---|---|---|
| **Breast** | | | |
| | Breast Conservation | | |
| | DCIS | Omission of radiotherapy to whole breast [27] | No survival benefit, small benefit in loco-regional recurrence |
| | Invasive disease<br>Low risk, older patients | Omission of radiotherapy to whole breast [[29, 47] | Endocrine therapy only sufficient in >70 (>65in PRIMEII) [29] |
| | Invasive disease<br>Genomic profile low risk | Omission of radiotherapy to whole breast | LUMINA, IDEA, PRECISION, PRIMETIME trials ongoing (caution outside of trial) |
| | Age ≥50, ER+, Her2- breast ca without other adverse pathologic features | Omission of boost radiotherapy [26, 48] | No survival benefit |
| | Post Mastectomy | | |
| | T1-2 N1 (Node+ Breast Cancer) | Omit radiotherapy | NSABP B-51/RTOG 1304 trials ongoing |
| **CNS** | | | |
| | Glioblastoma<br>Age > 60, methylated | Temozolamide only [49, 50] | Standard radiotherapy associated with poor outcomes |
| | Low grade glioma | Omit radiotherapy | |

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|---|---|---|---|
| | Asymptomatic meningioma Gr 1 - 2 | Omit radiotherapy | |
| | Asymptomatic AVM | Omit radiotherapy | |
| | | | |
| **Esophagus** | | | |
| | | Resection or chemoradiation rather than trimodality therapy | |
| **Gastric** | | | |
| | Resectable | Treat with chemotherapy only | |
| | Unresectable | Treat with chemotherapy only [51] | |
| **Lung** | | | |
| | SCLC, Extensive | Omit prophylactic cranial irradiation [52] | Also consider omission of consolidation thoracic radiotherapy in extensive stage disease |
| **Pancreas** | | | |
| | Unresectable | Omit radiotherapy [53] | Consider Chemotherapy or clinical trial |
| **Prostate** | | | |
| | Low, favorable intermediate risk | Active surveillance [54] | |
| **Benign Disease** | | | |
| | Keloid, Heterotopic Ossification, Actinic Keratosis | Omit radiotherapy | Not life-threatening, topicals (NSAIDS) may be reasonable alternatives (vs. delay in the far future). |
| **Palliative** | | | |
| | Painful mets, uncomplicated, other systemic options | | Ensure Medical Optimization (e.g. WHO Pain Ladder) |
| | Oligometastatic (e.g.Prostate Cancer) | Omit radiotherapy | Systemic treatment e.g. androgen deprivation therapy |
| | Postoperative RT (for pathologic fracture) [55] | Omit radiotherapy | Limited/ evidence of benefit |
| | CNS mets from NSCLC needing WBRT [19] | Omit radiotherapy | Best supportive care including steroids |

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|---|---|---|---|
| **Testicular** | | | |
| | Seminoma, stage I | Omit radiotherapy | Consider observation or carboplatin |

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**Table 3 – Palliative Radiotherapy Treatments where fractionation may be reduced**

| | Cohort/Eligibility | Dose/fraction (Gy) | # fractions | Interval between fractions | Technique | Other | OS benefit vs Obs | Evidence level | Group/Trial |
|---|---|---|---|---|---|---|---|---|---|
| Bone metastasis, no fracture, +/- cord compression - HS | Palliation | 6-10 | 1 | N/A | 3D | Risk of pain flare 25% with single fraction plus dexamethasone. Meta-analysis of 25 RCTs show difference between symptom relief single vs multifraction RT. Large studies show no difference in pain flare with single fraction compared to multifraction | | 1 - non-inferior | University of Toronto TROG 96.05, SCORAD III ICORG 05-03[15, 18, 56, 57] |
| Bone metastasis, fracture/surgery | | 4 | 5 | Daily | 3D | | | 1 - non-inferior | |
| Brain metastasis | 1-3 mets, good KPS, no extracranial disease | 15-20 | 1 | N/A | SRS | | | | |

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|---|---|---|---|---|---|---|---|---|---|
| | Palliation | 4 | 5 | Daily | 3D WBRT | A routine option in UK, UK, Europe, Asia, Canada, and Australia. Established in RTOG dose esclation studies. | Generally no, but benefit in some groups in QUARTZ | 1 - not different | RTOG QUARTZ[19, 58] |
| | Palliation, poor prognosis | 6 | 2 | Daily | 3D | On subanalysis seemed reasonable for poor prognosis; good prognosis benefited from longer fractionation. | Generally no, but benefit in some groups in QUARTZ | 1 - refer to abstract | Royal College of Radiologists[59] |
| Esophageal bleeding/dysphagia | | 3 | 4 | BID | 3D | Alternate = 5 Gy x 3 | | | Sharon Project [60] |
| | | 6 | 3 | Day 0,7,21 | 3D | | | | Adapted from other sites |
| GBM, poor KPS | Age ≥50, KPS 50-70, or age ≥65 KPS 50-100 | 5 | 5 | Daily | 3D, CTV was 2 cm margin as per EORTC | No Temozolamide | Yes but likely not curable Palliation benefit | 1 - noninferior | IAEA[61] |
| Head & Neck | Palliation | 6 | 5-6 | 2 fxs/week | | | None, palliation only | Prospective | HYPO trial[62] |

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| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Head & Neck | | 6-8 | 3 | Day 0,7,21 | 3D/IMRT | | | | [63] |
| SCV Syndrome/Lung cancer | Palliation | 8-10 | 1 | N/A | 3D | | | 1 | IAEA[64-66] |
| | | 8.5 | 2 | 1 Week | 3D | | | 1 | MRC [67] |
| Lymphoma, low grade | | 4 | 1 | N/A | 3D | | | | |
| Pelvic/GI bleeding | Palliation | 4 | 5-6 | Daily | 3D | | | | Reasonable BED equivalent for tolerance = 5.5 Gy x 4 |
| | | 4.5 | 4 | BID | 3D | | | Phase II | SHARON trial [68] |
| | | 3.7 | 4 | BID | 3D | Repeat q2-4 wks to total 44.4 Gy in 3 courses, QUAD SHOT | | Phase II, III | RTOG 8502[49, 69, 70] |
| | | 6-8 | 3 | Day 0,7,21 | 3D | | | Restrospective | [71] |

Journal Pre-proofs

Table 4 **Radical Radiotherapy Treatments where fractionation may be reduced**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Brain*** | | | | | | | | | | |
| | Glioblastoma Multiforme | Age ≥ 65 | 2.67 | 15 | Daily | 3D/IMRT<br>Retina, optics, brainstem <100% of dose. Lenses < 4 Gy | Concurrent Temozolamide | Yes but likely not curable<br>Palliation benefit | Likely non-inferior | CCTG/ EORTC/ TROG (with or without TMZ) [72, 73] |
| ***Bladder*** | | | | | | | | | | |
| | Muscle invasive, chemoradiation | cT2-4a N0 | 2.75 | 20 | Daily | 3D/IMRT<br>Full dose delivered to tumor and 80% dose (=44 Gy) to uninvolved bladder with CCB<br><br>(No dose constraints were outlined in BC2001.)<br>Use BED calculations<br>Small bowel <54 Gy.<br><br>If tumor is adjacent to small bowel, the high dose PTV may need to be undercovered | | Preservation is intention | Non-inferior | BC2001[74, 75] |
| ***Breast*** | | | | | | | | | | |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | Breast, Partial (APBI) EBRT | Early stage, ASTRO PBI criteria | 6 | 5 | Daily | IMRT was used. Consider also 3DCRT<br>PTV V28.5 = 100%<br>PTV max < 105% (31.5 Gy)<br>PTV min 28 Gy<br>uninvolved breast V15< 50%<br>ipsilateral lung V10< 20%<br>contralateral lung V5< 10%<br>heart V3< 10% | MRT PBI is equivalent to WBRT in LC. Adverse effects and cosmesis are actually improved with IMRT PBI. | Yes on meta-analysis | Equivalent, possibly superior to WBRT | University of Florence, Italy<br>UK meta-analysis[22, 76] |
| | Breast, Partial (APBI) EBRT | Early stage, ASTRO PBI criteria | 5.7 | 5 | Daily | (In FAST, dose constraints were limitations of cm of heart in field)<br>Dose constraints in FAST FORWARD (open protocol)<br>Heart V1.5< 30%, V7< 5%<br>Ipsilateral lung V8< 15% | Cosmetic outcomes were not different from standard fractionation. The cosmetic assessment was not as rigorous as in some other studies such as RAPID; nonetheless, in the data available, | Yes on meta-analysis | 1 - equivalent, possibly superior to WBR | UK FAST (10-yr f/u)<br>UK FAST FORWARD (ongoing study)<br>UK meta-analysis [21, 77, 78] |

Journal Pre-proofs

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| | | | | | | | there are similar late effects in FAST 28.5 Gy/ 5 fx weekly compared to conventional. | | | |
| | Breast , Whole breast +/- LN | early stage, >50s | 5.2 | 5 | Daily | 3D<br>Heart V1.5< 30%, V7< 5%<br>Ipsilateral lung V8< 15% | Ongoing protocol | | NA -ongoing | UK FAST FORWARD, UK NCRI / ICR[21] |
| | Breast, Partial (APBI) EBRT | Early stage, ASTRO PBI criteria | 3.85 | 10 | BID | RAPID<br>Ipsilateral lung V30% < 10%<br>Heart, right V5% < 5%<br>Heart, left outside LIQ V10% < 5%<br>Heart, LIQ, V15% < 5%<br>Contralateral lung V5% < 5%<br>Thyroid and contra breast max <3% | Noninferior to WBRT in regards to LC. However cosmetic adverse effects were slightly worse with EBRT PBI BID. | Yes on meta-analysis | Equivalent in LC | RTOG 0413<br>UK meta-analysis[76, 79] |
| | Breast, Partial (APBI) IORT | Early stage, ASTRO PBI criteria | 20 | 1 | IORT | Radiation is delivered over 20–45 min to the tumor bed. The surface of the tumor bed typically receives | | Yes on meta-analysis | 1 - noninferior, possibly superior to WBRT | TARGIT<br>UK meta-analysis [76, 80] |

Journal Pre-proofs

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| | | | | | | 20 Gy that attenuates to 5–7 Gy at 1 cm depth | | | | |
| | Whole breast + LNs | | 2.67 | 15 | Daily | 3D | | | | |
| | Chest wall PMRT | without implants (consider if + implants) | 2.67 or 2.9 | 15 | Daily | Beijing trial: Chest wall, SCV, level 3 axilla. Used 2D electron techniques for chest wall. 2D, 3D or IMRT for SCV.<br><br>RT CHARM<br>Chest wall, axilla, and SCV D95 > 95% (variation acceptable D90% > 90%)<br>IMN D90% > 90% (VA D90% > 80%)<br>Chest wall max V107% < 10 cc, V0.03 cc < 115% (or 130% for photon+electrons)<br>Ipsilateral lung V18 < 35% (VA V18 < 40%)<br>Heart V22.5 < 10%, mean < 3 Gy (VA V27 < 10% and mean < 5 | | Yes | Noninferior (without implants)<br><br>with implant trial ongoing | Beijing PMRT (Phase III) [81] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Gy)<br>Contralateral lung V4.8 < 10%<br>Contralateral CW/breast V3 < 10% | | | | |
| | Breast (Chest wall/whole breast/ RNI) | Elderly >70 years old | 5-6.25 | 6 | Weekly | | | | Observational, prospective | Hospital del Mar, Parc de Salut Mar, Barcelona, Spain[82] |
| | Chest wall PMRT | | | | | Omit boost | | No | Retrospective - worse toxicity, no LC benefit | Mass General Hospital [26] |
| ***Head and Neck*** | | | | | | | | | | |
| | HPV+ definitive | Localized HPV+ | 2 | 30 | Daily | IMRT<br>Standard dose constraints, concurrent cisplatin | Potential caution in applying. Not yet compared to standard fractionation in phase III | Yes | Phase II | NRG HN002[83] |

Journal Pre-proofs

| | | | | | | | | | | |
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| | | | | | | | trial. Consider planning first to 70 Gy, then at time of 60 Gy consider end of treatment based on status of patient, clinical response, and viral status in your community. | | | |
| | Definitive | | 2 | 33 | 6 fx/week | | Alone or with concurrent Nimorazole | Yes | 1 | DAHANCA [84, 85] |
| ***Lung*** | | | | | | | | | | |

Journal Preproofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | N0, medically inoperable | T1-T2 peripheral | 30-34 | 1 | N/A | SBRT<br>Spinal Cord V10 < 0.35cc, V7 < 1.2cc, $D_{max}$ 14 Gy<br>Esophagus V11.9 < 5 cc , $D_{max}$ 15.4 Gy<br>Brachial Plexus V14 < 3cc, $D_{max}$ 17.5 Gy<br>Heart/Pericardium V16 < 15cc, $D_{max}$ 22 Gy<br>Great Vessels V31 < 10cc, $D_{max}$ 37 Gy<br>Trachea/large bronchi V10.5 < 4cc, $D_{max}$ 20.2 Gy<br>Rib V22 < 1cc, $D_{max}$ 30 Gy<br>Skin V23 < 10cc, $D_{max}$ 26 Gy<br>Stomach V11.2 < 10cc, $D_{max}$ 12.4 Gy<br>Lung (L&R) for basic function: V7 < 1500cc<br>Lung (L&R) for pneumonitis: V7.4 <1000cc | | Yes | 1 - equivalent to 3 fxs | RTOG 0915, Roswell Park[86-88] |

Journal Pre-proofs

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N0, medically inoperable | Peripheral | 18 | 3 | Every other day | SBRT | | | | |
| | NSCLC, Concurrent chemoradiation | Locally advanced | 2.5 | 22 - 23 | Daily | 3D/IMRT | Caution in applying, especially to good performance status patients that seem curable. Not yet compared to 60 Gy/ 30 fx in phase III trial. Possibly similar when comparing to historical control. Routine option in UK. | Yes | Restrospective and Phase II. Not compared to standard. | UK, SOCCAR[89-91] |
| | NSCLC, Sequential chemoradiation | | 3 | 18 - 20 | Daily | 3D/IMRT | | | | |
| | NSCLC N+, Radiation only | | 4 | 15 | Daily | 3D/IMRT | | | | |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | SCLC, chemoradiation | | 2.67-2.8 | 15 | Daily | 3D/IMRT<br>Lung V20 ≤ 30% and mean < 20 Gy<br>Esophagus $D_{max}$ < 105% | | | Prospective, retrospective | Canada Norway[92, 93] |
| ***Pancreatic Cancer*** | | | | | | | | | | |
| | Locally advanced | NCCN borderline resectable and unresectable criteria | 5-10 Gy boost, consider 6.6 Gy to vessels | 5 | Every other day | SBRT CTV optional. Consider extending posteriorly to vessels. PTV 5 mm. Gating or 4DCT<br><br>TROG and AGITG guidelines (5 fractions)<br>Duodenum/small bowel/stomach Dmax 0.5 cc <33 Gy (VA <35)<br>V30 <5 Gy (VA <10)<br>Duodenum/small bowel/stomach PRV Dmax 0.5 cc <38 Gy (VA <40)<br>PTV40 D99 >30 (VA > 25)<br>PTV40 EVAL D90 >100 (VA > 90)<br>CTV D99 > 33 (VA > | | Likely no | Phse II | TROG and AGITG [94, 95] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 30)<br>PTV40 D0.05 max 110-130 (VA >140 or <110)<br><br>Koay et al, PRO, 2020 (Rx 50 Gy/5 fx with SIB 33 Gy)<br>iDuodenum V40 <0.5cc, V35 < 1cc, V30 <3cc<br>iStomach, sm bowel V 40 <0.5cc, V35 <1cc, V30 <2cc<br>Liver V12 <50%<br>Bile duct max <55 Gy<br>PTV high (50 Gy) covered to 90-95%<br>PTV low (33 Gy) covered to 98%<br>posterior tumor vessels covered to 40 Gy | | | | |
| ***Prostate*** | | | | | | | | | | |
| | Any risk | | 3 | 20 | Daily | IMRT<br>CHHiP<br>Rectum V20 <85%, V30 <57%, V40 <38%, V50 <22%, V60 <0.01% | No fiducials | in high risk | 1 - noninferior | CHHiP PROFIT[96, 97] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Bladder V60 <5%, V48.6 <25%, V40.8 <50% | | | | |
| | Intermediate/High Risk, Prostate only | T1c-3a, PSA 20 or less | 6.1 | 7 | Every other day | 3DCRT, IMRT, or VMAT (not SBRT)<br>Rectum V38.4 < 15%, V32 < 35%, V28 < 45%<br>(Bladder constraints were omitted)<br>Femoral heads max < 29.9 Gy<br>CTV $D_{min}$ > 95%<br>PTV D90 > 90%, V95% > 95% | Fiducials if possible | in high risk | 1 - noninferior | HYPO-RT-PC [35] |
| | High risk or M1 | Age 75+, or 70+ with moderate comorbidity | 6 | 6 | Weekly | The protocol allowed 3D and "equivalent coplanar techniques" that use MLCs: presumably both IMRT and SBRT<br>Rectum V50 <33.3 Gy, V60 <27.8, V80% <16.7<br>Bladder V25% <33.3, V50<27.8 | No fiducials | in high risk | 1 (vs no RT) | STAMPEDE [38] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | Low/Intermediate Risk, Prostate only | | 7.25-8 | 5 | Every other day | SBRT<br>NRG GU005<br>Rectum D0.03cc<38.06 Gy (variation acceptable <40), D3cc<34.4 Gy (VA <40), D10%<32.63 (VA <34), D20%<29 (VA <30), D50%<18.13 (VA < 19)<br>Bladder D0.03cc<38.06 (VA <40), D40%<18.13 (VA <20)<br>Urethra D0.03<38.78 (VA <43.5)<br>Rec but not required:<br>Penile bulb D0.03cc <100%, D3cc <19.9 Gy<br><br>SBRT, MSKCC phase I dose escalation<br>average PTV D95 within 95-101%<br>average PTV D98 within 89-100%<br>3 mm rectal wall: max < 103%, D1cc< | Need fiducials | in high risk | Phase I - II | MSKCC<br>NRG GU005 (Phase III ongoing)<br>NCCN [98] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 38.5 Gy, D53%< 24 Gy, V30.15 Gy < 8 cc Bladder wall: max < 105%, D1cc< 42 Gy, D53%< 24 Gy | | | | |
| | Post-prostatectomy, Fossa only | | 2.62 | 20 | Daily | IMRT RADICALS Bladder 40 Gy < 80%, 48 Gy < 50%, Rectum 24 Gy < 80%, 32 Gy < 70%, 40 Gy < 60%, 48 Gy < 50%, 52.5 Gy < 30% | | yes for SRT within 2 years of RP if PSA DY <6mo (JAMA. 2008;299(23):2760-2769) | Retrospective, prospective (an option on RADICALS - reported in abstract) | Christie RADICALS[99] |

Journal Pre-proofs

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|---|---|---|---|---|---|---|---|---|---|---|
| | Post-prostatectomy, Fossa only | | 2.5 | 25 | Daily | IMRT<br>NRG GU003<br>Rectum V36< 55 (variation acceptable <60), V59< 35 (VA <39)<br>Bladder V35< 70 (VA <77), V57< 50 (VA <55)<br>Femoral heads D44 <10 (VA <11)<br>Small bowel not specified - used BED calculations | | Yes for SRT within 2 years of RP if PSA DY <6mo (JAMA. 2008;299(23):2760-2769) | Ongoing protocol | NRG GU 003- trial ongoing |
| ***Rectal*** | | | | | | | | | | |
| | Preoperative | cT3-4 | 5 | 5 | Daily | 3D/IMRT<br>Field: traditional rectal pelvis fields. Dose constraints may not be required, only blocks? Avoid hotspots. WashU small bowel max < 25 Gy. If 4 field with FIF you should be able to meet this constraint with most plans (VA 2550 cGy small bowel max if it is completely in field). | | No | 1 | [100] |

Journal Pre-proofs

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| | | | | | | | | | | |
| Bladder | | | | | | | | | | |
| | Muscle invasive, N0 - Bladder only | cT2-4a N0 | 2 | 32 | Daily | 3D/IMRT | Omit nodes | | | [101] |
| CNS | | | | | | | | | | |
| | GBM | | 2.67 | 15 | Daily | 3D/IMRT | Smaller margins | | | [102] |
| | | | | | | | | | | [103] |
| Breast | | | | | | | | | | |
| | Post-menopausal ER+Her2-, G1-2, T1, 1-2 SLN (mi) | | 2.67 | 15 | Daily | 3D | WBRT only, Omit nodes | | | RCR Consensus Statement |

**Table 5**

**Radiotherapy Treatments that can be delayed**

Intermediate Priority: Patients who require service (e.g. treatment), but not critical (not immediately life threatening), other available options ~equivocal such as optimizing medical management (e.g. opioids for pain crisis). This will require individualized triaging based on resource availability (including risk of COVID transmission) and clinical outcomes. The delays should be as short as possible and triaged based on the risks of the pandemic (additional risks to the patient and/or system) being greater than the risk of delay to the patient.

| **Disease Site** | **Subsite** | **Eligibility** | **Modality** |
|---|---|---|---|
| **Breast** | | | |

Journal Preproofs

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|---|---|---|---|
| | **Breast conservation** | **T1-2 N0, luminal A+B** | **Start endocrine therapy, can wait up to 20 weeks for RT [30]** |
| **CNS** | | | |
| | **Asymptomatic meningioma** | ***WHO I Postop GTR and WHO Grade 1-2*** | ***Supportive care if minimally symptomatic Postop GTR & WHO I/benign -> observe*** |
| | **Asymptomatic AVM** | | ***Observation, medical management*** |
| | **Asymptomatic schwannoma** | | ***Observation, Supportive care if minimally symptomatic?*** |
| **Prostate** | | | |
| | | **Unfavorable Intermediate, High, Very High Risk** | **Longer neoadjuvant ADT reasonable for up to 6-7 months [32, 104]** |
| | | **Prostate, postop** | **Consider DECIPHER<br>No adjuvant treatment (only salvage), consider waiting for PSA>0.2, add ADT [38]** |
| **Skin** | | | |
| | **Basal cell carcinoma** | | **Observe<br>Can delay more than SCC** |
| | **Squamous cell carcinoma** | | **Observe** |
| **Other Benign Disease** | | | |
| | **Pituitary Adenoma** | | **Observation or supportive care** |
| | **Fibromatosis** | | |
| | **Other: Actinic Keratosis, Recurrent/Refractory Fasciitis, other rare benign** | | **Better outcomes earlier in the disease course Vs Omit** |
| **Palliative** | | | |

Journal Pre-proofs

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|---|---|---|---|
| | **(Progressively?) Painful metastases without impending structural/neurologic compromise** | | **Pain meds**<br>**Vs. omit (if other medical management can be optimized such as opioids)?** |

Journal Pre-proofs

**Table 6**

**P**repare, **C**ommunicate, **O**perate and **C**ompensate (PCOC).

| | Action |
|---|---|
| Prepare | Agree changes in treatment plans with colleagues in physics, planning and treatment<br><br>Look to increase capacity in preparation for reduced workforce by reducing fraction numbers and treatment courses.<br><br>Make physical adjustments to treatment areas<br><br>Order, fit and test Personal Protection equipment<br><br>Order and test IT to allow home working from self-isolation<br><br>Move clinic plans to remote monitoring / telemedicine /telephone wherever possible |
| Communicate | Explain to patients how COVID-19 changes the risk-benefit of standard treatment schedules of radiotherapy |

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|---|---|
| | Discuss personal protection, safety, hand washing and infection control procedures to all staff but especially radiation therapists with daily physical patient contact.<br><br>Alert staff groups to any suspected or proven COVID-19 case |
| Operate | Consolidate staff into small functional groups that do not depend on other groups and do not move to different clinical areas<br><br>Consider temperature screening for all users of the radiotherapy centre<br><br>Quickly disseminate information around COVID cases and agree with patient and staff if treatment will continue with PPE, stop or pause |
| Compensate | When treatment is paused agree radiobiological models and alpha/beta values for compensation on treatment restart.<br><br>Consider reassessing the CTV if growth may have taken place |

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**Online contributors**

Prof Michael Baum, UK
Dr Sushil Beriwal, USA
Dr Joaquín J Cabrera, Spain
Dr Garry Davenport, UK
Prof Corinne Faivre-Finn, UK
Prof Bobbie Farsides, UK
Dr Eric Ford, USA
Dr Erin Gillespie, USA
Prof Nick James, UK
Dr Brian Kavanagh, USA
Dr. Jonathan Livergant, Canada
Dr Join Y. Luh, USA
Prof Jane Maher, UK
Dr Michael Mejia, Singapore
Dr Robert C Miller, USA
Dr Esam Mohammad Murshid, Saudi Arabia
Prof Carlo Palmieri, UK
Prof Chris Parker , UK
Dr Miguel Panades, UK
Dr Clive Peedell, UK
Dr Marc-Emile Plourde, Canada
Dr Tom Roques, UK
Dr Shankar Siva, Australia
Dr Cormac Small, Republic of Ireland
Dr Daniel E Spratt, USA
Dr Sandra Turner, Australia
Prof Jayant Vaidya, UK
Dr Matthew Ward, USA

Journal Pre-proofs

Dr Henning Willers, USA
Dr Matt Williams, UK

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Richard Simcock, Sussex Cancer Centre, UK - Declarations of interest: none

Toms Vengaloor Thomas, University of Mississippi Medical Center, USA Declarations of interest: none

Christopher Estes, Mercy Hospital, Springfield, MO , USA Declarations of interest: none

Andrea R. Filippi, Radiation Oncology, Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy Declarations of interest: none

Matthew A Katz, Lowell, MA, USA Declarations of interest: none

Ian J Pereira, Ontario, Canada Declarations of interest: none

Hina Saeed, Medical College of Wisconsin, USA Declarations of interest: none

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As the global COVID-19 pandemic escalates there is a need within radiation oncology to work to support our patients in the best way possible. Measures are required to reduce infection spread between patients and within the workforce. Departments need contingency planning to create capacity and continue essential treatments despite a reduced workforce.
The #radonc community held an urgent online journal club in March 2020 to discuss these issues and create some consensus on urgent next steps. There were 121 global contributors. This document summarises these discussions around themes of infection prevention, rationalisation of workload and working practice in the presence of infection

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