FROM OUR PRESIDENT

COVID-19 CRISIS: Maintaining Brachytherapy Access and Strategies for Risk Mitigation

To begin with, no one ever imagined how the COVID-19 crisis would completely disrupt our lives in every way. I was recently “exposed” and quarantined at my cabin where I had plenty of time to reflect on what is happening, and how we can better serve our membership, staff and patients during these unprecedented times. I had finished writing my initial section amplifying a number of themes from Dr. Greg Merrick’s editorial from his 2019 Henschke award address, and how his recommendations will guide the 300 in 10 effort—a must read (January 2020 Brachytherapy). Then, COVID hit and changed our world. I will publish that editorial at a later date.

As with complex brachytherapy cases, patients, and life in general, we need to pivot and adapt. I asked our team to publish information relevant to our oncology and brachytherapy practice. Dr. Brandon Dyer and his team just completed a manuscript in less than 2 weeks, COVID-19 Impact of Timing of Brachytherapy Treatment and Strategies for Risk Mitigation, that is being co-published in our ABS Spring Newsletter and the Journal of Brachytherapy. A special thank you to Dr. Brandon Dyer and the co-authors for writing this critical information in record time. In addition, Drs. Mohindra, Beriwal and Kamrava have written Proposed Brachytherapy Recommendations (Practical Implementation, Indications and Dose-Fractionation) During COVID-19 Pandemic, that will be co-published. We are most grateful for their contribution as well. Relevant themes addressed that apply to our current pandemic include selectively delaying brachytherapy for some patients, continuing brachytherapy for those in which treatment delays would compromise cure rates, practical fractionation guidelines, anesthesia considerations and maintaining safely for both our patients and staff.

Dr. Emily Dunn, a brachytherapist in Eugene, Oregon, has been on the frontlines and has implemented a “home grown” system to sterilize PPEs (N95s) using UVC light, based upon the protocol from the University of Nebraska Medical Center. She wrote up a summary for the ABS newsletter and am grateful for the guidance she has given me. At our hospital in Rapid City, we just started

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sterilizing N95s with UVC lights. We were fortunate in that we had 4 UVC towers that were being used to sterilize rooms for C. Difficile. We as radiation oncologists and physicists are uniquely poised to assist our hospitals with this endeavor with our expertise in physics, radiation safely and verification of “dose” delivered. Finally, Dr. Louis Potters at Northwell Health in New York City, recently detailed their approach to the COVID crisis in the April ASTROgram/Blog: Leading the Storm: Lessons from the Epicenter, where they have had over 4,000 cases. From Dr. Potters, “we have maintained two guiding principles: Do everything to keep the staff well and safe and maintain access to cancer patients needing our services, through 5 key takeaways: actively manage your staff, decrease treatment volume, implement telehealth, maintain critical multidisciplinary discussions and keep patient safety as the highest priority”. (https://www.astro.org/Blog/March-2020/Leading-Through-the-Storm-Lessons-from-the-Epicent)

We are all looking forward to that time when life starts to normalize again. It is important for us as physicians, physicists and health care providers to maintain critical cancer access, promote patient and staff safety, and to be that presence in your community to help lead these efforts—be well and stay safe...

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President, ABS
Proposed Brachytherapy Recommendations
(Practical Implementation, Indications and Dose-Fractionation)
During COVID-19 Pandemic

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Shortened Running Title:
Proposed Brachytherapy Recommendations during COVID-19

Keywords:
Brachytherapy, COVID-19, Dose-fractionation

Summary:
Ongoing COVID-19 Pandemic has impacted availability
of health-care resources (personnel and material). This
has especially impacted cancer care who are at much
higher risk of contracting the infection and suffering
serious complications. Nationwide, there has been
reduction in conduct of elective surgeries including
some for cancer patients.

Brachytherapy is an integral part of radiotherapeu-
tic management in patients for a variety of clinical
indications. For many disease sites, brachytherapy
procedures are done with the support of anesthe-
sia and with utilization of hospital operating room
resources. As such, there is considerable pressure on
providers to judiciously select patients in need for
brachytherapy based on review of clinical indications,
disease type and available institutional resources. To
conserve resources, institutional policies have been
devised for personal protective equipment (PPE)
in normal clinical use or for care of patients with
influenza-like illness (ILI), persons under investiga-
tions (PUI) for COVID-19 with test results pending and
patients who may have tested positive for COVID-19
(COVID-19 +).

As a means to reduce burden on patient and staff
while reducing risk of exposure, there is urgent need
to define alternate dose-fractionation regimens to
allow completion of brachytherapy with fewer num-
ber of treatment fractions. Data on dose-response
for tumor and normal tissue in brachytherapy has
evolved through decades of institutional, national and
international collaborations which continues to refine
standard of care practice with the goal to improve the
therapeutic ratio.

Through data shown in the table on the following
pages, we seek to review practical implementation
considerations when using brachytherapy for a vari-
ety of clinical indications. We also summarize available
data supporting use of alternate higher dose-
per-fraction regimens to allow completion of the
brachytherapy course with using smaller number of
fractions. It is strongly recommended that for all such
modified fractionations being considered during the
Pandemic, strict respect for normal tissue dosimetric
constraints should be met using available published
data and by estimating dosimetric equivalence to
standard fractionation. When data on normal tissue
dosimetric constraints for higher dose-per-fraction
regimens is limited, use caution and clinical judge-
ment is warranted.

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<table>
<thead>
<tr>
<th>Disease Site</th>
<th>Indication</th>
<th>Practical Implementation Considerations during Pandemic</th>
<th>Common Dose/Fractionation</th>
<th>Suggested Dose/Fractionation during Pandemic</th>
<th>References</th>
</tr>
</thead>
</table>
| Gynecological Cancers | Intact Cervix    | 1. Effort should be made to complete treatment within 7-8 weeks for non-COVID-19 +/PU/ILI patients.  
2. Consider using MRI for first fraction only instead of all fractions especially if 1st MRI shows a minimal residual disease.  
3. When using brachytherapy consider spinal/epidural anesthesia, oral analgesia or intravenous conscious sedation over general endotracheal anesthesia.  
4. If patient is status COVID-19 +/PU/ILI then:  
a. If resources available continue brachytherapy boost with PPE precautions, or  
b. Delay till 10-14 days post-recovery from infection and try to increase dose of brachytherapy by 5 Gy cumulative dose for each week delay provided OAR constraints can be met. | HDR intracavitary +/- hybrid interstitial boost after 45-50.4 Gy: 5-6 Gy x 5 fractions, or 7 Gy x 4 fractions.  
HDR intracavitary +/- hybrid interstitial boost after 45 Gy: 7 Gy x 4 fractions, or 8 Gy x 3 fractions.  
9 Gy x 2 fractions showed inferior outcomes to 7 Gy x 4 and is not preferred. |                                                                                       |                                                                                                                                         | 1. retroEMBRACE, Tanderup et al. PMID: 27350396  
2. University of Pittsburgh, Beriwal et al. PMID 21908180  
3. ABS consensus guidelines, Viswanathan et al. PMID: 22265437  

continued ➡️
<p>| Inoperable Endometrial | 1. Consider using MRI for first fraction only instead of all fraction especially in good responder. |
| HDR intracavitary monotherapy (Stage I): 7-7.5 Gy x 5 fractions (^3) |
| HDR intracavitary boost after 45 Gy: 8.5 Gy x 2 fractions (^4), or 6.3-6.5 Gy x 3 fractions (^5), or 5.2 Gy x 4 fractions (^4) |
| HDR intracavitary boost after 50.4 Gy: 6 Gy x 2 fractions (^4), 3.75 Gy x 6 fractions (^4) |
| HDR intracavitary boost after 45 Gy: 8.5 Gy x 2 fractions (^4), or 6.3-6.5 Gy x 3 fractions (^4) |
| HDR intracavitary boost after 50.4 Gy: 6 Gy x 2 fractions (^4) |
| 1. University of Virginia, Staples et al. PMID: 29977988 |
| 2. SEER analysis. Yoo et al. PMID: 26083557 |
| 3. University of Pittsburgh, Gebhardt et al. PMID: 28923412 |
| 4. ABS consensus guidelines, Schwarz et al. PMID: 26186975 |
| 5. Compendium of fractionation choices for gynecologic HDR brachy. Albuquerque K et al. 2019. PMID 30979631 |
| 6. McGill University, Canada Niazi et al. PMID: 16099598 |
| Interstitial (template) | 1. If patient COVID-19+/PU/ILI during EBRT then: |
| HDR boost after 45-50.4 Gy: 4-6 Gy x 5 fractions (^3) |
| No consensus recommendation for re-irradiation. |
| HDR boost after 45 Gy: 7-8 Gy x 3 fractions (^2) |
| 6 Gy x 4 fraction, twice daily (^6) |
| 1. retroEMBRACE, Tanderup et al. PMID: 27350396 |
| 2. ABS Consensus Guidelines, Beriwal et al. PMID: 22265440 |
| 3. ABS consensus guidelines, Viswanathan et al. PMID: 22265437 |
| Post-operative vaginal cuff | 1. Can avoid brachytherapy boost after EBRT if no adverse factor like cervical involvement/LVSI, possibly using 50.4 Gy instead. | HDR cylinder monotherapy: 7 Gy ( \times ) 3 fractions to 5 mm, or 5-5.5 Gy ( \times ) 4-5 Fractions to surface, or 6-7.5 Gy ( \times ) 5 fractions to surface, or 4 Gy ( \times ) 6 fractions to surface(^3)(^4) | HDR cylinder monotherapy: 3 cm cylinder: 7 Gy ( \times ) 3 fractions to 5 mm ( \text{(PORTEC-2)} )(^5) [2.5 \text{ cm cylinder: 7 Gy} \times 3 \text{ fractions to surface}(^6)] | HDR cylinder boost after 45-50.4 Gy: 5-6 Gy ( \times ) 2-3 fractions to surface, or 4-5.5 Gy ( \times ) 3 fractions to 5 mm(^3)(^4) | HDR cylinder boost after 45 Gy (adverse factors): 5 Gy ( \times ) 2 fractions at 5 mm(^6)(^9), 5 Gy ( \times ) 1 fraction to surface(^7), or HDR Cylinder Boost after 50/50.4 Gy (adverse factors): 6 Gy ( \times ) 2 fractions to surface(^4) Add more fractions if positive margin | 1. University of Pisa, Fabrini et al. PMID: 22213303 | 2. Henry Ford Hospital, Michigan, Cattaneo et al. PMID: 24444785 | 3. ABS consensus guidelines, Small et al., PMID: 22265439 | 4. Compendium of fractionation choices for gynecologic HDR brachy. Albuquerque K et al. 2019. PMID 30979631 | 5. PORTEC-2, Nout et al. PMID: 20206777 | 6. Dana-Farber Cancer Institute/Brigham and Women’s Hospital, Alban et al. Brachytherapy 18 (2019) S12eS116 | 7. BC Canada, Bachand et al. <a href="https://www.brachyjournal.com/article/S1538-4721(13)00062-7/fulltext">https://www.brachyjournal.com/article/S1538-4721(13)00062-7/fulltext</a> | 8. PORTEC-3, de Boer et al. PMID: 31345626 | 9. University of Pittsburgh, He et al. PMID: 27527897 | Continued |</p>
<table>
<thead>
<tr>
<th>Prostate Cancer</th>
<th>Monotherapy, Boost or Salvage</th>
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<tbody>
<tr>
<td>1. All monotherapy should be deferred until pandemic resolves/resources become available.</td>
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<tr>
<td>2. Defer initiating EBRT and continue hormone therapy for unfavorable and high-risk prostate.</td>
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<tr>
<td>3. If already on EBRT, then consider brachytherapy boost if resources available with PPE precautions, else consider EBRT boost.</td>
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<tr>
<td>4. For salvage cases delay brachytherapy and consider hormone therapy until pandemic resolves/resources become available.</td>
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<tr>
<td>5. When using brachytherapy consider spinal/epidural anesthesia, or intravenous conscious sedation over general endotracheal anesthesia.</td>
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<tr>
<td>6. If patient is status COVID-19+/PUI/ILI during EBRT, then:</td>
<td></td>
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<tr>
<td>a. Consider interrupting treatment to allow 10-14 days post-recovery from infection before re-initiating EBRT/plan for brachytherapy.</td>
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### Interstitial monotherapy:
- HDR 13.5 Gy x 2
- (19 Gy x 1 is not appropriate)\(^1\)
- LDR dose per isotope used.

**HDR Interstitial boost after EBRT:**
- 45 Gy in 25 fraction pelvic RT or 37.5 Gy in 15 fraction (prostate alone) followed by HDR boost 15 Gy in one fraction (Standard arm of RTOG 0924 study)\(^2,3\)

**Salvage HDR brachytherapy:**
- 8 Gy x 4 fractions, single implant, twice daily\(^4\)
- 6 Gy x 6 fractions, two separate implants performed 1 week apart\(^5\)

**Interstitial monotherapy:**
- No change in fractionation needed.

**Interstitial boost after EBRT:**
- No change in fractionation needed.

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\(^1\) Sunnybrook Odette Cancer Center, Toronto, Morton G et al. Green Journal. 2020. PMID 32146259


\(^3\) Sunnybrook Odette Cancer Center, Toronto, Martell K et al. Green Journal. PMID 31522882

\(^4\) Memorial Sloan-Kettering Cancer Center, Yamada et al. PMID: 24373762

\(^5\) University of California-San Francisco, Chen et al. reference PMID: 23474112
If patient is status COVID-19 +/PUI/ILI, after 1st fraction HDR, then:
a. Consider delaying 2nd fraction to allow 10-14 days post-recovery from infection.

**Breast Cancer**

| Adjuvant | Delay adjuvant EBRT or interstitial brachytherapy for low risk breast cancer pts as no detrimental effect in outcome up until 16-20 weeks for ER+ invasive breast cancer, 12 weeks for DCIS.  

2. Balloon/Catheter-based intracavitary brachytherapy is dependent on presence of cavity and hence, needs to be done sooner.  

**Balloon/Catheter based HDR:**  
3.4 Gy x 10 fractions, single implant, twice daily over 5 days  
**IORT:** single fraction

**Balloon/Catheter based HDR:**  
7-7.5 Gy x 3 fractions, single implant, twice daily over 1.5 days  
or 7 Gy x 4 fractions, single implant, twice daily over 2 days  
**IORT:** No change in fractionation needed

1. British Columbia, Canada, Olivotto et al. PMID: 19018080  
2. Sahlgrenska University Hospital, Gothenburg, Sweden, Karlsson et al. PMID: 20729007  
3. Memorial Sloan Kettering Cancer Center, Shurell et al. PMID: 28960259  
4. ABS recommendations, Shah et al. PMID: 29074088  
5. Triumph-T trial, Khan et al. PMID:30611839  
6. Mayo Clinic Rochester, Jethwa et al. PMID 30583041  
7. Phase 1/2 trial, Wilkinson et al. PMID 28787281

**Skin Cancer**

| Delay brachytherapy until pandemic resolves/resources become available.  

**Surface applicators (dose to 3-5 mm below surface):**  
3 Gy x 17-18 fractions, thrice weekly, or 8 Gy x 5 fractions, twice daily or 10 Gy x 3 fraction, once weekly

1. GEC-ESTRO ACROP Recommendations, Guinot et al. PMID: 29455924  
2. Spanish brachytherapy group recommendations, Rodriguez et al. PMID: 28808925

*continued*
| **Esophageal Cancer** | **Palliative** | Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider short-course EBRT. | **Intraluminal HDR Monotherapy:** 12-21 Gy in 1-3 fractions, prescribed to 5-10 mm, or 12 Gy at 10 mm x 1 fraction, or 8 Gy at 10 mm x 2 fractions, once weekly combined with EBRT. | 1. Systematic review, Fuccio et al. PMID 31636025  
2. Netherlands multicentre, Horns et al. PMID 15500894  
3. IAEA, Rosenblatt et al. PMID: 20950882 |
| **Re-irradiation** | Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider conformal EBRT. | **Intraluminal HDR Monotherapy:** 5-7 Gy at 5 mm x 5-6 fractions, or 10-17.5 Gy at 7 mm x 3 fractions. | 1. Saint Louis Hospital, Paris, Wong Hee Kam et al. PMID 25906950  
2. Memorial Sloan Kettering Cancer Center, New York, Taggar et al. PMID 29496425 |
| **Hepato-biliary cancers** | **Hilar Cholangiocarcinoma (bridge to transplant)** | 1. Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider conformal EBRT. | **Intraluminal Boost after EBRT:** Mayo Clinic Protocol: 45 Gy/30 fractions EBRT with concurrent 5FU and 20-30 Gy intraluminal brachytherapy. | 1. Mayo Clinic, Rochester, Rea et al. PMID 16135931  
2. Mayo Clinic, Rochester, Deufel et al. PMID: 29776892 |
2. If patient is status COVID-19 +/PUI/ILI, then consider continuing EBRT instead of brachytherapy boost.

| Palliative Unresectable malignant biliary obstruction or Hepatocellular carcinoma (not for transplant) and metastatic lesions | Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider conformal EBRT. | Interstitial LDR malignant biliary obstruction: I-125 impregnated stents, 30-60 Gy at 15 mm<sup>4,5</sup> Interstitial HDR Hepatocellular carcinoma: 15-25 Gy 1-2 sessions<sup>6</sup> Interstitial HDR liver metastases: 15 Gy x 1 for breast cancer metastases 20 Gy x 1 for non-breast secondary liver cancers<sup>7</sup> | 1. Systematic review. Rim et al. PMID 29233562 2. Univ of Rochester, Stereotactic Hypofractionated RT. Katz et al. PMID 22172906 3. Multicenter phase II study, Hong et al. PMID 26668346 4. Multicenter study, China, Zhu et al. PMID: 29331343 5. Systematic review, Xu et al. PMID 29075881 6. Otto von Guericke University, Germany. Mohnike et al. PMID: 20056348 7. University Hospital Magdeburg, Magdeburg, Germany, Hass et al. PMID 31522972 |

| Rectal Cancer | Pre-operative | 1. Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from possible fecal spread. Consider conformal hypofractionated EBRT. | Intraluminal HDR Monotherapy: 26 Gy in 4 fractions prescribed to target volume Intraluminal HDR Boost after Chemoradiation: 10 Gy in 1-2 fractions at 10 mm | 1. Systematic review. Buckley et al. PMID 28816137 |

continued ➥
| Condition               | Treatment/Boost Options                                                                 | 2. If patient is status COVID-19+/PUI/ILI, then consider change to hypofractionated EBRT instead of brachytherapy boost. | 1. Delay brachytherapy until pandemic resolves/resources become available. Consider EBRT.  
2. If patient is status COVID-19+/PUI/ILI during EBRT, then consider continuing EBRT instead of brachytherapy boost. |
|-------------------------|-----------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| Sarcoma                 | BRT monotherapy or boost                                                                | **Interstitial HDR Monotherapy (Post-op, high-grade < 10 cm, negative margins):**  
30-50 Gy/8-14 fractions/4-7 days twice daily<sup>1</sup>  
**Interstitial HDR Boost (Post-op, low-grade deep > 5 cm or high-grade > 10 cm, negative margins):**  
12-20 Gy/2-3 days + EBRT 45-50 Gy EBRT  
Total Dose ≥ 60 Gy<sup>1</sup>  
**Interstitial HDR Boost (Post-op, positive surgical margins):**  
12-20 Gy/2-3 days + EBRT 45-50 Gy EBRT  
Total dose ≥ 65-70 Gy<sup>1,2</sup> | 1. ABS STS recommendation, Naghavi et al. PMID: 28342738  
2. Martínez-Monge et al. Univ. Navarre, Spain PMID: 21353160  
3. Itami et al., National Cancer Center Hospital, Japan PMID: 20692211  
4. Sharma et al., AIIMS, India, PMID: 25861894 |
| Head and Neck Definitive Reirradiation | Definitive/Boost Oral cavity/ Oropharynx, Boost Nasopharynx or any re-irradiation | **Interstitial HDR Monotherapy Oral cavity/ Oropharynx:**  
35-44 Gy/ 10-11 fractions/5-5.5 days/ twice daily<sup>1,2,3</sup>  
**Interstitial HDR Boost Oral cavity/ Oropharynx:**  
21-30 Gy/7-10 fractions/ 3-5 days + EBRT 40-50 Gy<sup>1,2,3</sup> | 1. GEC-ESTRO recommendations, Mazeron et al. PMID: 19329209  
2. GEC-ESTRO- ACROP recommendations, Kovacs et al. PMID: 27889184  
3. ABS Task Group Report, Takácsi-Nagy et al. PMID: 27592129 |
2. If patient is status COVID-19 +/-PUI/ILI, then consider continuing EBRT instead of brachytherapy boost.

**Interstitial HDR Boost**

Nasopharynx:
12-18/4-6 fractions/2-3 days + EBRT 60-70 Gy\textsuperscript{1,2,3}  

**Interstitial HDR Monotherapy**

Re-irradiation:
30-40 Gy/ 10 fractions/5 days/ twice daily\textsuperscript{4,5}

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4. Tselis et al., Sana Klinikum Offenbach GmbH, Germany, PMID: 21129799

5. Bhalavat et al., Jupiter Hospital, India, PMID: 30479619

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**Brain Tumors**

Primary brain tumors or brain metastases

Avoid brachytherapy until pandemic resolves/resources become available. Consider fractionated EBRT (glioma) or pre-operative or post-operative SRS/SRT (brain metastases).

**Interstitial LDR (gliomas):**

50-65Gy\textsuperscript{1,2}

**Interstitial LDR (brain metastases):**

60-70 Gy\textsuperscript{3}

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1. Nachbichler et al. PMID: 29393178

2. Barbarite et al. PMID: 27180560

3. Mahase et al. PMID: 30850332

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**Lung Cancers**

Palliative

Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider short-course EBRT.

**Endobronchial HDR:**

10 Gy@ 1cm/ 1 fraction to 30 Gy@ 1cm/ 6 fractions\textsuperscript{1}

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1. ABS recommendations, Stewart et al. PMID: 26561277

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Post-transplant stenosis

Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets.

**Endobronchial HDR:**

7-10 Gy@ 1 cm/ 1-2 fractions/ 2 weeks\textsuperscript{1}

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1. Allen et al., Rabin Medical Center, Israel. PMID: 22381651

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**Uveal Melanoma**

Definitive

70 to 100 Gy to the tumors apex 5-7 days\textsuperscript{1}

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1. ABS recommendations, Simpson et al. PMID: 24373763

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Many centers are looking ahead at the possibility of the current pandemic lasting for several more weeks to months. Our cancer patients will still require treatment, even with thoughtful delays. A shortage of PPEs is not only anticipated, but already noted in many high-risk areas. Creative measures are required to weather this storm.

You have likely seen recent articles about UVC or “germicidal” light and its potential use during this pandemic. UVC light is between 100-280 nm wavelength and notably filtered by the ozone layer. UVC light is found in artificial sources, such as mercury lamps. The wavelength of these bulbs is generally 254 nm. UVC radiation causes DNA/RNA damage by producing cyclobutane pyrimidine dimers altering DNA/RNA structure, and thus interfering with replication[1].

COVID-19 has been demonstrated to be an enveloped, positive-stranded RNA virus with nucleocapsid from the family of coronaviruses. The family of coronaviruses has been demonstrated to have sensitivity to UVC light at a 254 nm wavelength. The D_{37} of the coronavirus family is 3.1 J/m2 (equivalent to 0.31 mJ/cm2)[2]. The University of Nebraska Medical Center (UNMC) has started processing N95 masks with this technique and other hospitals have started to follow suit. 1000 mJ/cm2 is the dose that is being utilized by John Lowe, PhD, at UNMC to process N95 masks in the current pandemic. This dose is more than 10-fold higher than the D_{37}, based on laboratory data for a 6-log kill. The following link details their protocol (https://www.nebraskamed.com/sites/default/files/documents/covid-19/n-95-decon-process.pdf)

Duke University and Batelle Inc. have been using vaporized hydrogen peroxide, which provides a reprieve for these locations, but has yet to reach to the needs of each community. UVC light has previously been compared to microwave-generated steam, moist heat, bleach solution, ethylene oxide, and vaporized hydrogen peroxide[3-5]. UVC was favored based on N95 processing when evaluating filtration and fit of the mask.

There are elegant UVC medical devices made by companies within the U.S. It is possible your hospital currently owns one of these since they are used to sterilize rooms contaminated by C. Difficile. However, they are not readily available to many centers, are cost prohibitive, and currently on back order. There may be a potential to repurpose UVC lights from HVAC units, water filtration units, and laboratories within hospitals with some creativity. UVC lights can also be purchased from several lighting dealerships nationwide. It is imperative to utilize lights that are ozone free in a well-ventilated space. As with any radiation source, ALARA should be employed since UVC exposure can have carcinogenic and cataractogenic effects. We recommend they are used when humans are outside of the room.

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Time, distance, and output all are important in calculating the potential virucidal effects of the lamps, as is the wavelength of the bulbs used. Notably, the potential for exposure variability exists and should be verified with a UVGI (ultraviolet germicidal irradiation) meter. Alternatively, ultraviolet exposure strips could be considered in lieu of UVGI meter to confirm dose, though these are not reliable in confirming exposure. Medical physicist input is necessary for these measures.

CDC guidelines have allowed for homemade scarf or facemask in the time of crisis. Through transmission of these homemade devices is 97% and do not provide adequate protection for healthcare workers. They may, in fact, provide a false sense of security and are of limited benefit over no facemask. UVC light is one option that can be considered to conserve N95 masks in the time of crisis due to the critical shortage.


Patient Safety in the Brachytherapy Clinic During COVID-19

Tim Showalter, MD, MPH

University of Virginia

The ABS provided helpful guidance to practitioners regarding delivery of brachytherapy during the coronavirus outbreak (https://www.americanbrachytherapy.org/about-abs/abs-news/abs-statement-on-coronavirus/), recognizing the essential need for brachytherapy for cervical cancer and many patients with breast or uterine cancers. The ABS recognized the advisability of delaying some brachytherapy procedures for prostate cancer, as well. By limiting the number of brachytherapy procedures, radiation oncologists had help limit contact among people, conserve PPE, and limit the use of anesthesia services during the outbreak.

Given the continued need for brachytherapy services during this time, some additional guidance is offered to help improve the safety of brachytherapy practice:

**PPE During Procedures:**

Due the potential for viral shedding through a variety of avenues (including possibly vaginal mucosa), it is appropriate to wear protective equipment such as gown, gloves, facemask and eye protection during brachytherapy procedures. In order to conserve PPE, consider limiting the number of staff members involved with each procedure to the minimum requirement. At the University of Virginia (UVA), for example, we have not involved residents directly in brachytherapy procedures during the COVID outbreak, with the goals of minimizing exposure and conserving PPE.

*continued*
Cleaning Between Patients:
Attention should be given to cleaning and disinfecting all surfaces of the brachytherapy suite between procedures, following institutional guidance for cleaning during the COVID outbreak.

Social Distancing in the Brachytherapy Suite:
Staffing should be kept to the minimum required for safe practice, based on institutional input. Patient scheduling should be designed to avoid having patient appointments overlap. Consideration can be given toward having only one patient at a time in the brachytherapy suite, and only 1 family member allowed to accompany the patient. At UVA, our brachytherapy team has scheduled gaps between cases to allow intake, procedure and full recovery of each patient prior to admitting the next patient to the facility. The overall decrease in brachytherapy volume (from delaying prostate cancer procedures) has helped make this possible.

Shorten Radiation:
For multi-fraction brachytherapy courses, such as intracavitary GYN HDR brachytherapy, it is reasonable to consider using a shorter dose-fractionation schedule. The ABS guidelines are useful resources for fractionation schedules for brachytherapy. At UVA, we have historically delivered 5-fractions of tandem and ovoid brachytherapy for cervical cancer, but have adopted a 4-fraction schedule since the start of the COVID outbreak. We have also emphasized brachytherapy without needing anesthesia and intubation whenever possible to minimize the risks for our colleagues in anesthesiology.

Preparation for Staff Shortages:
Since a limited subset of radiation oncologists, medical physicists, nurses and other staff may be trained and credentialed for brachytherapy, each center may plan for contingencies in the event of having key stay members out (e.g., for quarantine or child care needs). At UVA, we are striving to alternate clinical versus work-from-home duties for our experienced brachytherapy practitioners to ensure that at least one competent physician and medical physicist are available to perform GYN brachytherapy cases.

Safety and Quality Checks:
The risk of errors may go up when staff dynamics change and when additional stressors enter into the equation. Now more than ever, it is vital to adhere to quality assurance and safety checklists to ensure patient safety during brachytherapy, and to communicate clearly among brachytherapy team members.
COVID-19 Impact on Timing of Brachytherapy Treatment and Strategies for Risk Mitigation

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Brachytherapy COVID-19 Response

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Introduction:
The novel SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) causing COronaVirus Disease-19 (COVID-19) has resulted in a global pandemic with unprecedented impact on medical resources and personnel, and patient care access issues. Given the ease of host-host transmission and impact on medical resources much of the world has implemented physical distancing and restrictions on when it is appropriate to leave home to further reduce transmission and subsequent strain on medical resources. There is some suggestion that patients with cancer who are infected with COVID-19 may have worse respiratory outcomes than patients without cancer; however, these data are preliminary.

Given the constantly evolving challenges surrounding COVID-19 and the potential impact on healthcare, we reviewed amassing evidence to help guide the management and timing of brachytherapy for gynecologic, breast, and prostate cancers. Where concrete
data could not be found, peer-reviewed expert opinion is provided. Importantly, these recommendations apply only to patients not known to be infected with SARS-CoV-2. For patients with symptoms concerning for COVID-19, or who have already tested positive, we recommend following the local clinic and/or hospital treatment policies and procedures given the unique resources of each institution. Delay of treatment until a negative COVID-19 test may be indicated in order to protect the patient, the treating team, and to maintain access to care for all other patients treated at that facility. Given this, the purpose of the following commentary is to highlight the importance of timely brachytherapy (BT) treatment for patients with breast, prostate, and gynecologic malignancies and provide a framework for clinical practice and management in response to the COVID-19 pandemic.

The Impact of Time on Treatment Outcomes

Cervix

During the COVID-19 pandemic, it is important to recognize that prolongation of the treatment duration has been shown to negatively impact tumor control outcomes through tumor repopulation. Fyles et al retrospectively assessed the impact of overall treatment time (external beam RT, EBRT, and BT) on pelvic control in FIGO stage I-IV cervical cancer patients. Over 800 women were included and the median treatment time (weekends excluded) was 36 days. The authors found that every delay in treatment of one day over the median was associated with a 1% loss of pelvic control. In a similar retrospective study by Peteriet et al in 209 patients with FIGO stage IIB-IIIB cervical cancer who received EBRT and BT the median duration of treatment was 55 days (duration included planned weekend breaks). They found that pelvic control (87% vs 72%, p=0.006) and 5 year survival (65% vs 54%, p=0.03) varied between treatment duration <55 days and duration ≥55 days, respectively. This study also identified time between EBRT and initiation of BT as the most common cause of treatment prolongation (combined with holidays). Several other studies confirmed that treatment prolongation over 55 days (> 8 weeks) adversely affected pelvic control in cervical cancer, and each additional day over this threshold was associated with ~1% decrement in both pelvic control and overall survival. The effect on tumor control and survival was examined by Song et al in the era of concurrent chemotherapy. In a retrospective review of 113 women with FIGO stage IIB-IIIB cervical cancer the authors found that time to completion of therapy (EBRT plus BT) > 56 vs ≤ 56 days was associated with pelvic failure rate of 26% vs 9% (p=0.04). Therefore, even with concurrent chemotherapy, prolongation of the total treatment interval remains an essential factor impacting pelvic control.

Uterus

Timing of adjuvant therapy for uterine malignancies is important to patient treatment outcomes. Ahmed et al reviewed the records of 195 patients following total abdominal hysterectomy with or without lymph node sampling and found that delay in the interval from surgery to the start of radiation > 6 weeks decreased disease specific survival (DSS) (p<0.005). Likewise, Fabrini et al investigated the impact of the interval between surgery to initiation of radiation in 177 patients with endometrial cancer. They found a significantly increased rate of local recurrence associated with a > 9 week interval between surgery and radiation (11% vs 0%, p=0.046). Cattaneo et al found that delay in the time to initiation of radiation following hysterectomy with or without lymph node dissection in women with uterine carcinomas ≥ 9 weeks was associated with worse recurrence free survival (39% vs 90%, p<0.001). Finally, a large, retrospective NCDB analysis reviewed the records of 16,520 patients with endometrial cancer for the impact of treatment interval on overall survival. They found that an interval between surgery and radiation ≤ 8 weeks was associated with improved 10 year overall survival (p=0.014).
**Special Cases:**

**Vaginal Cuff Brachytherapy and Medically Inoperable Endometrial Cancer**

Vaginal brachytherapy is often considered as adjuvant therapy for patients with early stage uterine carcinoma at intermediate or high risk of recurrence given that the vagina is the primary site of failure. There is limited data on the timing of vaginal brachytherapy relative to surgery. Timing of vaginal brachytherapy can be individualized based on risk of recurrence. Patients should be counseled that salvage of a vaginal cuff recurrence is about 60-70% at skilled centers (ranges 50-90%) with intensification of treatment required for salvage. The risk of recurrence, and the ability to deliver salvage therapy, are considerations when jointly deciding the delivery and timing of vaginal brachytherapy.

In low-grade, early-stage cases (FIGO stage I), medically operable endometrial cancer patients may be surgically delayed with an intra-uterine device (IUD) delivering hormonal therapy. Medically inoperable patients are those who are deemed inoperable following assessment by their gynecologic oncologist or other qualified health professional involved in their care based on medical comorbidities. Although no data exist for patients with high-grade uterine malignancies, following surgery these patients can be treated with brachytherapy alone or a combination of EBRT and BT (LDR or HDR). While it may be possible to delay surgery in patients with high-grade malignancies using an IUD delivering hormonal therapy during COVID-19, caution should be exercised as the long-term oncologic outcome in this situation is unknown.

**Vaginal Cancers**

Given the location of the vagina in close proximity to the bladder, rectum and urethra, organ preservation with radiation or chemoradiation is often the best definitive treatment option. After EBRT, for tumors > 0.5cm interstitial brachytherapy is required to ensure adequate dosing to achieve a cure. Extrapolating from cervical cancer, and given the aggressive nature of vaginal tumors, treatment should be initiated as soon as is feasible and completed within < 8 weeks.

**Breast Cancer**

In women with mammographically-detected ductal carcinoma in situ (DCIS) < 2.5 cm of low- or intermediate-grade and surgical margins > 2 mm, or > 70 years with invasive estrogen-receptor positive, node-negative tumors < 3 cm and negative surgical margins who are eligible to receive endocrine therapy, omission of RT is appropriate. The use of brachytherapy as adjuvant therapy is an alternative for select patients with early stage breast cancer. Consensus statements and guidelines have been published by ASTRO, ABS, and the American Society of Breast Surgeons. It is now an accepted standard of care for patients that fall into appropriate categories per guidelines. In the setting of single-catheter devices, timing is predicated by technical factors primarily the presence of a seroma cavity in which to place the device. In general, it is best practice to place the catheter and begin treatment within 4 weeks of breast conserving surgery (BCS). With an interstitial multi-catheter approach, the timing of BT is less dependent on the presence of a seroma cavity, and therefore falls in line with timing of external beam. For patients with DCIS radiation can be safely delayed up to 12 weeks following breast conserving surgery. For patients with invasive disease there is mixed data. Some studies show that RT treatment delay of 8-12 weeks following BCS was associated with inferior local control, and a large systematic review of 46 studies showed local recurrence rates to be significantly higher in patients receiving adjuvant RT more than 8 weeks after surgery compared with those treated within 8 weeks (OR 1.62, 95% CI 1.21-2.16). Other studies have shown that intervals up to 20 weeks may be safe and have no detriment to local control or overall survival (OS) for some patients without adverse tumor control or survival outcomes.
Prostate Cancer
There is conflicting data regarding whether postponement of treatment after diagnosis leads to worse outcomes in prostate cancer\textsuperscript{35}, for both surgery\textsuperscript{36-38} and RT\textsuperscript{39, 40}. It is likely that the retrospective nature of these studies and heterogeneous patient groups play a large role in the variability of findings. The largest of these studies involving surgery examined 3969 prostatectomy patients that underwent surgery within one year of diagnosis\textsuperscript{36}. It found no impact by time from biopsy to surgery on biochemical recurrence after a mean follow-up of 5.4 years; this remained true even when they examined the subset of higher risk patients. Similarly, the largest study on RT examined 1322 patients who underwent EBRT alone\textsuperscript{39}. They found no difference in OS, cause-specific survival (CSS), Distant metastasis (DM), or freedom from biochemical failure (FFBF) based on time to treatment (< 3, 3-6, 6-9, or > 9 months after diagnosis). They also found no difference in FFBF or DM in high-risk patients. Based on these studies, and others\textsuperscript{41}, the safe interval of postponement until definitive treatment may be 6-12 months. Even if there is a true detriment in cancer outcomes with postponement of therapy that is not fully captured by these studies. The conflicting data suggest a small magnitude that must be weighed against the risks posed to patients and society during the COVID-19 pandemic.

Overall, it is unlikely that postponement of a few months is unlikely to significantly impact disease outcomes. This is likely true for most grade group 1 and 2 cancers due to their more indolent rate of growth, and for most higher-grade cancers due to the efficacy of androgen deprivation therapy (ADT). Traditionally, two months of neoadjuvant ADT is given prior to RT, although recent evidence suggests this is not necessary\textsuperscript{42}. However, in the setting of COVID-19 and to attempt to reduce patient exposure, neoadjuvant ADT may be given for as many as 6 months (and possibly longer) prior to definitive therapy given the excellent and equivalent results seen in studies using this approach.

The use of brachytherapy in the treatment of prostate cancer is typically as definitive treatment alone in low-risk and favorable intermediate-risk patients, and in combination with EBRT in unfavorable intermediate-risk and high-risk patients. In lower risk patients, most evidence indicates the equivalence of brachytherapy alone compared to surgery or EBRT, and it has the advantage over EBRT of a much shorter time commitment for the patient to be in a health care setting. Similarly, combining brachytherapy with EBRT decreases the total time a patient would need to be away from home, and some data show improved biochemical progression-free survival in select patients\textsuperscript{43, 44}.

Treatment Recommendations
Timing of Therapy

Cervix
- For definitive therapy, the chemotherapy and external beam radiation plus brachytherapy total treatment package time should be < 8 weeks.
- For adjuvant external beam radiation therapy (with or without brachytherapy) following surgery in patients meeting GOG 92 criteria\textsuperscript{45}, external beam radiation should begin 4-6 weeks after surgery and treatment interruption should be kept to a minimum. For adjuvant chemotherapy and external beam radiation (with or without brachytherapy) following surgery in patients meeting GOG 109 criteria\textsuperscript{46}, chemotherapy and external beam radiation should begin 4-6 weeks after surgery and treatment interruption should be kept to a minimum.
Uterus
- For adjuvant vaginal cuff brachytherapy following surgery, brachytherapy should ideally begin < 8 weeks following surgery, but no more than 12 weeks.

Breast
- Physicians should consider department resources, patient COVID-19 infection risk (age, co-morbidities), and technical factors when deciding if EBRT or breast BT is the most appropriate treatment modality.
- For patients with early stage, favorable disease neoadjuvant endocrine therapy may be advised during the COVID-19 crisis as surgeries are being delayed. For patients requiring adjuvant treatment following BCS, breast BT is considered an equivalent option to EBRT. However, physicians should carefully consider the effect of neoadjuvant endocrine therapy on pathologic findings that are used to determine eligibility for APBI particularly in cases where endocrine therapy has extended beyond 3-6 months.
- For patients with DCIS who proceed with breast BT after BCS, treatment should start within 12 weeks following surgery.
- For patients with invasive breast disease who proceed with breast BT after BCS, treatment should start within 12 weeks following surgery, and not more than 20 weeks.

Prostate
- For definitive treatment of localized low- and intermediate-risk prostate cancer, BT alone is adequate treatment. In the setting of COVID-19 treatment can be postponed for at least 3-6 months. For patients anxious about delaying treatment during COVID-19, brachytherapy alone would minimize treatment time and healthcare exposure compared with other modalities.
- For patients with high-risk factors, having the patient on ADT for 3-6 months is recommended until definitive BT can be delivered. For patients receiving a prostate BT boost, BT should begin within 2-4 weeks following completion of EBRT. If significant delays are anticipated ADT should continue before initiating EBRT.

Fractionation Options
Cervix
The American Brachytherapy Society (ABS) lists several recommended fractionation schemes for cervical cancer. Consideration of the 7 Gy x 4 regimen is appropriate and shorter fractionation regimens may be considered to decrease treatment time, if appropriate. Table 1. Recent results from a prospective randomized trial done in India demonstrate that three fraction regimens may not increase toxicity greatly while providing equivalent tumor outcomes. However, caution should be used when deciding what fractionation schedule to use as there is data to suggest that two fractions may result in decreased tumor control. For interstitial cervical HDR brachytherapy the ABS recommend a single implantation with five treatments delivered twice daily with a minimum of 6 hours separation between fractions. Alternatively, if hospitalization is not possible, two separate insertions on consecutive weeks using 7 Gy x 4 and twice per day treatment separated by a 6 hour interval is an option. Various fractionation options are shown in Table 1. For tumors with distal vaginal extension or involvement, smaller fraction sizes and additional fractions may be necessary to minimize risk of high-grade toxicity and dose to organs at risk (OARs).
For early stage uterine cancer, adjuvant vaginal cuff monotherapy using HDR brachytherapy in three to six fractions is common. In the setting of COVID-19, minimizing patient exposure risk is imperative. The use of 7 Gy x 3 to a depth dose of 0.5 cm is common and safe\(^{55,56}\). However, in selected patients, such as those with anatomy requiring a cylinder size < 20 mm, consideration of a four to five fraction regimen may help prevent excessive vaginal dose and late toxicity\(^6\). A vaginal cuff boost may be delivered after EBRT in women with high-risk factors and should result in a vaginal surface LDR equivalent (EBRT and brachytherapy) of 65-70 Gy 50. A vaginal cuff boost following EBRT is of limited additional benefit and in the setting of COVID-19 should be restricted to the highest-risk patients (i.e., cervical invasion or positive surgical margins). Various fractionation options are shown in Table 1.

For breast cancer, accelerated partial breast irradiation (APBI) is an option. The TRIUMPH-T trial of 7.5 Gy x 3 fraction APBI in women treated with breast conserving surgery and tumors < 3 cm showed low toxicity with excellent cosmetic outcomes and good local control.

For prostate cancer, a boost can be completed using either LDR or HDR brachytherapy approaches. A brachytherapy boost can shorten overall treatment times and may improve biochemical disease control\(^44\). These shorter fractionation regimens have been recommended in instances where compliance and other logistic issues (i.e., COVID-19) make shorter treatment attractive, Table 1. For HDR monotherapy treatment of low- and intermediate-risk prostate cancer, 13.5 Gy x 2 fractions is preferred, and 19 Gy x 1 fraction is inferior\(^57\).

### Table 1

<table>
<thead>
<tr>
<th>Dose per fraction, Gy</th>
<th>Fx, #</th>
<th>EQD2 (+45 Gy EBRT, α/β=10)</th>
<th>Author/Reference</th>
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<tbody>
<tr>
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<tr>
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<td>6</td>
<td>81.8</td>
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<tr>
<td>HDR interstitial (1 insertion)</td>
<td>5-6</td>
<td>5 (BID)</td>
<td>75-84</td>
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<tr>
<td>HDR interstitial (2 insertions)</td>
<td>7</td>
<td>4</td>
<td>83.9</td>
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### Uterine Cancer

<table>
<thead>
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<th>Fraction</th>
<th>Surface Dose</th>
<th>Source</th>
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<tbody>
<tr>
<td>Vaginal cuff HDR monotherapy</td>
<td>7 Gy at 0.5 cm</td>
<td>3</td>
<td>57.8 (surface dose)</td>
<td>ABS Task Group Report 56&lt;br&gt; PORTEC-2 16</td>
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<tr>
<td></td>
<td>5.5 Gy at 0.5 cm</td>
<td>4</td>
<td>54.2 (surface dose)</td>
<td>ABS Task Group Report 50</td>
</tr>
<tr>
<td></td>
<td>5 Gy at 0.5 cm</td>
<td>5</td>
<td>58.9 (surface dose)</td>
<td>Jolly et al 62&lt;br&gt; ABS Task Group Report 56</td>
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<tr>
<td></td>
<td>8.5 Gy at surface</td>
<td>4</td>
<td>52.4 (surface dose)</td>
<td>MacLeod et al 63</td>
</tr>
<tr>
<td></td>
<td>6 Gy at surface</td>
<td>5</td>
<td>40 (surface dose)</td>
<td>ABS Task Group Report 50</td>
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<tr>
<td></td>
<td>4 Gy at surface</td>
<td>6</td>
<td>28 (surface dose)</td>
<td>Townamchai et al 64</td>
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<td>Vaginal cuff HDR boost</td>
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<td>60.3</td>
<td>RTOG 0921 65&lt;br&gt; RTOG 0418 66&lt;br&gt; ABS Task Group Report 56</td>
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<tr>
<td></td>
<td>6 Gy at surface</td>
<td>3</td>
<td>68.3</td>
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<td>4</td>
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<td></td>
<td>7.3 Gy at surface</td>
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<td>52.6 (no EBRT)</td>
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### Breast Cancer

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<td>42-45 (α/β=4-5)</td>
<td>RTOG 9517 67&lt;br&gt; Strnad et al 68&lt;br&gt; Khan et al 69</td>
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<td></td>
<td>7.5 Gy</td>
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### Prostate Cancer

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<th>Surface Dose</th>
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<tr>
<td>HDR monotherapy</td>
<td>13.5 Gy</td>
<td>2</td>
<td>104.6 (α/β=2)</td>
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<td>LDR monotherapy (I-125/Pd-103, Cs-131)</td>
<td>145/125/115</td>
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<td>NCCN Prostate CPG 70</td>
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<tr>
<td>HDR boost (EBRT 37.5 Gy/15 fx)</td>
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<td>1</td>
<td>105.9 (α/β=2)</td>
<td>Martell et al 71</td>
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<td>HDR boost (EBRT 45-50.4 Gy)</td>
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<td>~ 113 (α/β=2)</td>
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Anesthesia for Brachytherapy

A cornerstone of safe and effective brachytherapy is adequate patient analgesia. In the setting of COVID-19 many brachytherapy practitioners may have limited access to brachytherapy implantation in the operating room due to reductions in personnel and allocation of hospital resources elsewhere. To overcome these issues a variety of effective alternative analgesia options exist to allow for the timely completion of brachytherapy. 

As with patients receiving general analgesia, an individualized anesthesia plan should be developed, and a pre-procedural evaluation is required to better understand and minimize patient risks. The ongoing involvement of anesthesiology is strongly encouraged, and their input will be valuable for physicians without moderate sedation experience. Open communication with all team members is necessary to minimize the risk of aerosolizing particles during the brachytherapy procedure. For breast, prostate, and gynecologic implantations, procedural analgesia is possible with a combination of: neuraxial analgesia (epidural, spinal, or combined spinal-epidural anesthesia; CSE), pudendal nerve block, moderate sedation (midazolam and fentanyl) dosed per institutional policy, and local analgesia with topical/mucosal lidocaine and/or tissue infiltration with tumescent technique using buffered lidocaine with or without epinephrine. Buffered lidocaine is preferred as unbuffered lidocaine is acidic and painful when injected. 

If, after review of patient- and case-specific factors, it is felt that intubation and ventilation is necessary, strong consideration should be given to having only anesthesia staff in the room during intubation and extubation. Awareness of the ventilator filter system is important—particularly the viral filtration efficiency and use of a breathing system filter. Strong consideration should be given to high-efficiency particulate air (HIPA) filter system between the ventilator system and the patient, and disconnection of the system which the patient is being ventilated should be avoided.

Finally, early reports show that patients with COVID-19 may experience endothelial damage with severe coagulopathy and/or thromboembolism. In such patients who also require brachytherapy implantation with planned overnight hospitalization and immobilization, strong consideration should be given to the need for therapeutic anticoagulation and/or augmentation of the implantation technique as necessary.

Brachytherapy Analgesia Treatment Recommendations by Disease Site:

Gynecologic:
It is possible to successfully implant very large gynecologic tumors without the use of general anesthesia using a combination of moderate sedation, topical and local tumescent anesthesia tissue infiltration, and pudendal nerve block. Epidural anesthesia with or without spinal anesthesia using a hyperbaric block may significantly improve patient comfort for longer procedures, or implantations requiring overnight hospitalization in conjunction with patient-controlled analgesia (PCA). For centers with in-room imaging capabilities (CT or MRI) general anesthesia may be feasible; however, for the majority of centers without an in-room imaging solution general anesthesia should be avoided. This results from the need for patient extubation and/or transportation under anesthesia, and to avoid repeated disconnection of the respiratory circuit and potential staff exposure to patient respiratory secretions during imaging.

• For intracavitary (T&T, T&O) implantation, preference for moderate sedation with or without mucosal/injection lidocaine. Supplemental oxygen should be delivered with nasal cannula.

Furthermore, similar to patients with tuberculosis, consider implementing a wait period prior to staff re-entry into the room following extubation; however, this has not been studied for coronavirus to our knowledge.
with surgical mask in place on patient, or with facemask oxygen. All involved staff should wear appropriate surgical PPE.

- For hybrid implantation, preference for moderate sedation with mucosal/injection lidocaine, and with or without pudendal nerve block. Supplemental oxygen should be delivered with nasal cannula with surgical mask in place on patient, or with facemask oxygen. All involved staff should wear appropriate surgical PPE. Alternatively, for patients requiring general anesthesia, recommendations as above for full interstitial gynecologic implantation.

- For full interstitial implantation, preference for moderate sedation with mucosal/injection lidocaine, and with or without pudendal nerve block. Supplemental oxygen should be delivered with nasal cannula with surgical mask in place on patient, or with facemask oxygen. All involved staff should wear appropriate surgical PPE.

- For patients requiring general anesthesia, avoid tracheal intubation in favor of laryngeal mask airway (LMA) to decrease interaction with deep respiratory secretions. HIPA filter system between the patient and ventilator system is preferred. Avoid mask ventilation of the patient. At the very end of the implantation keep the ventilator system intact, then remove the LMA and place surgical mask on the patient.

Breast:
- For intracavitary cases requiring device exchange prior to brachytherapy, preference for oral pain and anxiolysis medication (oxycodone, lorazepam) as necessary. All involved staff should wear appropriate surgical PPE.

- For interstitial cases, preference for combined topical analgesia using EMLA cream, local tumescent infiltration of buffered lidocaine with epinephrine, and oral pain medication as above, or moderate sedation as necessary. Supplemental oxygen should be delivered with nasal cannula with surgical mask in place on patient, or with facemask oxygen. All involved staff should wear appropriate surgical PPE.

Prostate:
For patients undergoing prostate brachytherapy, preference for local and/or spinal or CSE anesthesia, supplemental oxygen should be delivered with nasal cannula with surgical mask in place on patient, or with facemask oxygen. All involved staff should wear appropriate surgical PPE.

Recommendations for Image-Guided Brachytherapy (IGBT) for Gynecologic Malignancies

In the era of COVID-19, it is imperative to be mindful of the exposure risks of our patients with every encounter, including diagnostic imaging. MRI improves soft tissue delineation and greater accuracy in creation of a HR-CTV for cervical brachytherapy. It would be reasonable to perform CT-based planning for patients with cervix-confined local disease and those with limited vaginal involvement (T1b-2a) and reserve MRI-based planning for patients with extracervical spread of disease where delineation of gray zones would be most impacted as with parametrial, uterine body, mid/distal vagina, bladder or rectal invasion (T2b-T4a).

For those patients where MRI is felt to improve their treatment delivery relative to risk of COVID, responsible utilization of MRI is necessary. MRI with applicator in situ for each fraction or application is ideal but may not be possible within the construct of each institution’s workflow and access to resources, and this is especially the case in the era of COVID-19. There are experiences with performing MRI-based brachytherapy with the applicator in situ while keeping the patient as an inpatient and delivering treatment in
2 applications\textsuperscript{83,84}. This strategy can be amended to perform all brachytherapy in a single well-placed application to avoid multiple admissions. For outpatient scenarios, a pre-brachytherapy MRI can be done and incorporated with CT done at time of implant. With this utilization, the MRI resulted in significant alterations in the HR-CTV in about 50\% of cases compared to CT alone in patients with parametrial invasion (T2b & T3b)\textsuperscript{85}.

Pre-brachytherapy MRI has been fused to a CT at time of implant using deformable image registration (DIR) as well. The GTV can be contoured on the MRI and HR-CTV on the MRI-CT fusion after DIR\textsuperscript{86}; however, limitations exist with this approach and should be recognized with clinical implementation\textsuperscript{87}. Another strategy utilized a Smit sleeve placed at time of first implant with CT-based planning. An MRI was then obtained with Smit sleeve in place with fusion of MRI to subsequent CT-based brachytherapy implant co-registered to the Smit sleeve\textsuperscript{88}. A third strategy, “cognitive fusion,” where the treating physician contours on a CT with applicator in place while directly referring to a pre-brachytherapy MRI, may also aid in defining an HRCTV in a time and resource efficient manner.

While integration of MRI is optimal and encouraged in the manners noted above, when logistical barriers exist to prevent this (which may potentially worsen with COVID-19), CT based volumetric brachytherapy planning remains a highly accessible method of both reducing toxicity and improving disease control, when compared to film based (point A) planning\textsuperscript{89}.

**Strategies to Preserve the Quality of Cancer Care While Minimizing Risk**

Temporizing options, such as endocrine therapy, exist for patients who wish to avoid traditional treatment paradigms to decrease the risk of COVID-19. As endometrioid precancerous lesions arise from the prolonged exposure of the endometrium to estrogen, progestins can act to inhibit endometrial proliferation and are used in the management of low risk or surgically inoperable women with endometrial cancer\textsuperscript{90}. These agents can be continuously for 3-6 months with reassessment for response every 6 months. If by 12 months there is not a complete response, definitive surgery should be pursued. A systematic review by Gunderson in 2012 indicated that 53\% of women experience a durable response to treatment with recurrence occurring in almost after response occurring in 35.4\% of women with invasive disease\textsuperscript{91}. A recent meta-analysis compared mechanism of progestin administration, either via levonorgestrel IUD or oral cyclic medroxyprogesterone acetate and found that the levonorgestrel IUD had a higher response rate that the oral formulation in non-obese women\textsuperscript{92}. Finally, a small Japanese prospective trial published in 2007 including 28 women with stage 1A endometrial cancer demonstrated a similar response rate of 55\% to that demonstrated in retrospective studies in women with stage 1A disease\textsuperscript{93}.

For breast and/or prostate cancer, delay of definitive or adjuvant therapy may also be possible using endocrine therapy temporizing measures.

**Discussion**

Patients who have gynecologic, breast, and prostate cancers where temporizing therapy is not available/appropriate and brachytherapy treatment is indicated should be considered “priority 1”—deemed critical for therapy and require services/treatment due to a clinical situation where delay or omission of therapy will result in severe negative impact on the oncologic outcome or life expectancy. If a delay is anticipated the treating physician should make alternative plans as early as possible and consider referral, if necessary, to another facility equipped and staffed to deliver treatment with minimal to no disruption in the treatment timeline. There are many potential reasons for treatment delay beyond physician-centric issues, Table 2. Impact of staff shortage, lack of social workers and ancillary support (housing, transportation), socioeconomic factors (loss of job, housing, insurance) may all play a role.

*continued*
Factors 4 and 5 Will Likely be of Most Concern During the COVID-19 Pandemic

While all hospital services and personnel are impacted by COVID-19 it is important to recognize strategies that may mitigate or lessen the impact, or delay treatment, Table 3.

In line with these strategies, the ABS94 and ASTRO95 recently issued recommendations in the setting of COVID-19, which are outlined in the sections above. While reduced patient exposure and resource utilization is important during COVID-19, it is critical to maintain brachytherapy services for patients. Furthermore, the use of brachytherapy may shorten treatment time and exposure for some patients.

The goal and scope of this work is to provide guidance and a framework of how to continue delivering high quality brachytherapy given the current, significant healthcare resource and personnel restrictions in the setting of the COVID-19 global pandemic. The recommendations made above are based on data (where available) and expert opinion. However, these are not formal policies, as data in this setting is limited. Given the unique and varied patient populations and resources available, beyond the above, we recommend that physicians keep open communication with patients and multidisciplinary care teams to optimize treatment at this challenging time, and continue to follow developing institutional, state, and federal guidelines/recommendations as challenges in delivering care during COVID-19 will continue to evolve.

References


Table 2 Factors Affecting Timely Delivery of Treatment

<table>
<thead>
<tr>
<th></th>
<th>Factors Affecting Timely Delivery of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Coordination of care among different sites</td>
</tr>
<tr>
<td>2</td>
<td>Multidisciplinary coordination of care</td>
</tr>
<tr>
<td>3</td>
<td>Poor patient navigation of system</td>
</tr>
<tr>
<td>4</td>
<td>Patient factors, i.e. – illness, socioeconomic challenges, transportation</td>
</tr>
<tr>
<td>5</td>
<td>Institution factors, i.e. – staffing shortage, equipment shortage, medication shortage</td>
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Table 3 Strategies to Preserve Cancer Care and Minimize Risk

<table>
<thead>
<tr>
<th></th>
<th>Strategies to Preserve Cancer Care and Minimize Risk</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Use of altered fractionation schedules</td>
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<tr>
<td>2</td>
<td>Endocrine therapy as a temporizing measure for breast, prostate, and uterine cancer (as appropriate)</td>
</tr>
<tr>
<td>3</td>
<td>Eliminate or consolidate non-essential OR procedures</td>
</tr>
<tr>
<td>4</td>
<td>Modify general anesthesia protocols or switch to neuraxial sedation and/or moderate sedation with local analgesia</td>
</tr>
<tr>
<td>5</td>
<td>Streamline staffing to minimize personnel exposure</td>
</tr>
<tr>
<td>6</td>
<td>Incorporate telemedicine where feasible</td>
</tr>
</tbody>
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continued ➤


75. Finsen V. Reduced pain when injecting lidocaine. *Tidsskr Nor Laegeforen*. 2017;137(9):629-630.
91. Gunderson CC, Fader AN, Carson KA, Bristow RE. Oncologic and Reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 Adenocarcinoma: A systematic review. *Gynecol Oncol*. 2012;125(2):477-482.
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RADIOACTIVE SEEDS
The American Brachytherapy Society, a nonprofit organization, has initiated the 300 in 10 program with the goal of training 30 competent brachytherapists per year over the next 10 years through a multifaceted approach. As part of the 6 phases for establishing brachytherapy competency, we have identified several institutions who will be offering 2-month “fellowships” at designated ABS certified centers for senior level residents. The goal is to provide hands-on clinical experience for senior level residents since low procedural volume has been identified as the major barrier to implementing a brachytherapy practice. These 2 months rotations will be offered for prostate and gynecologic cancer—using either LDR and/or HDR brachytherapy. Emphasis will be placed on patient selection, procedural skills, treatment planning as the dosimetry and physics of brachytherapy is essential, progressive thinking and methods to successfully implement a brachytherapy practice. If possible, senior level residents are encouraged to bring their physicist for 1 to 2 weeks.

Eligible applicants will include PGY4 and PGY5 residents. An ABS review committee will select the candidate. Emphasis will be placed on those candidates who can demonstrate a high likelihood of implementing a brachytherapy program. Due to the current COVID-19 crisis, these fellowships will start in the fall of 2020 or early 2021—pending the status of the current pandemic. However, senior level residents are encouraged to start planning for this opportunity during the 2020-2021 academic year.

FELLOWSHIP DETAILS

- Training will include interactive lectures centered on current concepts of prostate and gynecologic brachytherapy. Patient consultations and case presentations will address the spectrum of patients suitable for this procedure.
- Emphasis will be placed on progressive thinking. Participants are encouraged to share ideas and clinical cases from their own practice. Special breakout sessions will be available for treatment planning and for patient management.
- Finally, there will be an opportunity and expectation to participate in ongoing research projects. Opportunities include data collection, literature reviews, and abstract/manuscript preparation that highlight the favorable outcomes of brachytherapy.

SCHEDULE

- **Approximately** 7:00 am – 5:00 pm each day (will vary with each institution)
  - **Monday**: Implants, consultations, follow-ups, research, physics
  - **Tuesday**: Implants, consultations, follow-ups, physics
  - **Wednesday**: Implants, consultations, follow-ups, physics
  - **Thursday**: Implants, consultations, follow-ups, research
  - **Friday**: Implants, consultations, follow-ups, physics

continued ➤
Due to COVID-19, the 2020 Program was delayed. Stay tuned for more information.

LEARNING OBJECTIVES

♦ Identify clinical appropriateness
♦ Identify and utilize the latest techniques
♦ Understand the roles of each team member in the planning and treatment process
♦ Appreciate the workflow and materials involved in the treatment process
♦ Detail the risk and management of post implant complications
♦ Explain the concept and importance of radiation safety
♦ Participate in research opportunities

TRAINING FACILITIES

Coming Soon, will be announced in the near future.

COMPENSATION

Resident salaries will be funded from their own institution. ABS is working with industry to provide a stipend to offset the cost of transportation and lodging.

Your application should include the following:

♦ Curriculum Vitae
♦ Supporting letter from your department chair or program director
♦ Personal statement describing your brachytherapy experience and future goals, including your intention to develop a GYN and or prostate brachytherapy program
♦ Preference will be given to applicants who plan on starting a GYN/prostate brachytherapy practice as this is the primary goal of the 300 in 10 strategy.
♦ Member of the American Brachytherapy Society in good standing

Questions or concerns about fellowship details can be directed to:

Melissa Pomerene | Executive Director
American Brachytherapy Society
mpomerene@virtualinc.com
703.234.4078 | ext 4085

Due to COVID-19, the 2020 Program was delayed. Stay tuned for more information.