



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



COVID-19: Global radiation oncology's targeted response for pandemic preparedness



Richard Simcock^{a,*}, Toms Vengaloor Thomas^b, Christopher Estes^c, Andrea R. Filippi^d, Matthew S. Katz^e, Ian J. Pereira^f, Hina Saeed^g

^a Brighton and Sussex University Hospitals NHS Trust, UK

^b University of Mississippi Medical Center, USA

^c Mercy Hospital, Springfield, MO, USA

^d Radiation Oncology, Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy

^e Lowell General Hospital, Lowell, MA, USA

^f Queen's University, Ontario, Canada

^g Medical College of Wisconsin, USA

ARTICLE INFO

Article history:

Received 20 March 2020

Revised 22 March 2020

Accepted 22 March 2020

Available online 24 March 2020

Keywords:

Radiotherapy

COVID-19

Pandemic

Hypofractionation

Cancer

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 on Twitter in March 2020 to discuss these issues and create some consensus on crucial 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.

© 2020 The Authors. Published by Elsevier B.V. on behalf of European Society for Radiotherapy and Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

On 11th March 2020, WHO Director-General Tedros Adhanom Gebreyesus declared the novel coronavirus (COVID-19) outbreak a pandemic with over 118,000 cases and more than 4000 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 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. Of the 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 Prepare, Communicate, Operate and Compensate (PCOC). However, the COVID-19

* Corresponding author.

E-mail address: richard.simcock@nhs.net (R. Simcock).

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 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 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 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 Treatment bunkers may contain a large amount of equipment which in cases of 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 Extended treatments over many weeks are more vulnerable to interruption due to patient sickness or workforce shortage Chemoradiotherapy treatments also increase likelihood of serious infection Some treatments given for palliation or as adjuvant therapy may have altered risk benefit in the context of pandemic infections

situation is different. Unlike SARS, its scale is much larger (25× cases at the time of writing – 200 k vs. 8 k; 8× deaths – 8 k vs 800) making outbreak measures less effective. Unlike natural disasters, its impact is entirely biologic.

2. Methods

Over the weekend of 13–15th March 2020, an online Twitter discussion was held as part of the Radiation Oncology Journal Club (#RadOnc #jc) and moderated by the authors (MSK,IP,HS,RS). 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 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.

3. 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) 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].

3.1. 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 via 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 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.

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.

3.2. 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.

3.3. 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.

3.4. 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.

3.5. 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 8 Gy fraction to be as efficacious as a multiple-fraction course [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].

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.

3.6. Disease-specific 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 provide us with confidence to advise patients 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 link 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.

3.7. Breast cancer

3.7.1. Hypofractionation

Adjuvant breast radiotherapy is a significant proportion of fractions delivered for radiotherapy worldwide and is 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 are good data to suggest more extreme hypofractionation over 5 sessions in suitable patients either in whole breast or partial breast irradiation [21,22].

3.7.2. 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].

3.7.3. IORT

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 intraoperative breast radiation, these considerations may be outweighed pressures of a service in crisis [25].

3.7.4. 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].

Table 2
Radiotherapy Treatments that may be omitted.

Disease 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 Low risk, older patients	Omission of radiotherapy to whole breast [29,47]	Endocrine therapy only sufficient in > 70 (>65in PRIMEII) [29]
	Invasive disease 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 Post Mastectomy T1-2 N1 (Node + Breast Cancer)	Omission of boost radiotherapy [26,48]	No survival benefit
CNS	Glioblastoma Age > 60, methylated	Temozolamide only [49,50]	Standard radiotherapy associated with poor outcomes
	Low grade glioma 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 radiotherapy (for pathologic fracture) [55]	Omit radiotherapy	Limited/evidence of benefit
	CNS mets from NSCLC needing WBRT [19]	Omit radiotherapy	Best supportive care including steroids
Testicular	Seminoma, stage I	Omit radiotherapy	Consider observation or carboplatin

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.

3.8. Prostate cancer

Early prostate cancer may be managed with active surveillance, radiotherapy or surgery. During a pandemic, overall strategies for prostate 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 of ADT or else extending the ADT – in either case delaying the start of radiotherapy for at least 4–5 months and even extending ADT out to 8 months, as shown by safety data, is reasonable [32].

For patients with high risk disease shorter delays of 2–4 months 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].

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 (60 Gy) or ultra hypo-fractionated regimens (42.7Gy in seven fractions, 3 days per week for 2.5 weeks) [35] or 36 Gy in 6 weeks [36]. Ultrahypofractionation (5 fraction) stereotactic body radiotherapy may be most preferred if staff are available to support planning and delivery [37].

3.8.1. 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.

Table 3
Palliative Radiotherapy Treatments where fractionation may be reduced.

	Cohort/Eligibility	Dose/ fraction (Gy)	# fractions	Interval between fractions	Technique	Other	OS benefit vs Observation	Evidence level	Group/Trial
Bone metastasis, no fracture, +/- cord compression	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				
	Palliation	4	5	Daily	3D WBRT	A routine option in UK, UK, Europe, Asia, Canada, and Australia. Established in RTOG dose escalation 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 × 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]
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 × 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			Retrospective	[71]

Table 4
Radical Radiotherapy Treatments where fractionation may be reduced.

	Cohort	Eligibility	Dose/ fraction (Gy)	# fractions	Interval between fractions	Technique	Other	OS benefit vs Observation	Evidence level	Group/Trial
Brain	Glioblastoma Multiforme	Age \geq 65	2.67	15	Daily	3D/IMRT Retina, optics, brainstem < 100% of dose. Lenses < 4 Gy	Concurrent Temozolamide	Yes but likely not curable 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 Full dose delivered to tumor and 80% dose (=44 Gy) to uninvolved bladder with CCB (No dose constraints were outlined in BC2001) Use BED calculations Small bowel < 54 Gy 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	Breast, Partial (APBI) EBRT	Early stage, ASTRO PBI criteria	6	5	Daily	IMRT was used. Consider also 3DCRT PTV V28.5 = 100% PTV max < 105% (31.5 Gy) PTV min 28 Gy uninvolved breast V15 < 50% ipsilateral lung V10 < 20% contralateral lung V5 < 10% 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 UK meta- analysis [22,76]
	Breast, Whole breast, node negative	Early stage, ASTRO PBI criteria	5.7	5	Daily	(In FAST, dose constraints were limitations of cm of heart in field) Dose constraints in FAST FORWARD (open protocol) Heart V1.5 < 30%, V7 < 5% 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, there are similar late effects in FAST 28.5 Gy/5 fx weekly compared to conventional	Yes on meta- analysis	1 – equivalent, possibly superior to WBR	UK FAST (10-yr f/u) UK FAST FORWARD (ongoing study) UK meta- analysis [21,77,78]
	Breast, Whole breast +/- LN	early stage, >50 s	5.2	5	Daily	3D Heart V1.5 < 30%, V7 < 5% 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 Ipsilateral lung V30% < 10% Heart, right V5% < 5% Heart, left outside LIQ V10% < 5% Heart, LIQ, V15% < 5% Contralateral lung V5% < 5% 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 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 20 Gy that attenuates to 5–7 Gy at 1 cm depth		Yes on meta- analysis	1 – noninferior, possibly superior to WBRT	TARGET UK meta- analysis [76,80]

Table 4 (continued)

	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 RT CHARM Chest wall, axilla, and SCV D95 > 95% (variation acceptable D90% > 90%) IMN D90% > 90% (VA D90% > 80%) Chest wall max V107% < 10 cc, V0.03 cc < 115% (or 130% for photon + electrons) Ipsilateral lung V18 < 35% (VA V18 < 40%) Heart V22.5 < 10%, mean < 3 Gy (VA V27 < 10% and mean < 5 Gy) Contralateral lung V4.8 < 10% Contralateral CW/breast V3 < 10%	Yes	Noninferior (without implants) with implant trial ongoing	Beijing PMRT (Phase III) [81]	
	Breast (Chest wall/whole breast/RNI)	> 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 Standard dose constraints, concurrent cisplatin	Potential caution in applying. Not yet compared to standard fractionation in phase III 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	Yes	Phase II	NRG HN002 [83]
	Definitive		2	33	6 fx/ week		Alone or with concurrent Nimorazole	Yes	1	DAHANCA [84,85]
Lung	N0, medically inoperable	T1-T2 peripheral	30–34	1	N/A	SBRT Spinal Cord V10 < 0.35 cc, V7 < 1.2 cc, D _{max} 14 Gy Esophagus V11.9 < 5 cc, D _{max} 15.4 Gy Brachial Plexus V14 < 3 cc, D _{max} 17.5 Gy Heart/Pericardium V16 < 15 cc, D _{max} 22 Gy Great Vessels V31 < 10 cc, D _{max} 37 Gy Trachea/large bronchi V10.5 < 4 cc, D _{max} 20.2 Gy Rib V22 < 1 cc, D _{max} 30 Gy Skin V23 < 10 cc, D _{max} 26 Gy Stomach V11.2 < 10 cc, D _{max} 12.4 Gy Lung (L&R) for basic function: V7 < 1500 cc Lung (L&R) for pneumonitis: V7.4 < 1000 cc	Yes	1 – equivalent to 3 fxs	RTOG 0915, Roswell Park [86–88]	

Table 4 (continued)

	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	Retrospective 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				
	SCLC, chemoradiation		2.67–2.8	15	Daily	3D/IMRT Lung V20 < 30% and mean < 20 Gy 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 TROG and AGITG guidelines (5 fractions) Duodenum/small bowel/stomach Dmax 0.5 cc < 33 Gy (VA < 35) V30 < 5 Gy (VA < 10) Duodenum/small bowel/stomach PRV Dmax 0.5 cc < 38 Gy (VA < 40) PTV40 D99 > 30 (VA > 25) PTV40 EVAL D90 > 100 (VA > 90) CTV D99 > 33 (VA > 30) PTV40 D0.05 max 110–130 (VA > 140 or 110) Koay et al, PRO, 2020 (Rx 50 Gy/5 fx with SIB 33 Gy) iDuodenum V40 < 0.5 cc, V35 < 1 cc, V30 < 3 cc iStomach, sm bowel V 40 < 0.5 cc, V35 < 1 cc, V30 < 2 cc Liver V12 < 50% Bile duct max < 55 Gy PTV high (50 Gy) covered to 90–95% PTV low (33 Gy) covered to 98% posterior tumor vessels covered to 40 Gy		Likely no	Phase II	TROG and AGITG [94,95]
Prostate	Any risk		3	20	Daily	IMRT CHHiP Rectum V20 < 85%, V30 < 57%, V40 < 38%, V50 < 22%, V60 < 0.01% Bladder V60 < 5%, V48.6 < 25%, V40.8 < 50%	No fiducials	in high risk	1 – noninferior	CHHiP PROFIT [96,97]
	Intermediate/ High Risk, Prostate only	T1c-3a, PSA 20 or less	6.1	7	Every other day	3DCRT, IMRT, or VMAT (not SBRT) Rectum V38.4 < 15%, V32 < 35%, V28 < 45% (Bladder constraints were omitted) Femoral heads max < 29.9 Gy CTV D _{min} > 95% PTV D90 > 90%, V95% > 95%	Fiducials if possible	in high risk	1 – noninferior	HYPO-RT-PC [35]

Table 4 (continued)

	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 Rectum V50 < 33.3 Gy, V60 < 27.8, V80% <16.7 Bladder V25% <33.3, V50 < 27.8	No fiducials	in high risk	1 (vs no RT)	STAMPEDE [38]
	Low/ Intermediate Risk, Prostate only		7.25–8	5	Every other day	SBRT NRG GU005 Rectum D0.03 cc < 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) Bladder D0.03 cc < 38.06 (VA < 40), D40% <18.13 (VA < 20) Urethra D0.03 < 38.78 (VA < 43.5) Rec but not required: Penile bulb D0.03 cc < 100%, D3cc < 19.9 Gy SBRT, MSKCC phase I dose escalation average PTV D95 within 95–101% average PTV D98 within 89–100% 3 mm rectal wall: max < 103%, D1cc < 38.5 Gy, D53%< 24 Gy, V30.15 Gy < 8 cc Bladder wall: max < 105%, D1cc < 42 Gy, D53%< 24 Gy	Need fiducials	in high risk	Phase I–II	MSKCC NRG GU005 (Phase III ongoing) NCCN [98]
	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]
	Post-prostatectomy, Fossa only		2.5	25	Daily	IMRT NRG GU003 Rectum V36 < 55 (variation acceptable < 60), V59 < 35 (VA < 39) Bladder V35 < 70 (VA < 77), V57 < 50 (VA < 55) Femoral heads D44 < 10 (VA < 11) 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 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]

(continued on next page)

Table 4 (continued)

Bladder	Muscle invasive, cT2–4a N0 NO – Bladder only	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

For low-volume metastatic disease where higher quality evidence suggests treatment of the primary [38] delaying radiotherapy for 4–6 months while on ADT if newly diagnosed is reasonable.

3.9. 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.

3.10. 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 indicated significant reduction of all operating theatre capacity with the exception of 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.

4. 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 of 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 entering the department. Some departments may choose to do temperature screening of staff, patients and any other visitors entering the department, as was employed during SARS [1]. When patients arrive for treatment and before they leave the department, they

Table 5
Radiotherapy Treatments that can be delayed.

Disease Site	Subsite	Eligibility	Modality
Breast	Breast conservation	T1-2N0, 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 Prostate, postop	Longer neoadjuvant ADT reasonable for up to 6–7 months [32,104] Consider DECIPHER No adjuvant treatment (only salvage), consider waiting for PSA > 0.2, add ADT [38]
Skin	Basal cell carcinoma		Observe Can delay more than SCC
	Squamous cell carcinoma		Observe
Other	Benign Disease		
	Pituitary Adenoma		Observation or supportive care
Palliative	Fibromatosis Other: Actinic Keratosis, Recurrent/Refractory Fasciitis, other rare benign		Better outcomes earlier in the disease course Vs Omit
	(Progressively?) Painful metastases without impending structural/neurologic compromise		Pain meds vs. omit (if other medical management can be optimized such as opioids)?

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.

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 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 practiced 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 the risks associated with increased infection and 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. 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 that all patients are requested to wear protective masks during their stay in the radiotherapy department, even if asymptomatic (no cough), 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 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 all be fitted with appropriate PPE. Store fixation devices (breast boards, thermoplastic masks etc) used by infected patients should be stored 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 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 support 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.

5. 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 Prepare, Communicate, Operate and Compensate (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.

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.

Table 6
Prepare, Communicate, Operate and Compensate (PCOC).

	Action
Prepare	<p>Agree changes in treatment plans with colleagues in physics, planning and treatment</p> <p>Look to increase capacity in preparation for reduced workforce by reducing fraction numbers and treatment courses</p> <p>Make physical adjustments to treatment areas</p> <p>Order, fit and test Personal Protection equipment</p> <p>Order and test IT to allow home working from self-isolation</p> <p>Move clinic plans to remote monitoring/telemedicine / telephone wherever possible</p>
Communicate	<p>Explain to patients how COVID-19 changes the risk–benefit of standard treatment schedules of radiotherapy</p> <p>Discuss personal protection, safety, hand washing and infection control procedures to all staff but especially radiation therapists with daily physical patient contact</p> <p>Alert staff groups to any suspected or proven COVID-19 case</p>
Operate	<p>Consolidate staff into small functional groups that do not depend on other groups and do not move to different clinical areas</p> <p>Consider temperature screening for all users of the radiotherapy centre</p> <p>Quickly disseminate information around COVID cases and agree with patient and staff if treatment will continue with PPE, stop or pause</p>
Compensate	<p>When treatment is paused agree radiobiological models and alpha/beta values for compensation on treatment restart</p> <p>Consider reassessing the CTV if growth may have taken place</p>

6. Declarations of interest

None.

Appendix. 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, Phillipines
 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
 Dr Henning Willers, USA
 Dr Matt Williams, UK

References

- [1] Mukherjee R et al. Hiding in the bunker: challenges for a radiation oncology department operating in the Severe Acute Respiratory Syndrome outbreak. *Australas Radiol* 2003;47(2):143–5.
- [2] Gay HA et al. Lessons learned from Hurricane Maria in Puerto Rico: practical measures to mitigate the impact of a catastrophic natural disaster on radiation oncology patients. *Practical Radiat Oncol* 2019;9(5):305–21.
- [3] @Rad_Nation. RadOnc Journal Club - COVID19 response. 2020 17/03/2020; Available from: <https://wke.lt/w/s/cehkH6>.
- [4] Slotman BJ, Ricardi U, Lievens Y. Radiotherapy in a time of crisis, ESTRO Presidents' statement. 2020.
- [5] Eichler TJ. COVID-19 recommendations to radiation oncology practices. *American Society of Therapeutic Radiation Oncology*; 2020.
- [6] Beaver K et al. Comparing hospital and telephone follow-up for patients treated for stage-I endometrial cancer (ENDCAT trial): a randomised, multicentre, non-inferiority trial. *BJOG* 2017;124(1):150–60.
- [7] Frankland J et al. Follow-up care after treatment for prostate cancer: evaluation of a supported self-management and remote surveillance programme. *BMC Cancer* 2019;19(1):368.
- [8] Schmidt-Hansen M, Baldwin DR, Hasler E. What is the most effective follow-up model for lung cancer patients? A systematic review. *J Thoracic Oncol* 2012;7(5):821–4.
- [9] Cusack M, Taylor C. A literature review of the potential of telephone follow-up in colorectal cancer. *J Clin Nurs* 2010;19(17–18):2394–405.
- [10] Zhou M et al. The utilization of telephone follow-up in the advanced cancer population: a review of the literature. *J Comp Eff Res* 2012;1(6):509–17.
- [11] Beaver K et al. Comparing hospital and telephone follow-up after treatment for breast cancer: randomised equivalence trial. *BMJ* 2009;338:a3147.
- [12] Kimman ML et al. Patient satisfaction with nurse-led telephone follow-up after curative treatment for breast cancer. *BMC Cancer* 2010;10(1):174.
- [13] Greenhalgh T et al. Video consultations for covid-19. *BMJ* 2020;368:m998.
- [14] Hoskin P et al. A multicenter randomized trial of ibandronate compared with single-dose radiotherapy for localized metastatic bone pain in prostate cancer. *JNCI* 2015;107(10).
- [15] Chow R et al. Single vs multiple fraction palliative radiation therapy for bone metastases: cumulative meta-analysis. *Radiother Oncol* 2019;141:56–61.

- [16] Yu JB et al. Persistent use of extended fractionation palliative radiotherapy for medicare beneficiaries with metastatic breast cancer, 2011 to 2014. *Am J Clin Oncol* 2019;42(6):493–9.
- [17] Ong WL et al. Variation in the use of single-versus multifraction palliative radiation therapy for bone metastases in Australia. *Int J Radiat Oncol Biol Phys* 2020;106(1):61–6.
- [18] Hoskin PJ et al. Effect of single-fraction vs multifraction radiotherapy on ambulatory status among patients with spinal canal compression from metastatic cancer: the SCORAD randomized clinical trial. *JAMA* 2019;322(21):2084–94.
- [19] Mulvenna P et al. Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial. *Lancet* 2016;388(10055):2004–14.
- [20] Haviland JS et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol* 2013;14(11):1086–94.
- [21] Brunt AM et al. Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3-week regimen delivered in the UK FAST-Forward Trial. *Radiother Oncol* 2016;120(1):114–8.
- [22] Livi L et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. *Eur J Cancer* 2015;51(4):451–63.
- [23] Bartlett FR et al. The UK HeartSpare Study (Stage II): multicentre evaluation of a voluntary breath-hold technique in patients receiving breast radiotherapy. *Clin Oncol (R Coll Radiol)* 2017;29(3):e51–6.
- [24] Vaidya JS et al. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. *Lancet* 2010;376(9735):91–102.
- [25] Esposito E, Douek M. Update on intraoperative radiotherapy: new challenges and issues. *Ecanermedscience* 2018;12:793.
- [26] Naoum GE et al. The impact of chest wall boost on reconstruction complications and local control in patients treated for breast cancer. *Int J Radiat Oncol Biol Phys* 2019;105(1):155–64.
- [27] Early Breast Cancer Trialists' Collaborative, G., et al., Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. *J Natl Cancer Inst. Monographs*, 2010. 2010(41): p. 162–177.
- [28] Hughes KS et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343. *J Clin Oncol* 2013;31(19):2382–7.
- [29] Matuschek C et al. The benefit of adjuvant radiotherapy after breast conserving surgery in older patients with low risk breast cancer - a meta-analysis of randomized trials. *Radiat Oncol (London, England)* 2017;12(1):60.
- [30] Olivetto IA et al. Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy. *J Clin Oncol* 2009;27(1):16–23.
- [31] Neal DE et al. Ten-year mortality, disease progression, and treatment-related side effects in men with localised prostate cancer from the ProtecT randomised controlled trial according to treatment received. *Eur Urol* 2020;77(3):320–30.
- [32] Crook J et al. Final report of multicenter Canadian Phase III randomized trial of 3 versus 8 months of neoadjuvant androgen deprivation therapy before conventional-dose radiotherapy for clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2009;73(2):327–33.
- [33] Ghadjjar P et al. Use of androgen deprivation and salvage radiation therapy for patients with prostate cancer and biochemical recurrence after prostatectomy. *Strahlenther Onkol* 2018;194(7):619–26.
- [34] Dearnaley DP et al. Escalated-dose versus control-dose conformal radiotherapy for prostate cancer: long-term results from the MRC RT01 randomised controlled trial. *Lancet Oncol* 2014;15(4):464–73.
- [35] Widmark A et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. *Lancet* 2019;394(10196):385–95.
- [36] Dearnaley D et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol* 2016;17(8):1047–60.
- [37] Brand DH et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. *Lancet Oncol* 2019;20(11):1531–43.
- [38] Parker CC et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet* 2018;392(10162):2353–66.
- [39] Salehi S et al. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol* 2019;2020:1–7.
- [40] Videtic GM et al. 30 Gy or 34 Gy? Comparing 2 single-fraction SBRT dose schedules for stage I medically inoperable non-small cell lung cancer. *Int J Radiat Oncol Biol Phys* 2014;90(1):203–8.
- [41] Siva S, Ball DL. Single fraction SBRT for early stage lung cancer; less is more? *Int J Radiat Oncol Biol Phys* 2019;103(5):1085–7.
- [42] World Health Organization. Rational use of personal protective equipment for coronavirus disease 2019 (COVID-19). 2020.
- [43] Ferguson N et al. Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand. Imperial College London; 2020.
- [44] National Health Service England. COVID 19 Information Governance Advice. 2020.
- [45] Filippi AR et al. COVID-19 outbreak in Northern Italy: First practical indications for radiotherapy departments. *Int J Radiat Oncol Biol Phys* 2020.
- [46] Royal College of Radiologists UK. The timely delivery of radical radiotherapy: standards and guidelines for the management of unscheduled treatment interruptions. Royal College of Radiologists; 2019.
- [47] Kunkler IH et al. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. *Lancet Oncol* 2015;16(3):266–73.
- [48] Bartelink H et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. *Lancet Oncol* 2015;16(1):47–56.
- [49] Malmström A et al. Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial. *Lancet Oncol* 2012;13(9):916–26.
- [50] Wick W et al. Temozolomide chemotherapy alone versus radiotherapy alone for malignant astrocytoma in the elderly: the NOA-08 randomised, phase 3 trial. *Lancet Oncol* 2012;13(7):707–15.
- [51] Suzuki A et al. Localized gastric cancer treated with chemoradiation without surgery: UTMD Anderson Cancer Center experience. *Oncology* 2012;82(6):347–51.
- [52] Rusthoven CG, Kavanagh BD. Prophylactic Cranial Irradiation (PCI) versus active MRI surveillance for small cell lung cancer: the case for Equipoise. *J Thoracic Oncol* 2017;12(12):1746–54.
- [53] Chauffert B et al. Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000–01 FFCD/SFRO study. *Ann Oncol* 2008;19(9):1592–9.
- [54] Hamdy FC et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016;375(15):1415–24.
- [55] Willeumier JJ, van der Linden YM, Dijkstra PDS. Lack of clinical evidence for postoperative radiotherapy after surgical fixation of impending or actual pathologic fractures in the long bones in patients with cancer; a systematic review. *Radiother Oncol* 2016;121(1):138–42.
- [56] Chow E et al. Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial. *Lancet Oncol* 2014;15(2):164–71.
- [57] Thirion PG et al. Non-inferiority randomised phase 3 trial comparing two radiation schedules (single vs. five fractions) in malignant spinal cord compression. *Br J Cancer* 2020.
- [58] Borgelt B et al. The palliation of brain metastases: final results of the first two studies by the radiation therapy oncology group. *Int J Radiat Oncol Biol Phys* 1980;6(1):1–9.
- [59] Priestman TJ et al. Final results of the Royal College of Radiologists' trial comparing two different radiotherapy schedules in the treatment of cerebral metastases. *Clin Oncol* 1996;8(5):308–15.
- [60] Deressa BT et al. Short-course 2-dimensional radiation therapy in the palliative treatment of esophageal cancer in a developing country: a Phase II study (Sharon Project). *Int J Radiat Oncol Biol Phys* 2020;106(1):67–72.
- [61] Roa W et al. International atomic energy agency randomized phase III study of radiation therapy in elderly and/or frail patients with newly diagnosed glioblastoma multiforme. *J Clin Oncol* 2015;33(35):4145–50.
- [62] Porceddu SV et al. Hypofractionated radiotherapy for the palliation of advanced head and neck cancer in patients unsuitable for curative treatment—"Hypo Trial". *Radiother Oncol* 2007;85(3):456–62.
- [63] Nguyen NTA et al. 0-7-21 hypofractionated palliative radiotherapy: an effective treatment for advanced head and neck cancers. *British J Radiol* 2015;88(1049):20140646.
- [64] Jeremic B et al. The International Atomic Energy Agency (IAEA) randomized trial of palliative treatment of incurable locally advanced non small cell lung cancer (NSCLC) using radiotherapy (RT) and chemotherapy (CHT) in limited resource setting. *Radiother Oncol* 2015;116(1):21–6.
- [65] Rathod S et al. Quality of life outcomes in a phase 3 Randomized trial of optimization of treatment of advanced non-small cell lung cancer using radiation therapy and chemotherapy: IAEA multicentric randomized phase 3 study (NCT00864331). *Int J Radiat Oncol Biol Phys* 2017;99(2):S103.
- [66] Report to the Medical Research Council by its Lung Cancer Working, P., Inoperable non-small-cell lung cancer (NSCLC): a Medical Research Council randomised trial of palliative radiotherapy with two fractions or ten fractions. *British J Cancer*, 1991. 63(2): p. 265–270.
- [67] A Medical Research Council (MRC) randomised trial of palliative radiotherapy with two fractions or a single fraction in patients with inoperable non-small-cell lung cancer (NSCLC) and poor performance status. Medical Research Council Lung Cancer Working Party. *Br J Cancer*, 1992. 65(6): p. 934–41.
- [68] Farina E et al. Palliative short-course radiotherapy in advanced pelvic cancer: a phase II study (SHARON Project). *Anticancer Res* 2019;39(8):4237–42.
- [69] Spanos Jr W et al. Phase II study of multiple daily fractionations in the palliation of advanced pelvic malignancies: preliminary report of RTOG 8502. *Int J Radiat Oncol Biol Phys* 1989;17(3):659–61.

- [70] Spanos Jr WJ et al. Effect of rest interval on tumor and normal tissue response—a report of phase III study of accelerated split course palliative radiation for advanced pelvic malignancies (RTOG-8502). *Int J Radiat Oncol Biol Phys* 1993;25(3):399–403.
- [71] Yan J et al. A hypofractionated radiotherapy regimen (0-7-21) for advanced gynaecological cancer patients. *Clin Oncol* 2011;23(7):476–81.
- [72] Perry JR et al. A phase III randomized controlled trial of short-course radiotherapy with or without concomitant and adjuvant temozolomide in elderly patients with glioblastoma (CTG CE.6, EORTC 26062–22061, TROG 08.02, NCT00482677). *J Clin Oncol* 2016;34(18_suppl). p. LBA2-LBA2.
- [73] Roa W et al. Abbreviated course of radiation therapy in older patients with glioblastoma multiforme: a prospective randomized clinical trial. *J Clin Oncol* 2004;22(9):1583–8.
- [74] Hall E et al. BC2001 long-term outcomes: a phase III randomized trial of chemoradiotherapy versus radiotherapy (RT) alone and standard RT versus reduced high-dose volume RT in muscle-invasive bladder cancer. *J Clin Oncol* 2017;35(6_suppl). p. 280-280.
- [75] Porta N et al. Hypo-fractionation in muscle-invasive bladder cancer: an individual patient data (IPD) meta-analysis of the BC2001 and BCON trials. *Int J Radiat Oncol Biol Phys* 2019;105(1):S138.
- [76] Vaidya JS et al. Reduced mortality with partial-breast irradiation for early breast cancer: a meta-analysis of randomized trials. *Int J Radiat Oncol Biol Phys* 2016;96(2):259–65.
- [77] Agrawal RK et al. First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015). *Radiother Oncol* 2011;100(1):93–100.
- [78] Brunt AM et al. FAST phase III RCT of radiotherapy hypofractionation for treatment of early breast cancer: 10-year results (CRUKE/04/015). *Int J Radiat Oncol Biol Phys* 2018;102(5):1603–4.
- [79] Vicini FA et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *Lancet* 2019;394(10215):2155–64.
- [80] Vaidya JS et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. *Lancet* 2014;383(9917):603–13.
- [81] Wang SL et al. Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial. *Lancet Oncol* 2019;20(3):352–60.
- [82] Sanz J et al. Once-weekly hypofractionated radiotherapy for breast cancer in elderly patients: efficacy and tolerance in 486 patients. *Biomed Res Int* 2018;2018:8321871.
- [83] Yom SS et al. NRG-HN002: a randomized phase II trial for patients with p16-positive, non-smoking-associated, locoregionally advanced oropharyngeal cancer. *Int J Radiat Oncol Biol Phys* 2019;105(3):684–5.
- [84] Lyhne NM et al. The DAHANCA 6 randomized trial: effect of 6 vs 5 weekly fractions of radiotherapy in patients with glottic squamous cell carcinoma. *Radiother Oncol* 2015;117(1):91–8.
- [85] Overgaard J et al. 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* 2003;362(9388):933–40.
- [86] Singh AK et al. One versus three fractions of stereotactic body radiation therapy for peripheral stage I to II non-small cell lung cancer: a randomized, multi-institution, phase 2 trial. *Int J Radiat Oncol Biol Phys* 2019;105(4):752–9.
- [87] Videtic GM et al. Long-term follow-up on NRG oncology RTOG 0915 (NCCTG N0927): a randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer. *Int J Radiat Oncol Biol Phys* 2019;103(5):1077–84.
- [88] Videtic GMM et al. A randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer: NRG oncology RTOG 0915 (NCCTG N0927). *Int J Radiat Oncol Biol Phys* 2015;93(4):757–64.
- [89] Din OS et al. Accelerated hypo-fractionated radiotherapy for non small cell lung cancer: results from 4 UK centres. *Radiother Oncol* 2013;109(1):8–12.
- [90] Iqbal MS et al. Hypofractionated concomitant chemoradiation in inoperable locally advanced non-small cell lung cancer: a report on 100 patients and a systematic review. *Clin Oncol* 2019;31(2):e1–e10.
- [91] Maguire J et al. SOCCAR: a randomised phase II trial comparing sequential versus concurrent chemotherapy and radical hypofractionated radiotherapy in patients with inoperable stage III non-small cell lung cancer and good performance status. *Eur J Cancer* 2014;50(17):2939–49.
- [92] Giuliani ME et al. Correlation of dosimetric and clinical factors with the development of esophagitis and radiation pneumonitis in patients with limited-stage small-cell lung carcinoma. *Clinical Lung Cancer* 2015;16(3):216–20.
- [93] Halvorsen TO et al. Tumour size reduction after the first chemotherapy-course and outcomes of chemoradiotherapy in limited disease small-cell lung cancer. *Lung Cancer* 2016;102:9–14.
- [94] Koay EJ et al. Dose-escalated radiation therapy for pancreatic cancer: a simultaneous integrated boost approach. *Pract Radiat Oncol* 2020.
- [95] Oar A et al. Australasian Gastrointestinal Trials Group (AGITG) and Trans-Tasman Radiation Oncology Group (TROG) guidelines for Pancreatic Stereotactic Body Radiation Therapy (SBRT). *Pract Radiat Oncol* 2019.
- [96] Catton CN et al. Randomized trial of a hypofractionated radiation regimen for the treatment of localized prostate cancer. *J Clin Oncol* 2017;35(17):1884–90.
- [97] Staffurth J et al. Impact of prostate cancer hypofractionation on patient reported outcomes: baseline to 5 years change in the CHHIP trial. *Int J Radiat Oncol Biol Phys* 2018;102(3):S1–2.
- [98] Zelefsky MJ et al. Five-year outcomes of a phase 1 dose-escalation study using stereotactic body radiosurgery for patients with low-risk and intermediate-risk prostate cancer. *Int J Radiat Oncol Biol Phys* 2019;104(1):42–9.
- [99] S. Chin et al. Ten-year outcomes of moderately hypofractionated salvage postprostatectomy radiation therapy and external validation; contemporary multivariable nomogram for biochemical failure *Int J Radiat Oncol Biol Phys*.
- [100] Zhou ZR et al. Short-course preoperative radiotherapy with immediate surgery versus long-course chemoradiation with delayed surgery in the treatment of rectal cancer: a systematic review and meta-analysis. *Surg Oncol* 2014;23(4):211–21.
- [101] Tunio MA et al. Whole-pelvis or bladder-only chemoradiation for lymph node-negative invasive bladder cancer: single-institution experience. *Int J Radiat Oncol Biol Phys* 2012;82(3):e457–62.
- [102] Byun HK et al. Clinical predictors of radiation-induced lymphopenia in patients receiving chemoradiation for glioblastoma: clinical usefulness of intensity-modulated radiotherapy in the immuno-oncology era. *Radiat Oncol* 2019;14(1):51.
- [103] Wernicke AG et al. Glioblastoma: radiation treatment margins, how small is large enough? *Pract Radiat Oncol* 2016;6(5):298–305.
- [104] Pisansky TM et al. Duration of androgen suppression before radiotherapy for localized prostate cancer: radiation therapy oncology group randomized clinical trial 9910. *J Clin Oncol* 2015;33(4):332–9.