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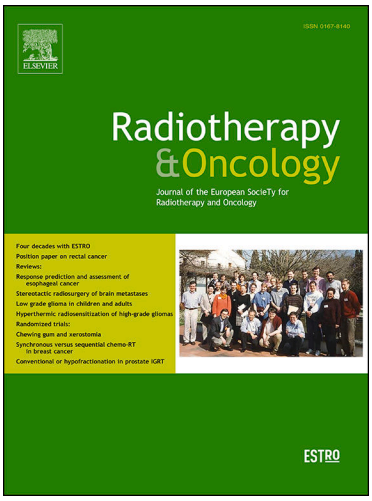

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PII: S0167-8140(20)30182-1
DOI: https://doi.org/10.1016/j.radonc.2020.04.001
Reference: RADION 8252

To appear in: *Radiotherapy and Oncology*

Received Date: 1 April 2020
Accepted Date: 1 April 2020

Please cite this article as: Guckenberger, M., Belka, C., Bezjak, A., Bradley, J., Daly, M.E., DeRuysscher, D., Dziadziuszko, R., Faivre-Finn, C., Flentje, M., Gore, E., Higgins, K.A., Iyengar, P., Kavanagh, B.D., Kumar, S., Le Pechoux, C., Lievens, Y., Lindberg, K., McDonald, F., Ramella, S., Rengan, R., Ricardi, U., Rimner, A., Rodrigues, G.B., Schild, S.E., Senan, S., Simone II, C.B., Slotman, B.J., Stuschke, M., Videtic, G., Widder, J., Yom, S.S., Palma, D., Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: An ESTRO-ASTRO consensus statement, *Radiotherapy and Oncology* (2020), doi: https://doi.org/10.1016/j.radonc.2020.04.001

Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: An ESTRO-ASTRO consensus statement

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Abstract

Background: The COVID-19 pandemic has caused radiotherapy resource pressures and led to increased risks for lung cancer patients and healthcare staff. An international group of experts in lung cancer radiotherapy established this practice recommendation pertaining to whether and how to adapt radiotherapy for lung cancer in the COVID-19 pandemic.

Methods: For this ESTRO & ASTRO endorsed project, 32 experts in lung cancer radiotherapy contributed to the consensus process using a modified Delphi process. We assessed potential adaptations of radiotherapy in two pandemic scenarios. The first, the early pandemic scenario of risk mitigation, is characterized by an altered risk-benefit ratio of radiotherapy for lung cancer patients due to their increased susceptibility for severe COVID-19 infection, and minimization of patient travelling and exposure of our radiotherapy staff. The second, a later pandemic scenario, is characterized by reduced radiotherapy resources. Six common lung cancer cases were assessed for both scenarios: peripherally located stage I NSCLC, locally advanced NSCLC, postoperative radiotherapy after resection of pN2 NSCLC, thoracic radiotherapy and prophylactic cranial irradiation for SCLC and palliative thoracic radiotherapy for stage IV NSCLC.

Results: In a risk-mitigation pandemic scenario, efforts should be made not to compromise the prognosis of lung cancer patients by departing from guideline-recommended radiotherapy practice. In that same scenario, postponement or interruption of radiotherapy treatment of COVID-19 positive patients is generally recommended to avoid exposure of cancer patients and staff to an increased risk of COVID-19 infection. In a severe pandemic scenario characterized by reduced resources, if patients must be triaged, important factors for triage include potential for cure, relative benefit of radiation, life expectancy, and performance status. Case-specific consensus recommendations regarding multimodality treatment strategies and fractionation of radiotherapy are provided.

Conclusion: This joint ESTRO-ASTRO practice recommendation established pragmatic and balanced consensus recommendations in common clinical scenarios of radiotherapy for lung cancer in order to address the challenges of the COVID-19 pandemic.

Background:

After the outbreak of the coronavirus 2019-nCov (COVID-19) in Wuhan, China, in December 2019,[1] the disease rapidly became a global pandemic. Infection rates peaked and began to decline in some Asian countries by March 2020, but Europe and the US are now among the most affected regions.[2] Most COVID-19 infections are characterized by only mild symptoms of fever and cough; however, there is a high risk of severe pulmonary infection and death, in particular for the elderly and populations with comorbidities such as diabetes, hypertension and cardiopulmonary diseases.[3,4] Cancer patients have been reported to be at increased risk of mortality.[5] Therefore, many countries have implemented strategies to reduce the risk of spread, aiming to slow-down or "flatten" the infection rate of the coronavirus and to stay within the capacity of the healthcare services, especially intensive care units.[6]

The pandemic mitigation strategies of most countries also apply to medical care in general and to oncology in particular, and include reduction of elective services, a focus on remote visits (e.g. telemedicine and video), and use of personal protective equipment. However, most health authorities maintain emergency services (e.g. for accidents) and services for diagnosis and treatment of severe diseases such as cancer. These dramatic developments related to COVID-19 are associated with challenges for the practice of radiation oncology,[7,8] especially for radiotherapy of lung cancer patients, who represent one of the highest-risk groups, with high risks of death from both cancer and COVID-19 illness.

It may be challenging for radiation oncologists to continue to follow accepted practice guidelines, given these limitations, and delivering standard therapies may even become inappropriate. There are two potential scenarios that may unfold, with different radiation practice patterns.[9] In a ***first (early) pandemic scenario***, sufficient radiotherapy resources are still available to deliver radiation. This is sometimes referred to as the "contingency standard of care" [10]. However, suppression strategies aiming to slow down the virus spread may also impact the practice of lung cancer radiotherapy due to: a) the need for suppression of the coronavirus and, therefore, the need to minimize the travel of patients[11] and exposure of our radiotherapy staff;[12] b) an altered risk-benefit ratio of radiotherapy for lung cancer patients due to their increased susceptibility for severe COVID-19 infection when repeatedly leaving their home and traveling to radiotherapy treatment. For example, a patient who contracts COVID-19 during a visit for radiation is at a high risk of morbidity and death due to that visit. In this scenario of the COVID-19 pandemic, standard-of-care practice of curative or palliative radiotherapy for lung cancer might require adaptations and lead to treatment recommendations that are outside current guidelines.[13] Hypofractionation is an option that could at least partially address these issues.

In a ***second (later) pandemic scenario***, radiotherapy resources may not be available in sufficient quantity for treatment of all patients. A severe shortage of radiotherapy resources may result from sickness or home-quarantine of our department staffing. Service or repair of radiotherapy software and hardware might be restricted or unavailable by radiotherapy vendors. These issues would require the allocation of resources and triage of patients,[14,15] in addition to the potential need to make changes to lung cancer radiotherapy prescriptions. This phase is sometimes referred to as the "crisis standard of care" [10].

In this setting of the COVID-19 pandemic, hypofractionation is an attractive treatment option, one that is actively being discussed within the radiotherapy community on social media platforms such as Twitter and theMednet. However, the results of such *ad hoc* discussions do not address the needs of our radiotherapy community in an optimal way. Individual opinions may not be clinically appropriate and might expose cancer patients to potential harm from suboptimal radiotherapy practice. On the other end of the spectrum, adoption of appropriate hypofractionation might be low if that practice is outside of international guidelines and not endorsed by recognized experts and professional societies, yet such guidelines often take many months to develop.

In this practice recommendation, which is endorsed by the European Society for Radiotherapy and Oncology (ESTRO) and the American Society for Radiation Oncology (ASTRO), an international group of experts in lung cancer radiotherapy aims to rapidly provide guidance about the potential need to adapt the practice and fractionation of radiotherapy for lung cancer in the current COVID-19 pandemic.

Methods

On March 22nd, 32 experts in lung cancer radiotherapy were invited to participate in this project, 16 European and 16 US/Canadian experts. By March 24th, 97% had agreed, and a replacement was found for the single invitee who was unavailable, to keep the total at 32 with a balance between groups. All invited participants are co-authors of recent national and international lung cancer practice guidelines or principal investigators of lung cancer clinical trials. A Delphi process was used to establish consensus about whether and how to adapt radiotherapy for lung cancer in the COVID-19 pandemic.[16] Surveys were circulated to all individual participants using the online survey tool SurveyMonkey. All respondents agreed to participate in a rapid Delphi process, with 24 hours to complete each round and successive rounds starting 24 hours after the closure of the previous round.

Two scenarios of the COVID-19 pandemic were assessed, both of which were already occurring in some geographical regions:

- **Early pandemic scenario 1 - risk mitigation**: In this scenario, we asked if respondents would recommend changes to standard practice during the early phase, considering these challenges: The altered risk-benefit ratio of radiotherapy for lung cancer patients due to their increased susceptibility for severe COVID-19 infection, and minimization of patient traveling and exposure of our radiotherapy staff.
- **Later pandemic scenario 2 - reduced radiotherapy resources:** In this scenario, we asked respondents to consider how their above recommendations from scenario 1 would change if a lack of radiotherapy resources prevented some patients at their centre from receiving radiation treatment.

Six common lung cancer cases were assessed for both pandemic scenarios (Table 1). For all six, we assumed a patient with average / standard characteristics for the lung cancer population. The standard treatment for each option was provided, consistent with guideline-recommended radiotherapy according to current versions of the National Comprehensive Cancer Network (NCCN), ESTRO, ASTRO and European Organization for Research and Treatment of Cancer (EORTC) guidelines.

Table 1. The six lung cancer cases described, including the diagnosis and the presumed standard guideline-recommended therapy.

Case 1: Stage I NSCLC	New diagnosis of stage I, inoperable, peripherally located NSCLC
	Institutional standard fractionation of SBRT according to NCCN: 3-4 Fx total dose 45 – 54 Gy
Case 2: Stage III	Locally advanced stage IIIA (bulky N2) NSCLC

NSCLC	Standard fractionation of radiochemotherapy: 30-33 Fx over 6-6.5 weeks, total dose 60-66 Gy
Case 3: PORT NSCLC	Resected N2 (multi-station and extra nodal spread) NSCLC
	Standard fractionation of radiotherapy: 27 Fx over 5.5 weeks, total dose 54 Gy
Case 4: LS SCLC	SCLC, limited stage
	Standard fractionation of radiochemotherapy: 30 Fx over 3 weeks, BID, total dose 45 Gy, OR 33 Fx over 6.5 weeks, total dose 66 Gy
Case 5: PCI LS SCLC	PCI for SCLC limited stage after good response to radiochemotherapy
	Standard fractionation of radiotherapy: 10 Fx over 2 weeks, total dose 25 Gy
Case 6: palliative NSCLC	Palliative metastatic NSCLC with failure after first-line chemo-IO combination and symptoms due to mediastinal/hilar disease progression and severe cough and moderate dyspnea.
	Standard fractionation of radiotherapy: 10 Fx over 2 weeks, total dose 30 Gy

The questions for the first round of the Delphi process are shown in Table 2. All responses were analyzed and consolidated by two investigators (MG and DAP). A threshold of ≥66% for agreement or disagreement was required for each item to reach consensus and a threshold of ≥80% for strong consensus. For questions voting on prioritizing the cases, the results of the vote are presented without necessarily achieving consensus. In the second and third rounds, participants received the results and summary of comments from prior rounds, and were asked to vote again on items that had not reached ≥66% agreement. New questions were constructed (by MG and DAP) in order to gain clarification or to raise issues noted in the comments from participants. Following the third round, any items still lacking consensus were not considered a recommendation, but some important issues raised by a large minority of respondents are reflected below.

Table 2. Questions in the first round of the Delphi process.

Early pandemic scenario 1 - risk mitigation	
All cases	Do you recommend that physicians change their radiotherapy practice to

	address the challenges in this early phase of the COVID-19 pandemic? (i.e. risks due to multiple visits, susceptibility of lung cancer patients to COVID-19 morbidity/mortality)
All cases	Would you recommend postponing the initiation of treatment by 4-6 weeks?
All cases	Would you recommend hypofractionating beyond your usual fractionation?
Case 1-3	Would your answers to questions #2 and #3 above change if the tumor was mutation positive (EGFR or ALK) or PD-L1 positive (i.e. >50%)?
Case 2	Would you recommend induction therapy in this case?
All cases	If you recommended hypofractionation, what would be the maximum degree of hypofractionation you would propose to a patient in your clinical service? Specify the total dose, number of fractions, total treatment time, and provide any pertinent references if available.
All cases	If this patient was COVID-19 positive before starting treatment, would you postpone RT until the patient becomes asymptomatic and the test for COVID-19 negative?
All cases	If this patient became COVID-19 positive after starting treatment, would you recommend interrupting RT until the patient becomes asymptomatic and the test for COVID-19 negative?
Later pandemic scenario 2 - reduced radiotherapy resources	
All cases	How highly would you prioritize this patient's treatment compared to all other cancer patients in your centre?
All cases	If there was a critical shortage of RT capacity, would you recommend further hypofractionation beyond what you have described above?
All cases	If you answered yes to the question above, what would be the maximum degree of hypofractionation you would propose to a patient in your clinical service? Specify the total dose, number of fractions, total treatment time, and provide any pertinent references if available.
All cases	In the setting of reduced RT capacity, if this patient was COVID-19 positive before the start of treatment, what would be the maximum duration to postpone the initiation of radiotherapy (in weeks)?
All cases	In the setting of reduced RT capacity, if this patient became COVID-19 positive after starting treatment, would you recommend interrupting RT until the patient becomes asymptomatic and the test for COVID-19 negative?
Case 1	Case 1B: An operable patient with stage I NSCLC is referred to you by a thoracic surgeon because timely access to surgery is not available due to surgical capacity issues. Would you treat with SABR?
Case 2	Would you recommend starting with induction chemotherapy to postpone the start of radiation?
Overall	Please rank the six cases in order of priority, starting with the highest-priority case, in the setting of reduced resources.
Overall	If you were to triage patients for treatment, in the setting of reduced RT

	resources, please provide up to 5 factors that you would use to decide who gets treatment, in order of importance.

Results

A total of three Delphi rounds were conducted. Surveys remained open for 24 hours and response rates were 29/32 (March 23rd, round 1), 31/32 (March 25th, round 2) and 30/32 (March 27th, round 3).

Early phase of the COVID-19 pandemic: risk mitigation

Question: Would you recommend postponing the initiation of treatment by 4-6 weeks?
In the early phase of the COVID-19 pandemic, decisions on delay of treatment depended on the clinical case (Table 3). There was a strong consensus not to postpone curative treatment for case 2 (stage III NSCLC), case 4 (LS SCLC) and case 6 (palliative NSCLC). In contrast, there was a strong consensus to postpone treatment for case 3 (PORT NSCLC) and a consensus to postpone for case 5 (PCI SCLC).

Table 3. Recommendations regarding postponement of treatment

Would you recommend postponing the initiation of treatment by 4-6 weeks?	
Case	**Response**
Case 1: stage I NSCLC	Yes: 43% No: 57%
Case 2: stage III NSCLC	Yes: 4% **No: 96% (strong consensus)**
Case 3: PORT NSCLC	**Yes: 82% (strong consensus)** No: 18%
Case 4: LS SCLC	Yes: 11% **No: 89% (strong consensus)**
Case 5: PCI SCLC	**Yes: 70% (consensus)** No: 30%
Case 6: Palliative NSCLC	Yes: 4% **No: 96% (strong consensus)**

For case 1 (stage I NSCLC), answers on postponement were balanced and we asked for factors influencing the decision whether or not to postpone. There was strong consensus that tumor growth rate (87%) should be used in the decision-making process and some support for these other factors (33-66%): patient preference, solid component vs GGO, patient performance status, T1 vs T2, current and future status of pandemic.

For case 5 (PCI SCLC) we asked about regular contrast-enhanced cranial MRI follow up as an alternative to PCI: this strategy was supported by 46% without reaching consensus.

Question: Would you recommend hypofractionating beyond your usual fractionation?

In the early phase of the COVID-19 pandemic, there was consensus not to universally change radiotherapy practice to more hypofractionated regimens (table 4). There was consensus or strong consensus not to change to more hypofractionated approaches in case 3 (PORT NSCLC), case 4 (LS SCLC) and case 5 (PCI SCLC). In contrast, there was strong consensus to change to more hypofractionation in case 6 (palliative NSCLC).

Table 4. Fractionation recommendations.

Would you recommend hypofractionating beyond your usual fractionation?			
Case	**Standard fractionations**	**Response**	**Maximum degree of hypofractionation supported**
Case 1: stage I NSCLC	SBRT: 45-54 Gy in 3 Fx, 48 Gy in 4 fractions	Yes: 50% No: 50%	30-34 in 1 Fx [17]: 90% support if choosing hypofractionation **(strong consensus)**
Case 2: stage III NSCLC	Radiochemotherapy 60-66 Gy in 30-33 Fx over 6-6.5 weeks	Yes: 46% No: 54%	
Case 3: PORT NSCLC	PORT: 50-60 Gy over 5-6 weeks	Yes: 29% **No: 71% (consensus)**	
Case 4: LS SCLC	Radiochemotherapy 60-66 Gy in 30-33 Fx over 6-6.5 weeks, or 45 Gy in 30 Fx over 3 weeks using BID fractions of 1.5 Gy	Yes: 33% **No: 67% (consensus)**	
Case 5: PCI SCLC	PCI: 25 Gy in 10 Fx over 2 weeks	Yes: 7% **No: 93% (strong consensus)**	

Case 6: Palliative NSCLC	30Gy in 10 Fx over 2 weeks	**Yes: 89% (strong consensus)** No: 11%	Favored fractionations : 20Gy in 5 Fx (30%) [18] 17Gy in 2 Fx (37%) [19] 8-10Gy in 1Fx (33%) [20]

If a decision was made for hypofractionation beyond standard fractionations, there was strong consensus for using a single fraction SBRT of 30-34 Gy in case 1 (stage I NSCLC). In case 6 (palliative NSCLC), palliative regimens in 5 fractions, 2 fractions and a 1 fraction all had similar support.

For case 2 (stage III NSCLC), we further differentiated fractionations based on whether the patient was treated with radiotherapy only, with sequential radiochemotherapy or concomitant radiochemotherapy. There was strong consensus that hypofractionated radiotherapy is appropriate in radiotherapy alone or sequential radiochemotherapy; however, there was consensus against hypofractionation in concomitant radiochemotherapy (Table 5). Various fractionations were considered as appropriate, with total doses between 50Gy and 66Gy delivered in 15 - 30 fractions.

Table 5. Recommended hypofractionation regimens based on availability/use of concurrent and sequential radiochemotherapy, or radiotherapy alone.

Would you consider hypofractionated radiotherapy as appropriate?		
Case 2 stage III NSCLC	**Response**	**Maximum degree of hypofractionation supported**
Radiotherapy only	**Yes: 97% (strong consensus)** No: 3%	60 Gy in 15 Fx (33%) [21,22] 60 Gy in 20 Fx (27%) [23] 60-66 Gy in 24-30 Fx (2.2-2.75 Gy/day) (23%) [24] 55 Gy in 20 Fx (13%) [25] None (3%)
Sequential radiochemotherapy	**Yes: 97% (strong consensus)** No: 3%	60-66 Gy in 24-30 Fx (2.2-2.75 Gy/day) (27%) [24] 55 Gy in 20 Fx (27%) [25] 60 Gy in 15 Fx (23%) [21,22] 60 Gy in 20 Fx (20%) [23] None (3%)
Concomitant radiochemotherapy	Yes: 27% **No: 73% (consensus)**	See footnote*

***Although there was consensus not to recommend hypofractionation, the respondents supportive of hypofractionation (n=11) were asked which fractionation(s) they would support, with multiple answers allowed. The favored options were 60-66 Gy in 22-30 Fx, given at 2.2-2.75 Gy/day, (75%) and 55 Gy in 20 Fx (63%)

Question: An operable patient with stage I NSCLC is referred to you by a thoracic surgeon because timely access to surgery is not available due to surgical capacity issues. Would you treat with SBRT?

Surgical capacities might become especially at risk because of the strong need for intensive care and ventilators in patients with severe COVID-19 infection. We therefore addressed a situation where an operable patient with stage I NSCLC is referred to radiation oncology by a thoracic surgeon because timely access to surgery is not available due to surgical capacity issues: it was asked whether treatment with SBRT would be offered. There was a 100% consensus to offer SBRT.

Question: Which multi-modality strategies would you consider as reasonable in order to address the challenges in this early phase of the COVID-19 pandemic?

This question was asked for the curative stage III NSCLC (case 2) only. It was explicitly described that the patient does not have any contraindications against the guideline recommended standard-of-care concomitant radiochemotherapy. Concurrent radiochemotherapy achieved strong consensus as the preferred treatment strategy. Radiotherapy alone, chemotherapy followed by radiotherapy and chemotherapy followed by radiochemotherapy were not considered as reasonable treatment strategies by >33% of participants.

We also asked if respondents would recommend against any standard concurrent chemotherapy agents (e.g. cisplatin-etoposide, cisplatin-vinka alkaloid, cisplatin-pemetrexed, carboplatin-paclitaxel, or carboplatin monotherapy), and there was no consensus to recommend against any of these. The carboplatin-paclitaxel regimen was chosen as a regimen of concern most often (by 37% of respondents), potentially due to risks of myelosuppression and/or pneumonitis.

Question: Would your multi-modality treatment strategy change if the tumor was mutation positive (EGFR or ALK) or highly PD-L1 positive (i.e. >50%)? (Cases 1-3)

There was strong consensus (96%) not to change the treatment strategy for case 1 (stage I NSCLC) and almost consensus (64%) for case 3 (PORT NSCLC).

For case 2 (stage III NSCLC), we asked about induction strategies to postpone the start of radiotherapy for the populations described in this question, although these are not yet evidence-based treatment options. There was limited support but no consensus to consider induction EGFR-targeting TKI for EGFR mutated NSCLC or induction ALK-targeting TKI for NSCLC with ALK rearrangement (38%); induction chemo-IO for cancers highly PD-L1 positive was not supported (17%).

For case 3 (PORT NSCLC) we asked about EGFR/ALK targeting TKIs and about immune-checkpoint inhibition (+/- chemotherapy) as options to postpone radiotherapy or as alternatives to radiotherapy (although these are not yet evidence-based treatment options): none of these strategies was supported by >25% of the participants.

Question: Handling of COVID-19 positive patients?

There was consensus in all cases to postpone initiation of radiotherapy until the patient becomes asymptomatic and the test for COVID-19 becomes negative (Table 6). When patients are diagnosed as COVID-19 positive during radiotherapy treatment, there was consensus to interrupt radiotherapy until the patient becomes asymptomatic and the test for COVID-19 is negative in the three cases of non-curative intent radiotherapy (cases 3, 5 and 6) whereas opinions were evenly split for the cases with curative radiotherapy at the time of primary diagnosis (cases 1, 2 and 4).

Table 6. Recommendations on delay or interruption of treatment in COVID-19 positive patients.

Patient case	**Time patient is diagnosed as COVID-19 positive**	**Postpone or interrupt RT?**
Case 1: Stage I NSCLC	Start of Tx	**Yes: 96% (Strong consensus)**
	After start of Tx	Yes: 54%
Case 2: Stage III NSCLC	Start of Tx	**Yes: 100% (Strong consensus)**
	After start of Tx	Yes: 57%
Case 3: PORT NSCLC	Start of Tx	**Yes: 96% (Strong consensus)**
	After start of Tx	**Yes: 68% (Consensus)**
Case 4: LS SCLC	Start of Tx	**Yes: 89% (Strong consensus)**
	After start of Tx	Yes: 48%
Case 5: PCI SCLC	Start of Tx	**Yes: 93% (Strong consensus)**
	After start of Tx	**Yes: 67% (consensus)**
Case 6: Palliative NSCLC	Start of Tx	**Yes: 74% (Consensus)**

	After start of Tx	**Yes: 78% (Consensus)**

For case 2 (stage III NSCLC) and case 4 (LS SCLC) with longer radiotherapy treatments, the following factors were described as relevant in the decision-making process of whether or not to interrupt radiotherapy in patients diagnosed as COVID-19 positive: COVID-19 related symptoms, symptoms of lung cancer, and infection with COVID-19 near the end of treatment.

Later phase of the COVID-19 pandemic: lack of radiotherapy resources and need for patient triage

For the later phase of the COVID-19 pandemic with potentially reduced radiotherapy resources, we addressed the questions whether further hypofractionation or postponement of radiotherapy for COVID-19 positive patients would be considered as reasonable and how to prioritize and triage patients. Results are summarized in Table 7. For case 3 (PCI SCLC) there was strong consensus (83%) for regular contrast-enhanced cranial MRI follow up instead of PCI. Availability of MRI may, however, be limited during a pandemic situation.

Table 7. Recommendations regarding hypofractionation of treatment in the later phase of the COVID-19 pandemic characterized by a lack of radiotherapy resources

Case	**Maximum hypofractionation considered as appropriate (66% threshold)**
Case 1: stage I NSCLC	30-34 Gy in 1Fx
Case 2: stage III NSCLC	55-60Gy in 20Fx
Case 3: PORT NSCLC	Consensus against hypofractionation
Case 4: LS SCLC	40-45 Gy in 15Fx
Case 5: PCI SCLC	Consensus against hypofractionation
Case 6: Palliative NSCLC	8-10Gy in 1Fx

Regarding postponement or interruption of treatment for COVID-19 positive patients during scenario 2, since the consensus in Scenario 1 was to postpone and interrupt in all situations, it was concluded that treatment would be postponed/interrupted until the patient recovers and is COVID-19 negative in Scenario 2 as well, since it is a more extreme example.

Prioritization of Cases and Triage of Patients

Table 8 shows the ranking of cases based on relative priority, their perceived priority relative to all other types of cancer cases, and the top 5 factors recommended in order to triage patients in a setting where not all patients can receive radiotherapy due to capacity shortages.

Table 8 Prioritization of lung cancer patients and factor for triaging of patients

Prioritization of lung cancer patients			**Top 5 factors for triaging patients across all radiotherapy cases**
Rank	**Case***	**Relative Priority Compared All Other Types Cancer Cases in Department****	
1.	Stage III NSCLC	Very high/high (71% consensus)	1. Potential for cure
2.	LS-SCLC SCLC	Very high/high (78% consensus)	2. Relative benefit of RT vs. other treatment options
3.	Stage I NSCLC	High/average (near consensus: 65%)	3. Active COVID-19 infection (absence thereof)
4.	Palliative NSCLC	No consensus. Widely dispersed responses.	4. Life expectancy
5.	PORT NSCLC	Low/very low (68% consensus)	5. Performance Status
6.	SCLC PCI	Low/very low (81% consensus)	

*The six cases were ranked, with 6 points given for a #1 ranking, 5 points for #2, etc, and the average number of points was determined. The average scores, in order of ranking as listed in the table, were 5.2, 4.9, 4.1, 3.0, 2.1 and 1.7, respectively.

**Respondents were asked to prioritize each case as very high, high, average, low, or very low, corresponding to quintiles of priority (e.g. very high = top 20%, very low = bottom 20%), compared to all types of cancers treated in their department. Adjacent categories were combined to determine consensus.

Discussion

This Delphi process was able to achieve consensus in many important aspects of lung cancer radiotherapy in the current COVID-19 pandemic. A total of 32 international experts in lung cancer radiotherapy completed 3 rounds of a consensus-building process and addressed six common lung cancer cases within the context of two different scenarios of the COVID-19

pandemic. Beyond detailed recommendations shown above, the following three take-home messages should be considered in lung cancer radiotherapy.

First, in a risk-mitigation pandemic scenario where radiotherapy resources remain available, efforts should be made to not compromise the prognosis of lung cancer patients by departing from guideline-recommended radiotherapy practice. Second, in that same scenario, postponement or interruption of radiotherapy treatment of COVID-19 positive patients should be considered to avoid exposure of cancer patients and staff to an increased risk of COVID-19 infection. Third, in a severe pandemic scenario characterized by reduced resources, if patients must be triaged, important factors included potential for cure, relative benefit of radiation, life expectancy, and performance status.

This joint ESTRO-ASTRO practice recommendation aims to provide rapid, pragmatic and balanced guidance in common clinical scenarios of radiotherapy for lung cancer. Practitioners must use their clinical judgement when considering how these consensus statements apply to their individual clinical practice. These consensus statements are not absolute clinical practice recommendations. Clinical decisions should take into account all clinical factors, and in some settings the consensus recommendations may not be appropriate. The decision-making process will be influenced by various stakeholders (governments, health care authorities, hospital and university administration), will be restricted by logistical and financial aspects, will need to follow the appropriate legal frameworks, and will need to be put into political and cultural context. The ability to implement hypofractionation may depend on departmental resources available (e.g. physicist).

This ESTRO-ASTRO practice recommendation used methodologies that are established quality indicators for regular consensus and guideline processes:[26] the practice recommendation was officially endorsed by the ESTRO and ASTRO societies, a sufficiently large group of international experts in lung cancer radiotherapy contributed to this recommendation, the modified Delphi process started with open questions aiming to comprehensively collect the knowledge and opinions of all participants and consensus was established by follow-up rounds of feedback and voting. A systematic review was not part of the practice recommendation due to time constraints, and especially due to a lack of evidence for pandemic situations.

All co-authors therefore encourage practitioners to consider the results of this ESTRO-ASTRO practice recommendation on whether and how to adapt radiotherapy for lung cancer to the COVID-19 pandemic. Finally, we want to express our gratitude to all colleagues of all professions and disciplines who continue delivering optimal cancer care in serious situations such as now - take care of yourselves as well as your patients.

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Practice recommendations for lung cancer radiotherapy during the COVID-19 pandemic: An ESTRO-ASTRO consensus statement

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Conflict of Interest Disclosures:

A. Bezjak: AstraZeneca advisory board.
J. Bradley: AstraZeneca Scientific Advisory Board; Mevion Medical Systems Scientific Advisory Board; Genentech Scientific Advisory Board.
M. Daly: Research funding from EMD Serono and Genentech, Boston Scientific Advisory Board, Triptych Health Partners consulting.
R. Dziadziuszko: AstraZeneca, Pfizer, Roche, Seattle Genetics, Takeda Advisory Boards.
C. Faivre-Finn: research funding from AstraZeneca and Elekta and Astra Zeneca Advisory Boards.
M Guckenberger: research funding from AstraZeneca.
K. Higgins: Astra Zenenca Advisory Board/Consultant, Genetech Advisory Board, Varian Consultant. Research Funding RefleXion Medical.
C. Le Pechoux: Participation in Astra Zeneca, Nanobiotix and Roche Advisory Boards, Participation in educational meetings Amgen, Astra Zeneca, Lilly, Medscape, PrimeOncology.
Y Lievens: personal fees from AstraZeneca and RaySearch.
U Ricardo: Astra Zeneca Advisory Board.
A. Rimner: Research funding from Varian Medical Systems, Boehringer Ingelheim, Pfizer, AstraZeneca, Merck; Personal fees from: AstraZeneca, Merck, Research to Practice, Cybrexa, More Health.
S. Schild: UpToDate.
S. Senan: consulting/advisory fees from AstraZeneca, Merck, Celgene, and departmental research funding from ViewRay Inc., Varian Medical Systems and AstraZeneca.
M Stuschke: research funding from AstraZeneca.
S. Yom: research funding from Genentech, Merck, Bristol-Myers Squibb, BioMimetix;
The other authors declare no conflicts of interest.

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Highlights:

- Risk-mitigation pandemic scenario: efforts should be made not to compromise the prognosis of lung cancer patients by departing from guideline-recommended radiotherapy practice.
- Postponement or interruption of radiotherapy of COVID-19 positive patients is generally recommended to avoid exposure of cancer patients and staff to an increased risk of COVID-19 infection.
- Severe pandemic scenario characterized by reduced resources: important factors for patient triage include potential for cure, relative benefit of radiation, life expectancy, and performance status.