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Yale Radiation Oncology COVID19 Guidelines

Disclaimer

*These guidelines were based on best available evidence and expert opinion and were created by the Yale School of Medicine Department of Therapeutic Radiology faculty. Some elements of this guideline are based on pre-publication figures and tables from Zaorsky et al. Adv Radiat Oncol 2020. (*https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/COVID-Zaorsky-et-al(ADRO).pdf)

These guidelines are being provided for voluntary, educational use by health care providers during an urgent and evolving COVID-19 pandemic. They are not medical or legal advice and are not intended to be used for diagnosis or treatment of individual conditions. They do not endorse or recommend specific products or therapies, mandate any specific course of medical care, or constitute a statement of the standard of care. The answers are not deemed inclusive of all proper approaches or exclusive of other methods reasonably directed to obtaining the same results. Each health care provider must make the ultimate judgment regarding treatment and management approaches considering all the circumstances presented. Neither Yale School of Medicine, nor authors of this manuscript or Yale New Haven Hospital or Yale Medicine assume liability for the information, conclusions, and recommendations contained in the guidelines or any injury or damage to persons or property arising out of or related to any use of this information or any errors or omissions. The guidelines are based on information available at the time the workgroup prepared the responses. There may be new developments that are not reflected here.

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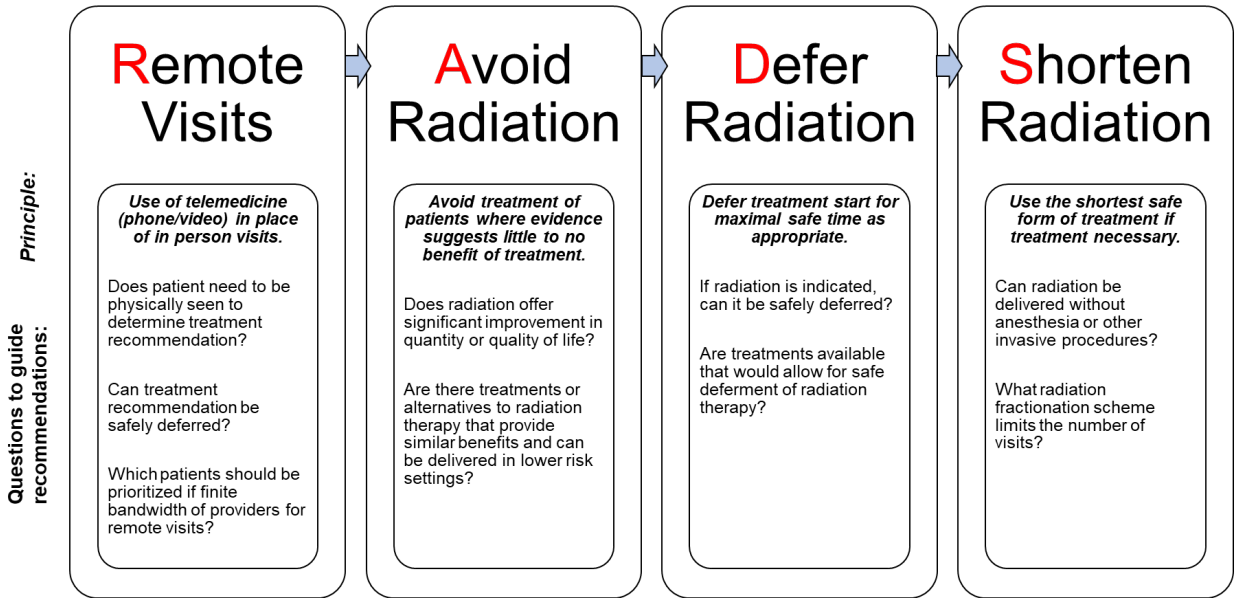
RADS FRAMEWORK

(Figure developed by Robert Dess MD, from Zaorsky et al. Adv Rad Oncol. 2020. In Press https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/COVID-Zaorsky-et-al(ADRO).pdf)



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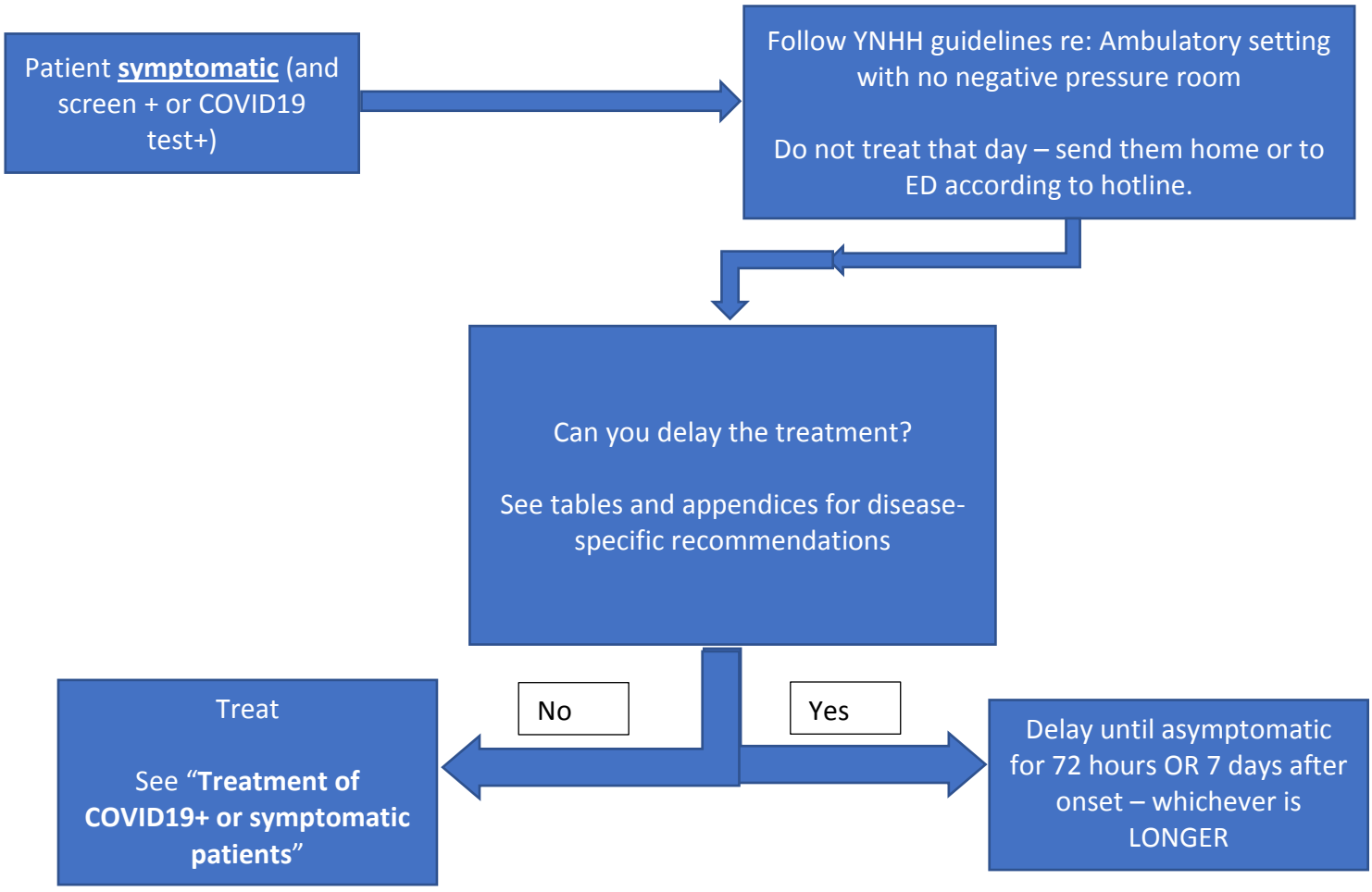
[SYMPTOMATIC PATIENTS AND SCREEN+] or [SYMPTOMATIC AND COVID19 TEST+]



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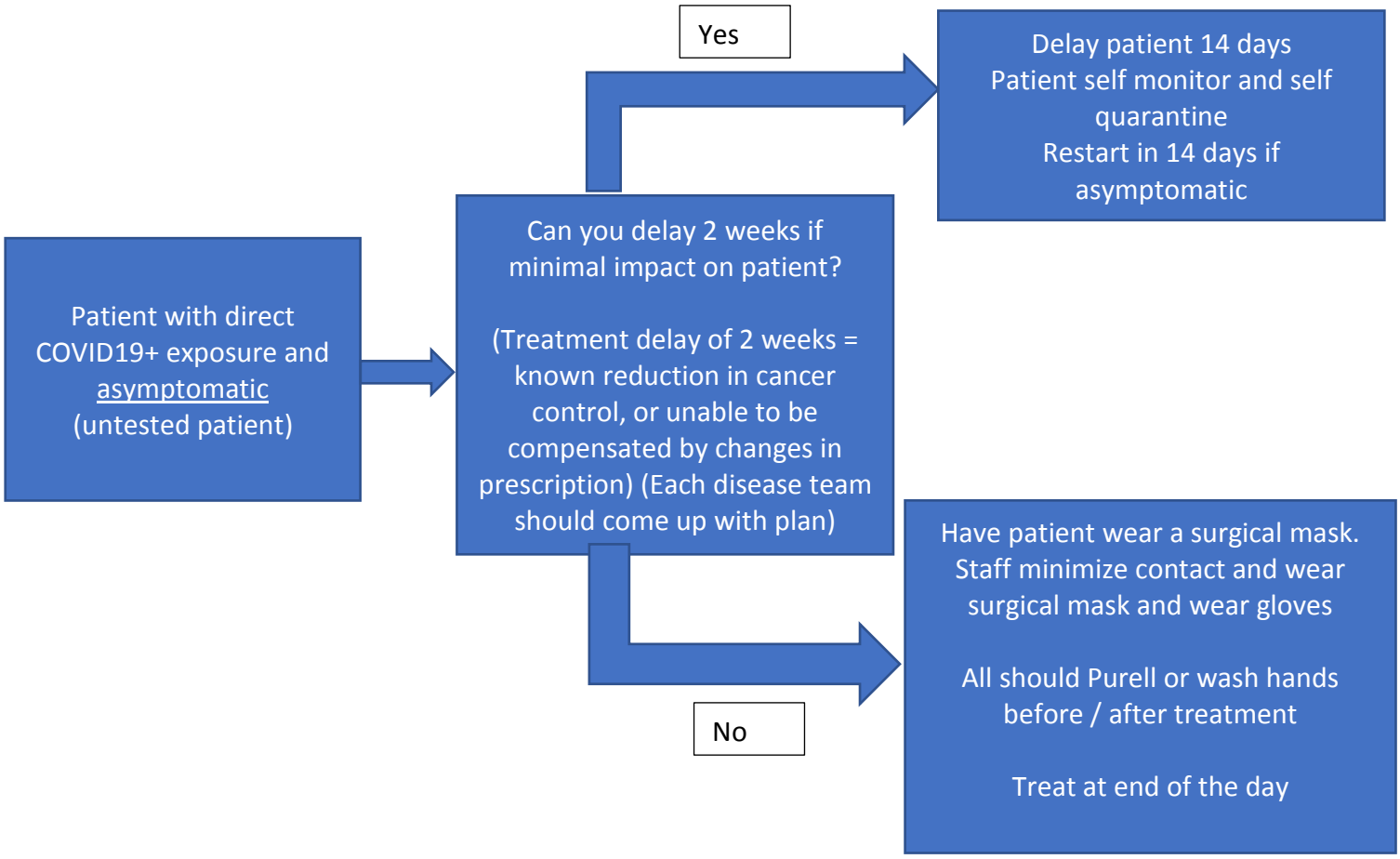
ASYMPTOMATIC PATIENTS WITH DIRECT EXPOSURE



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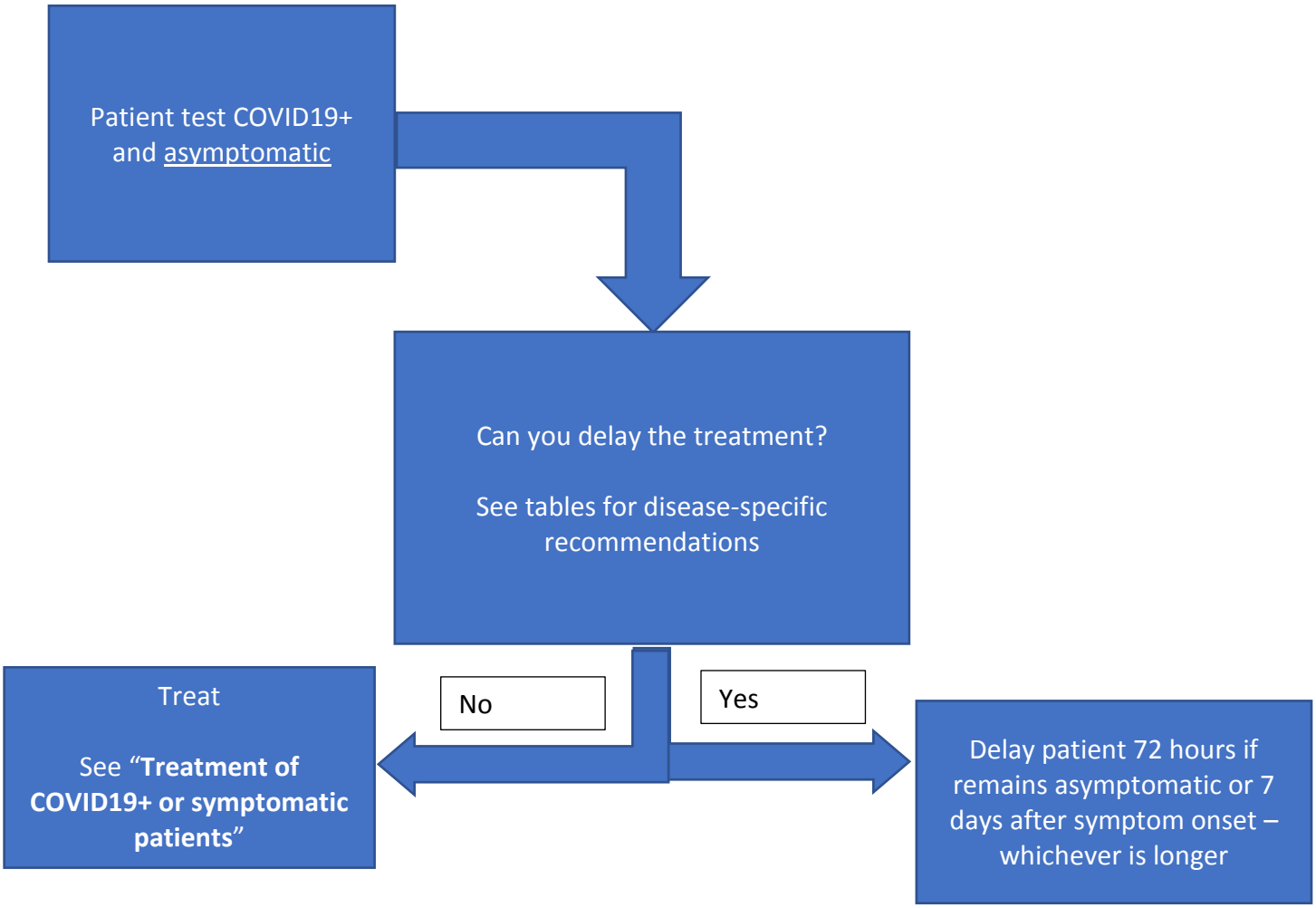
COVID19+ AND ASYMPTOMATIC



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Approach to palliative treatment

Life threatening or morbid without immediate treatment **and** **patient overall survival expected to be > 3 months?**	**Strategy**
Yes Acceptable indications for treatment while symptomatic or COVID19+: Cord compression Microvascular bleeding that is life threatening (note: named vessel / large vessel bleeds do not respond well to radiotherapy) Grade 4 or 5 per SVC algorithm (see SVC algorithm)	Treat single fraction if possible. 8 Gy x 1 for pain or bony lesion 10 Gy x 1 for bleeding if not involving spine If single fraction not possible, hypofractionate as much as possible Brain metastases can be deferred per algorithm, and treated with single fraction gamma knife For endobronchial obstruction consider 8 Gy x 1 or 17 Gy in 2 weekly fractions
No	Maximize medical therapy. Treat after algorithm allows

***Ventilated patients who absolutely require radiation treatment should be discussed with physician. This should be an extremely rare and unlikely occurrence given the amount of staff required and the infection control risk that will be caused by the movement of a ventilated patient through the hospital to the radiation unit.**

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Approach to curative intent therapy

Disease site	Criteria for delay	Mitigation strategy
Prostate cancer (intact)	All intermediate risk patients with localized disease undergoing moderately hypofractionated or standard fractionated treatment can be delayed up to 2 weeks without mitigation. If delayed up to 3 weeks see mitigation strategy For intermediate risk patients undergoing SBRT see mitigation strategy If treatment has reached >72 Gy can complete therapy if a delay over 2 weeks is likely See appendix for further recommendations	It patients delayed 3 weeks consider additional 1-3 fractions if standard fractionation (1.8-2.0 Gy). If hypofractionated, no mitigation required. SpaceOAR disintegration after 12 weeks may require replanning or additional CBCT scrutiny, but does not by itself require patients to be treated while COVID19+ or symptomatic especially if fiducial markers have been placed Patients undergoing SBRT should be considered for increased dose per fraction (8 Gy per fraction) or completing with treatment every day to minimize treatment length. See appendix for further recommendations
Prostate cancer (postop)	All patients can be delayed up to 3 weeks If treatment has reached 64 Gy (salvage/adjuvant) can complete therapy if a delay over 2 weeks is likely See appendix for further recommendations	If patients delayed 3 weeks consider additional fraction to total 72 Gy See appendix for further recommendations
Bladder cancer	All patients can be delayed up to 2 weeks without mitigation	Can use the 2 week break for a second look cystoscopy if

		concerns about disease progression
Breast cancer	Whole breast radiotherapy [WBRT] (Impact of treatment [TX] break is low) (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**	Do not change WBRT dose in the setting of a TX break (continue original hypofractionated or conventional TX). Boost portion can be adjusted as follows: - ASSUMING SEQUENTIAL BOOST AFTER WBRT: • IF NO BOOST ORIGINALLY INTENDED, ADD BOOST AFTER WBRT (10 Gy/5 fx conventional fractionation [CF] or 10 Gy/4 fx hypofractionated [HF]) - If initially plan DID have a sequential boost and treatment interuption: • Can add additional 2 Gy fractions up to 66 Gy (CF) or additional 2.5 Gy fraction to 52.55 Gy (HF) If original intended dose was 66 Gy (high risk patient), can increase dose to 70 Gy/2 Gy Fx (CF) and consider reducing the volume to the highest risk region. (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**

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Breast cancer	Chest wall RT (Impact of treatment break is low) (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**	Similar to above, but substitute lumpectomy cavity PTV for mastectomy scar PTV (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**
Breast cancer	RNI (SCV, ax, IM) with WBRT/PMRT (Impact of treatment break is low) (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**	Dose max of 50 Gy in 2 Gy fractions (unless boosting IM nodes) (see: **Yale Breast Team COVID-19 Clinical Patient Guidelines)**
Esophagus cancer	Defer patients who have received 10 Gy or less; deliver definitive dose later Continue treatment for definitive CRT patients at >10 Gy if at all possible Reduce dose for pre-operative patients to 41.4 Gy	Start induction chemotherapy to defer new starts For patients delayed after 10 Gy or less, escalate dose by 4-10 Gy when completing treatment
Pancreatic cancer	Delay and convert to hypofractionated plan	Continue chemotherapy to defer new starts as much as possible Utilize SBRT rather than CRT Convert to hypofractionated plan to complete delayed courses
Rectal cancer	Delay and convert to hypofractionated / short course plan	Start FOLFOX to delay all new starts Convert delayed patients to short course plan (equivalent of 5 Gy x5)

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Anal cancer	Delay patients who have received 10 Gy or less; deliver definitive dose later Continue treatment for definitive CRT patients at >10 Gy if at all possible	Consider induction chemo to delay new starts For patients delayed after 10 Gy or less, escalate dose by 4-10 Gy when completing treatment
Lung cancer - Patients already on treatment who already have already received more than approximately 15-20 Gy):	Patients who may be OK for a break or discontinuation: -palliative -oligomets -consolidative thoracic RT or PCI for extensive-stage SCLC -PCI for limited-stage SCLC -postop for incidental N2 NSCLC Patients who need to continue if at all possible: -definitive chemo-RT for locally advanced NSCLC (top priority) -definitive chemo-RT for limited-stage SCLC -SBRT for early-stage NSCLC (especially if biopsy-proven, growing fast, younger age, fewer comorbidities, fewer number of previous lung cancers) **See lung cancer recommendations**	**See lung cancer recommendations**
Lung cancer - Patients not on treatment yet or who have received less than 15-20 Gy so far (threshold set here since it may still be possible to deliver a definitive dose in the future if interrupted	Can defer -early-stage lung cancers especially if not biopsied, growing slowly, lepidic adeno, older age or more comorbidities (at increased risk of COVID complications), and higher number of previous lung cancers (suggesting they may easily develop more)	**See lung cancer recommendations**

this early in treatment):	-oligomets -consolidative thoracic RT or PCI for extensive-stage SCLC -PCI for limited-stage SCLC -postop for incidental N2 NSCLC Start as early as possible -Definitive chemo-RT for locally advanced NSCLC -Definitive chemo-RT for limited-stage **See lung cancer recommendations**	
Head and neck cancer	Discuss with attending. Head and neck cancer treatment break or deferral may lead to reduced tumor control given rapid tumor doubling time. **See head and neck recommendations**	Consider mitigating with additional radiation dose after treatment or addition of chemotherapy. **See head and neck recommendations**
Cervical cancer	Discuss with attending. Cervical cancer radiation treatment break or deferral may lead to reduced tumor control given rapid tumor doubling time.	Consider mitigating with additional radiation dose after treatment or addition of chemotherapy.
Endometrial, high-intermedate risk or stage II, brachytherapy alone	Brachytherapy initiation can be delayed, but should start no later than 9 weeks post hysterectomy; if already started on treatment, then up to 14 days between fractions is acceptable	Discuss with attending. No default mitigation needed
Endometrial, high intermediate risk or stage II, pelvic RT alone	Pelvic radiotherapy can be delayed, but should start no later than 8 weeks post hysterectomy; consider if brachytherapy alone is a reasonable substitute for these patients after weighing risks and benefits	Discuss with attending. No default mitigation needed

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Endometrial, early stage, high risk histology (MMMT, UPSC, CC, DD/UD), brachy + chemo	Brachytherapy initiation can be delayed, but should start no later than 9 weeks post hysterectomy; if already started on treatment, then up to 14 days between fractions is acceptable.	Discuss with attending. No default mitigation needed
Endometrial, advanced stage, high risk, pelvic RT + chemo	Unless there are positive margins, these patients may receive all 6 cycles of Carbo-Taxol up-front and then delay the pelvic RT until after all the chemotherapy has completed. Pelvic RT can start 3-4 weeks from last chemo.	Discuss with attending. No default mitigation needed
Low grade glioma	Initiation of radiation therapy can and should be delayed at initial diagnosis	Discuss with attending. No default mitigation needed
High grade glioma	Treatment decisions must be individualized, delay may not be feasible in patients without significant resection, with neurologic symptoms, or with significant steroid requirement.	If treatment breaks occur due to illness, conversion to hypo-fractionation can be considered upon return in order to complete the course in a similar time frame. If treatment breaks occur due to access, temodar should be continued and dosing (daily vs 5days/week) coordinated with neuro-oncology.
Meningioma and Schwannoma	Initiation of radiation therapy can and should be delayed at initial diagnosis	
Spine tumors	Low grade tumors (ependymomas, schwannomas, meningiomas) or surgically resected tumors can be	Patients undergoing potentially curative therapy may need treatment through

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	delayed for 4 weeks and re-evaluated Primary or metastatic tumors causing neurologic symptoms should proceed with treatment	infection and will need to be assessed on a case by case basis

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Head and Neck OR Cervical cancers - additional guidelines

Given the abundance of data showing treatment delays or protracted treatment times results in significantly reduced cancer outcomes for head and neck cancer OR cervical cancer, any treatment delay/interruption will require thorough evaluation.

For patients that have NOT started treatment, but have COVID+ test, or suspicion, treatment start should be delayed until testing results negative, or asymptomatic for 72 hours, or 7 days after onset (whichever is longer). For certain patients, (ie larynx), at risk for airway compromise if long delay in start, starting treatment under COVID+ protocol may be necessary or other multidisciplinary input regarding alternate treatment options.

For patients that are MID-treatment, treatment interruption more than 7 days would preferably be prevented.

- If SYMPTOMATIC, patient can be delayed 1 week to see if symptoms abate, and then treated as per COVID+ protocol.
- If Asymptomatic, but COVID+, would prefer to treat as long as asymptomatic, per COVID+ protocol.
- For a delay of more than 1 week, altered fractionation once patient is safe (clinically stable) to resume treatment, or potentially additional fractions can be considered once treatment resumes.

In general interruptions of greater than 1 week are to be avoided. If due to clinical instability, patient unable to receive treatment due to infection, attending will determine whether to resume treatment once stable, change treatment plan, or coordinate alternate treatment with multi-D team as appropriate

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Lung cancer – additional recommendations to limiting fractionation as much as possible:

General principles:

- If RT can be safely deferred or avoided for now, consider doing so since it is currently unknown how pneumonitis/fibrosis will affect patients who may eventually contract COVID. If it cannot be safely deferred or avoided, then try not to escalate beyond minimum effective dose even if meeting constraints,

SBRT:

- Peripheral tumors for whom you would otherwise prescribe 50-55 Gy in 5 fractions rather than 54 Gy in 3 fractions (i.e. close to chest wall, multiple isocenters, older patient with multiple comorbid illnesses, etc): consider prescribing 45 Gy in 3 fractions aiming for 150% max dose (Nordic regimen)
- Central tumors (within 2 cm of proximal tracheobronchial tree): no more than 50 Gy in 5 fractions (investigator-initiated trial "DD3" using 45 Gy in 3 fractions is currently on hold along with most other Cancer Center trials)
- Central tumors (within 2 cm of non-TBT structures like heart, great vessels, esophagus, or spine): no more than 50 Gy in 5 fractions, or in select circumstances consider 45 Gy in 3 fractions off-trial but risks/benefits need to be weighed carefully (investigator-initiated trial "DD3" using 45 Gy in 3 fractions is currently on hold along with most other Cancer Center trials)
- Ultracentral or very large tumors: do what you might normally do to be safe while still giving a definitive dose if indicated (i.e. 60-72 Gy in 15-18 fractions vs. 60 Gy in 8 fractions)

LA-NSCLC:

- Minimize dose escalation above 60 Gy in 30 fractions (RTOG 0617 regimen)
- If no chemo, then consider 52.5-60 Gy in 15 fractions

LS-SCLC:

- Consider 40-42 Gy in 15 fractions rather than 45 Gy in 30 BID fractions or 60-66 Gy in 30-33 fractions

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Prostate cancer – additional recommendations

(From Zaorsky et al. Adv Rad Oncol. 2020.)

	Visits		Simulation/Preparation			If Treatment is Warranted During Pandemic			
Disease State	**New Consults***	**RVs***	**Fiducials****	**Rectal Spacers****	**Simulation scans**	**Preferred Treatment During Pandemic**	**Brachytherapy*****	**EBRT type**	**ADT**
Localized/Locally advanced									
Very low/low	Delay until safe	Delay until safe	Delay until safe	Delay until safe	Delay until safe	AS	Delay until safe	Delay until safe	Do not use
F/R	Delay 3 months	Delay until safe	Delay until safe	Delay until safe	Delay until safe	AS	Delay until safe	Delay until safe	Do not use
U/R	Delay 1-3 months	Delay 4 months	Consider if performing SBRT	Consider if performing SBRT	Delay up to 4-6 months if ADT given	RT+ADT	Do not use	5 fx (preferred) or 20 fx	Can use ADT to delay RT 4-6 months. Consider 6 month depot
High/very high	Delay up to 1 month	Delay 3 months	Consider if performing SBRT	If experienced to place, consider only if performing SBRT	Delay 4-6 months if ADT given	RT+ADT	Do not use	5 fx (preferred) or 20 fx	Can use ADT to delay RT 4-6 months. Consider 6 month depot
N+	Delay 2-4 weeks	Delay 3 months	Consider if performing SBRT	Not recommended	Delay 4-6 months if ADT given	RT+ADT	Do not use	5 fx or 20 fx	Can use ADT to delay RT 4-6 months. Consider 6 month depot
Post-Prostatectomy									
Adjuvant	Strongly consider use of early salvage RT	Delay 4 months	-	-	Delay up to allowing treatment 120 days after surgery	RT +/- ADT	-	20 fx	Can use ADT to delay RT 4-6 months. Consider 6 month depot
Salvage	Delay up to 1 month	Delay 3 months	-	-	Delay depending on PSA level and doubling time	RT +/- ADT	-	20 fx	Can use ADT to delay RT 4-6 months. Consider 6 month depot

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Yale Breast Team COVID-19 Clinical Patient Guidelines V.2

Low-risk patients:

- Luminal patients
- Age >65-70
- Patients HR+ who have been started on endocrine therapy
- Small, node negative tumors
- DCIS (particularly GI/II)

Higher risk patients:

- Locally advanced
- Node +
- TNBC
- Palliative (pain or other symptoms)
- Surgical margin positive or gross ECE (> 2 mm)
- Neoadjuvant chemotherapy with residual disease
- DCIS GIII in a young patient <50 yrs

*HER2+ patients should be individualized based on other factors such as nodal involvement, tumor size, receipt of chemo, HR+ vs. HR- etc.
*Special attention should be paid for individualized decision making for RT timing vulnerable populations, such as small TNBC in women >65, with multidisciplinary discussion.
*Ideally, aim to start RT ≤10-12 wks from surgery/chemo for higher risk patients and up to 16 weeks for lower risk patients on endocrine therapy

Radiation Oncology attending to screen all incoming consults and follow-ups for their clinic
Determine if new patient needs:

1) Immediate consult-----Palliative/inflammatory etc. (need to start RT)
2) Defer consultation 6-8 weeks- post-operative /post-chemo (to start RT within 12 weeks of last treatment)
3) Defer consultation 12-16 weeks---no chemo, on endocrine therapy, luminal pts, low oncotype dx score (start RT 16 weeks or more, low-risk, on endocrine therapy and/or omission of RT being considered)

*Emphasize no survival benefit in elderly population for omission of WBRT (>65-70) for patients willing to take endocrine therapy

*Medical Oncology and Surgery to initiate up-front discussion for endocrine therapy in HR+ pts and get Oncotype Dx score early-so that RT consultations can be deferred for these patients.

*Perform breast examination at time of simulation

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*For any patients requiring consultations, video teleconsultations can be performed by attending MD (watch video and follow instructions)

Recommendations for patient interruptions:

Breast	Breast-only treatment	Low	Do not change the whole-breast dose in the setting of a treatment break (continue the original 42.56 Gy in 16 fractions or 50 Gy in 25 fractions). The boost portion of the treatment dose gets adjusted as follows: • Initial treatment plan did not include a sequential boost to the lumpectomy cavity PTV: 10 Gy in 5 fractions boost. • Initial treatment plan included a sequential boost to the lumpectomy cavity PTV: Add one 2 Gy fraction per week missed up to 66 Gy; alternatively, a 2.3 Gy × 5 boost. If the intended boost was to 66 Gy, increase the dose up to 70 Gy, and consider reducing the volume to the highest risk region.
	Chest wall after mastectomy	Low	Similar to above, but substitute lumpectomy cavity PTV for mastectomy scar PTV.
	Regional nodal (supraclavicular, axillary, internal mammary chain) with breast or chest wall	Low	Dose is adjusted to a maximum of 50 Gy in 2 Gy fractions.

From: Gay HA, Santiago R, Gil B, Remedios C, Montes PJ, López-Araujo J, 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 radiation oncology. 2019;9(5):305-21.

Yale Version:

Cancer	Clinical Scenario	Impact of Gap	Recommendations
Breast	WBRT	Low	Do not change WBRT dose in the setting of a TX break (continue original hypofractionated or conventional TX). Boost portion can be adjusted as follows: - ASSUMING SEQUENTIAL BOOST AFTER WBRT: • IF NO BOOST ORIGINALLY INTENDED, ADD BOOST AFTER WBRT (10 Gy/5 fx CF or 10 Gy/4 fx HF) - If initially plan DID have a sequential boost and treatment interuption: • Can add additional 2 Gy fractions up to 66 Gy (CF) or additional 2.5 Gy fraction to 52.55 Gy (HF) • If original intended dose was 66 Gy (high risk patient), can increase dose to 70 Gy/2 Gy Fx (CF) and consider reducing the volume to the highest risk region.
	Chest Wall RT	Low	Similar to above, but substitute lumpectomy cavity PTV for mastectomy scar PTV

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	RNI (SCV, ax, IM) with WBRT/PMRT	Low	Dose max of 50 Gy in 2 Gy fractions (unless boosting IM nodes)

*We can further discuss as group as interruptions occur- may consider increasing boost dose to 14-16Gy (CF) or additional single fraction 12.5 Gy (HF)

Boost considerations during this period should be personalized (not routinely delivered)- Consider adoption of the following: (combination of ASTRO WBI and our institutional policy):

- Consider omitting tumor bed boost for:
  - All patients >65-70 yrs(DCIS and invasive)
  - Low grade DCIS in >50 yrs
  - Any patient who meets <u>all</u> of the following criteria:
    - >50 yrs
    - hormone receptor + (agrees to take endocrine therapy)
    - Grade I/II
    - widely negative (≥2 mm) margins
- Continue tumor bed boost for:
  - All patients under the age of 50 yrs after BCT (DCIS and invasive)
  - All inflammatory breast cancer
  - All NAC patients with residual disease in the breast after BCS
  - High grade tumors (invasive or DCIS) between ages of 51-65/70 yrs.
  - Patients with focally positive margins
  -

*Of course, as with all guidelines, individualized decision-making is required and should incorporate and be sensitive to patient preferences and values regarding the modest expected disease control benefit compared with the modest increase in treatment-related burden and toxicity associated with boost RT.

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Superior Vena Cava (SVC) Syndrome grading (Yu JB et al. JTO. 2008;3:811-4).

Grade	Category	Estimated Incidence (%)	Definition[a]
0	Asymptomatic	10	Radiographic superior vena cava obstruction in the absence of symptoms
1	Mild	25	Edema in head or neck (vascular distention), cyanosis, plethora
2	Moderate	50	Edema in head or neck with functional impairment (mild dysphagia, cough, mild or moderate impairment of head, jaw or eyelid movements, visual disturbances caused by ocular edema)
3	Severe	10	Mild or moderate cerebral edema (headache, dizziness) or mild/moderate laryngeal edema or diminished cardiac reserve (syncope after bending)
4	Life-threatening	5	Significant cerebral edema (confusion, obtundation) or significant laryngeal edema (stridor) or significant hemodynamic compromise (syncope without precipitating factors, hypotension, renal insufficiency)
5	Fatal	<1	Death

a Each sign or symptom must be thought due to superior vena cava obstruction and the effects of cerebral or laryngeal edema or effects on cardiac function. Symptoms caused by other factors (e.g., vocal cord paralysis, compromise of the tracheobronchial tree, or heart as a result of mass effect) should be not be considered as they are due to mass effect on other organs and not superior vena cava obstruction.

Red box: Do not treat until COVID19 test negative, or asymptomatic 72 hours or 7 days after symptom onset- whichever is longer.

All others – URGENT STENT recommended, or thrombolytics if thrombus. If no stent possible, proceed to treatment.

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Treatment of screening positive or test positive COVID19+ symptomatic patients

General radiation planning guidelines

Minimize fractions as much as possible. Use single fraction treatment for palliation. Hypofractionate as much as possible.

Staff safety guidelines

Treatment performed at end of day after all machines have stopped treating. Minimum staffing required. If N95 mask required, will require rapid fit testing with mask.

Patients should call ahead before coming to department. To reduce contact, banding of patient arm is not required – escorting staff will carry the patient ID band. Verbal check in and time out at treatment machine still required. All staff that comes into direct contact with patient should wear PPE, including front desk staff. Patient time in the department should absolutely be minimized. If patients have to wait, they should be placed in the previously designated isolation room with door closed. After patient leaves the isolation room the door to the room should be closed for an hour and terminal cleaned. Patient should not be waiting in waiting rooms or any rooms with carpeting or non-impervious upholstered chairs.

Given recent changes (3/18/20) in Personal Protective Equipment guidelines for the acute care setting, given the proximity of patients to therapy staff, **Modified Airborne/Contact** precautions should be used.

1) Alert therapy and nursing leadership
2) Alert environmental services leadership
3) After 5pm, after hours with absolute minimum staff
4) Mask patient with surgical mask. For patients with aquaplast immobilization – if the patient can tolerate it, place mask on the aquaplast mask as well.
5) All staff engaging in direct patient care should wear PPE (gown, glove, face shield, N95 mask with eye protection*) All staff watch video how to don/doff
6) Radiation therapy staff wipes down all radiation equipment with disinfectant wipes
7) Close LINAC door for 1 hour
8) Call environmental services and alert them
9) Terminal clean linac before treating next day

*If your hospital system can sustain this use. Surgical mask with eye protection is acceptable if N95 not released for ambulatory use.