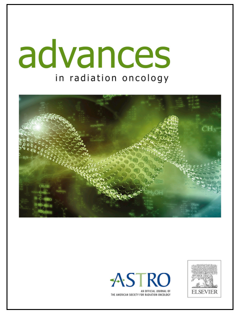
Journal Pre-proof



Concerns for activated breathing control (ABC) with breast cancer in the era of COVID-19: Maximizing infection control while minimizing heart dose

Andrew Song, MD, Gregor Manukian, MD, Amy Taylor, MS, Pramila R. Anne, MD, Nicole L. Simone, MD

PII: S2452-1094(20)30060-9

DOI: https://doi.org/10.1016/j.adro.2020.03.009

Reference: ADRO 426

To appear in: *Advances in Radiation Oncology*

Received Date: 21 March 2020

Revised Date: 23 March 2020

Accepted Date: 24 March 2020

Please cite this article as: Song A, Manukian G, Taylor A, Anne PR, Simone NL, Concerns for activated breathing control (ABC) with breast cancer in the era of COVID-19: Maximizing infection control while minimizing heart dose, *Advances in Radiation Oncology* (2020), doi: https://doi.org/10.1016/j.adro.2020.03.009.

Journal: Advances in Radiation Oncology

Article Type: Short Communication/Brief Opinions

Title: Concerns for activated breathing control (ABC) with breast cancer in the era of COVID-19: Maximizing infection control while minimizing heart dose

Authors: Andrew Song MD[1], Gregor Manukian MD[1], Amy Taylor MS[1], Pramila R. Anne MD[1], Nicole L. Simone MD[1]

Affiliations:

1) Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, PA

Corresponding Author:

Nicole L. Simone, MD

111 South 11th St., G-301G

Philadelphia, PA 19107

215-503-0554

nicole.simone@jefferson.edu

Word Count (max 2,000): 640

References: 16

Tables/Figures (max 6): N/A

Fee: $750

COI Disclosures: The authors have no conflicts of interest to declare.

Acknowledgements: This work was supported in part by the NCI Cancer Center Grant P30CA056036.

Active Breathing Control (ABC) devices employ moderate deep inspiration breath hold (DIBH) techniques in order to spare cardiac structures from dosing in left breast cancer (LBC) patients and is more commonly practiced than prone positioning[1]. ABC also helps in reducing dose to other organs at risk, including lungs and liver[2]. However, in the era of the COVID-19 pandemic, there are concerns regarding the safety of using such devices with risks of transmission amongst multiple patients, especially since the virus has a relatively high transmission rate and increased risk for fatality for elderly patients[3]. This issue is particularly poignant to cancer patients who may be immunocompromised and are at increased risk of invasive ventilation, ICU admission, or death (39% vs 8%) with COVID-19[4]. In addition, alternatives to ABC, such as prone positioning, may provide comparable benefits to ABC without placing LBC patients in situations at risk for direct exposure from shared respiratory devices.

At our institution, we utilize Active Breathing Coordinator™ (Elekta; Stockholm, Sweden) for our LBC patients. We previously published the results from a prospective trial using this device in which we demonstrated a median reduction in mean heart dose (MHD) of 1.7 Gy with a 8-year locoregional relapse rate of 7 percent[5]. Additionally, a systematic review of ten studies showed similar results with DIBH, including a reduction of MHD up to 3.4 Gy, translating to a 13.6 percent decrease in risk of heart disease[6]. This includes reduction of dose to the left anterior descending artery, with mean dose reduced by nearly half and coronary events at 10 years down to 2.55 percent from 4.03 percent[7].

Respiratory droplets are one of the main methods of transmitting the SARS-CoV-2 virus[8]. These can be generated through coughing, sneezing, mouth and nose breathing, and talking. The size and the number of droplets can vary based on the expiratory activity, the region of origin in the respiratory tract, and the type of pathogen[9]. SARS-CoV-2 particles have had reported diameters ranging from 0.06 to 0.14 microns[10]. SARS-CoV-2 viral particles in aerosols can remain viable for up to 3 hours and up to 72 hours on plastic and stainless steel surfaces[11]. Aerosol models in healthy humans have measured droplets from coughing as small as 0.1 microns, with the vast majority (97 percent) of droplets as submicron in size[12]. Viral aerosols, such as those generated by influenza, tend to skew towards this submicron size distribution[13].

The Active Breathing Coordinator™ utilizes a mouthpiece and filter kit which are designed for single patient use. The ViroMax® viral/bacterial filter is constructed of a Styrene-Acrylonitrile Copolymer which supports the filter media constructed from a blend of modacrylic and polypropylene fibers. This has been tested and certified to >99.99% viral and >99.999% bacterial efficiency (FDA GMP, ISO 13485:2016, FDA 510(k) clearance K063526). The filter has been tested to 0.1 micron size particles which should technically provide adequate protection from transmission. Since the SARS-CoV-2 virus may be as small as 0.06 microns, however, we have elected in our clinic to decide whether or not to use ABC on a case-by-case basis due to these concerns.

As an extra precaution during this time of the pandemic, providers can consider alternatives to ABC. Prospective trials comparing prone positioning vs DIPBH have found similar rates of cardiac sparing[14, 15]. A randomized clinical trial comparing voluntary DIBH with ABC DIBH found *no significant differences* in doses to normal structures and was preferred by patients[16]. Both prone positioning and voluntary DIBH can provide cardiac sparing comparable to ABC, and droplet precautions do not have to be considered. During this current pandemic, our institution has been favoring prone positioning over ABC for cardiac sparing. Prone positioning is not ideal for all LBC patients, however, including for those needing regional nodal irradiation, very medial or lateral lumpectomy cavities, and for situations where anterior displacement of the heart towards the chest wall may not lead to effective cardiac sparing[17]. Therefore, one can consider simulating patients in both prone and supine positions and selecting a treatment plan that is most suitable for the patient.

In addition, emphasis should be placed on optimizing treatment planning techniques such as field-in-field and IMRT[18].

In summary, the COVID-19 pandemic gives radiation oncologists an opportunity to evaluate our standard practices and create institutional guidelines taking into account: 1) the size of SARS-CoV-2 virus and 2) the type of device used for respiratory gating, in order to determine the risk-benefit ratio acceptable for our patients during this time. Alternatives to ABC, including voluntary DIBH, prone positioning, and optimizing treatment planning should also be considered to mitigate risk between patients.

References

1. Desai N, Currey A, Kelly T, et al: Nationwide Trends in Heart-Sparing Techniques Utilized in Radiation Therapy for Breast Cancer [Internet]. Adv Radiat Oncol 4:246–252, 2019[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/31011669

2. Lin CH, Lin LC, Que J, et al: A seven-year experience of using moderate deep inspiration breath-hold for patients with early-stage breast cancer and dosimetric comparison. Medicine (Baltimore) 98:e15510, 2019

3. Sun P, Lu X, Xu C, et al: Understanding of COVID□19 based on current evidence [Internet]. J Med Virol jmv.25722, 2020[cited 2020 Mar 20] Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25722

4. Liang W, Guan W, Chen R, et al: Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China [Internet]. Lancet Oncol 21:335–337, 2020[cited 2020 Mar 20] Available from: https://linkinghub.elsevier.com/retrieve/pii/S1470204520300966

5. Eldredge-Hindy H, Lockamy V, Crawford A, et al: Active Breathing Coordinator reduces radiation dose to the heart and preserves local control in patients with left breast cancer: Report of a prospective trial [Internet]. Pract Radiat Oncol 5:4–10, 2015[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/25567159

6. Smyth LM, Knight KA, Aarons YK, et al: The cardiac dose-sparing benefits of deep inspiration breath-hold in left breast irradiation: a systematic review. J Med Radiat Sci 62:66–73, 2015

7. Joo JH, Kim SS, Ahn S Do, et al: Cardiac dose reduction during tangential breast irradiation using deep inspiration breath hold: A dose comparison study based on deformable image registration [Internet]. Radiat Oncol 10:264, 2015[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/26715382

8. Transmission of Coronavirus Disease 2019 (COVID-19) | CDC [Internet][cited 2020 Mar 20] Available from: https://www.cdc.gov/coronavirus/2019-ncov/prepare/transmission.html

9. Morawska L: Droplet fate in indoor environments, or can we prevent the spread of infection? [Internet]. Indoor Air 16:335–347, 2006[cited 2020 Mar 21] Available from: http://doi.wiley.com/10.1111/j.1600-0668.2006.00432.x

10. Zhu N, Zhang D, Wang W, et al: A novel coronavirus from patients with pneumonia in China, 2019 [Internet]. N Engl J Med 382:727–733, 2020[cited 2020 Mar 20] Available from: http://www.nejm.org/doi/10.1056/NEJMoa2001017

11. van Doremalen N, Bushmaker T, Morris DH, et al: Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. [Internet]. N Engl J Med NEJMc2004973, 2020[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/32182409

12. Zayas G, Chiang MC, Wong E, et al: Cough aerosol in healthy participants: Fundamental knowledge to optimize droplet-spread infectious respiratory disease management [Internet]. BMC Pulm Med 12:11, 2012[cited 2020 Mar 20] Available from: https://bmcpulmmed.biomedcentral.com/articles/10.1186/1471-

2466-12-11

13. Fabian P, McDevitt JJ, DeHaan WH, et al: Influenza virus in human exhaled breath: An observational study. PLoS One 3, 2008

14. Yan SX, Maisonet OG, Perez CA, et al: Radiation effect on late cardiopulmonary toxicity: An analysis comparing supine DIBH versus prone techniques for breast treatment. Breast J , 2020

15. Gerber NK, Yan SX, Levinson BA, et al: A prospective trial to compare deep inspiratory breath hold (DIBH) with prone breast irradiation [Internet]. Pract Radiat Oncol , 2020[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/32014615

16. Bartlett FR, Colgan RM, Carr K, et al: The UK HeartSpare Study: Randomised evaluation of voluntary deep-inspiratory breath-hold in women undergoing breast radiotherapy [Internet]. Radiother Oncol 108:242–247, 2013[cited 2020 Mar 20] Available from: http://www.ncbi.nlm.nih.gov/pubmed/23726115

17. Haffty BG: Supine or Prone Breast Radiation: Upsides and Downsides [Internet]. Int J Radiat Oncol Biol Phys 101:510–512, 2018[cited 2020 Mar 23] Available from: http://www.ncbi.nlm.nih.gov/pubmed/29893266

18. Li JS, Freedman GM, Price R, et al: Clinical implementation of intensity-modulated tangential beam irradiation for breast cancer [Internet]. Med Phys 31:1023–1031, 2004[cited 2020 Mar 23] Available from: http://doi.wiley.com/10.1118/1.1690195