e-ISSN 2083–4640
ISSN 1507–1367

LETTER TO THE EDITOR

Reports of Practical Oncology and Radiotherapy
2022, Volume 27, Number 3, pages: 583–588
DOI: 10.5603/RPOR.a2022.0064
Submitted: 11.02.2022
Accepted: 06.05.2022

Navigator-assisted hypofractionation (NAVAH) to address radiation therapy access disparities facing African-Americans with breast cancer

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ABSTRACT

Background: African-Americans have the highest overall cancer death rate and shortest survival time of any racial or ethnic group in the United States. The most common cancer studied in African-American radiation therapy (RT) access disparities research is breast cancer. The goal of this study is to evaluate the impact of patient navigation on RT access for African-American breast cancer patients.

Material and methods: This study is a prospective survey-based evaluation of the impact of patient navigation on access to hypofractionated RT and financial toxicity in African-American breast cancer patients. The impact of patient navigation on RT access will be collated and analyzed from survey results pre-RT versus post-RT as well as for patients with versus without receipt of patient navigation. The validated COST-Functional Assessment of Chronic Illness Therapy score will be used to compare hypofractionation versus standard fractionated RT financial toxicity for patients with early-stage breast cancer who have received lumpectomy.

Conclusion: This is the first study to investigate the impact of patient navigation on reducing RT access disparities facing African-American breast cancer patients. The natural progression of this work will be to expand this model to include additional breast cancer populations most vulnerable to suffering RT access disparities (Native American, Hispanic American, Appalachian) within the United States.

Key words: breast cancer; adjuvant radiation therapy; African-American race; hypofractionation; patient navigation; health disparities

Rep Pract Oncol Radiother 2022;27(3):583–588

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Introduction

African-Americans have disparately limited access to optimal cancer care

Despite residing in the most opulent nation on earth (2021 gross domestic product exceeding 22 trillion dollars), African-Americans have been plagued with the reality of disparately limited access to optimal medical intervention, even when Level I evidence has demonstrated the superiority of said intervention. This has unfortunately been demonstrated repeatedly in many aspects of procedure-based treatment, remaining prevalent even after accounting for income and insurance status [1–5], and has manifested in some instances as being disproportionately triaged to lower-reimbursement treatment modalities [6, 7].

The field of Radiation Oncology in the 21st century has markedly increased its role in patient care, as advances in the precision of radiation delivery have allowed advanced techniques to provide comparable outcomes to operative intervention for many cancer patients [8]. As a result, any disparity in access to radiation therapy (RT) will prove more harmful now than at any previous era.

African-Americans have the highest overall cancer death rate and shortest survival time of any racial or ethnic group in the United States [9]. Elucidation of disparities in access to cancer care are important since previous work has indicated that when equal access to RT in Radiation Therapy Oncology Group (RTOG) prospective randomized trials is granted, race does not independently affect outcomes [10], a finding similar to Level I clinical data assessing evidence-proven optimal management of curable neurologic conditions [11].

Breast cancer is the most common cancer in African-American women

The most common cancer studied in African-American RT access disparities research has been breast cancer, which is by far the most common diagnosed form of cancer among African-American women (32%) [9, 12]. Health disparities research in Radiation Oncology is a relatively new field of study; as of 2016 more than 70% of Radiation Oncology disparities peer-reviewed work had been published since the beginning of 2014 [8] — this number has likely substantially increased given the relative explosion of interest in Radiation Oncology diversity, equity and inclusion since 2016.

As such, breast cancer provides a prime opportunity to address barriers impeding equal access to treatments which improve quality-of-life, reduce financial toxicity and increase overall survival. The equivalence of breast conservation therapy including radiation as compared to mastectomy for early-stage disease has been established for more than 40 years while indications for post-mastectomy radiation have expanded in the past decade, making RT essential in the optimal treatment of breast cancer [13].

Based on the Early Breast Cancer Trialists' Collaborative Group landmark meta-analysis (nearly 11,000 patients from 17 randomized trials), it is well-established that radiation treatment not only offers a substantial improvement in local control of breast cancer but also improves overall survival from this disease [14]. As a result, any access disparity facing African-Americans which restricts optimal radiation use results in consequences that are at least deleterious and at worst fatal.

The appropriate use of optimal RT is essential in reducing the rate of local recurrence in the conserved breast, which has further been associated with reduction of 15-year overall mortality[15]. Although there is a range of RT techniques for providing optimal breast cancer treatment, standard of care regimens for whole breast RT prescribe either at least 46 Gray (Gy) in 1.8–2.0 Gy/fraction given over 5–7 weeks as "standard fractionation", or at least 40 Gy in 2.66–2.70 Gy/fraction given over 3–4 weeks as "hypofractionation" [16, 17].

African-American breast cancer patients are less likely to receive standard-of-care radiation therapy

Previous work has identified that compared to Caucasian women with breast cancer, African-American women are 48% more likely to have RT omission during treatment [18], 167% less likely to receive timely completion of RT after breast-conserving surgery [19], 40% less likely to complete RT [20], and significantly more likely to experience RT treatment delays [21]. Furthermore, African-American patients with Stage I breast cancer are significantly less likely to receive post-lumpectomy RT [22], and are more likely to be adversely impacted by increased distance from a cancer center with

regard to RT use [18], possibly related to a significantly increased likelihood of reliance on public transportation [20].

Shorter course radiation therapy may reduce disparities in radiation therapy care facing African-American breast cancer patients

With equivalent outcome and side-effect profiles between hypofractionated and standard fractionation breast cancer RT regimens firmly established by Level I evidence [15, 23], the 30–40% reduction in overall treatment time provided by hypofractionation reduces acute toxicities such as pain and fatigue and increases RT completion rates by 42-fold compared to standard fractionation [24, 25]. The impact of hypofractionation on alleviating the monetary burden of cancer care for African-American patients cannot be overstated, particularly given the present landscape where income disparity in the United States (the top 0.1% of incomes equaling the bottom 90%) even before the COVID19 pandemic was approaching a rate not seen since prior to the Great Depression [26]. As of 2017, median Caucasian household income is 86 times more than that of African-Americans and projected to increase to 99 times by 2024 [27] — these projections were before the COVID19 pandemic, which has only exacerbated underlying racial disparities. Furthermore, prospective analysis has demonstrated African-Americans receive hypofractionation following breast-conserving surgery less frequently than Caucasians [28]. It is therefore not surprising that African-Americans suffer disproportionate financial toxicity following RT compared to Caucasian patients [29, 30].

While moderate hypofractionation over 3–4 weeks has steadily increased in the United States by approximately 5% per year since 2004 [24], recent Level I evidence provided by the FAST-Forward trial has established the noninferiority of an even more extremely hypofractionated regimen. That trial compared 1 week versus 3 weeks of hypofractionation in treating early-stage breast cancer at five years post-treatment as measured by ipsilateral breast tumor recurrence rate [31]. Additionally, the one-week regimen of 26 Gy in 5 fractions demonstrated non-inferiority of local control compared to a three-week regimen (40 Gy in 15 fractions) while providing a comparably low risk of normal tissue effects/breast shrinkage compared to the 40 Gy regimen [31].

These findings offer a tremendous opportunity to potentially further decrease the duration of radiation therapy in this patient population [32] and, consequently, further reduce financial toxicity and increase treatment completion rates without compromising tumor control or normal tissue effects; this has been noted in the recently published European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations [33]. Given documented race-related differences in pain following breast radiation therapy, reducing toxicity may benefit African-American women more [34]. Although the radiation oncology community remains divided as to whether sufficient evidence exists to support the use of one-week regimens of hypofractionated adjuvant RT for breast cancer after breast-conserving surgery, the abundant evidence to support 3-week moderately hypofractionated regimens has led to consensus guidelines explicitly naming that approach as preferred over conventional fractionation for most patients receiving whole breast irradiation [35].

Innovation

We are implementing a patient navigator model in a novel manner to increase access to hypofractionated RT, termed the Navigator-Assisted Hypofractionation (NAVAH) program. NAVAH is highly innovative in that it is the first to use: 1) patient navigation to increase hypofractionation, 2) targeted recruitment of the African-American breast cancer community for hypofractionation, 3) objective assessment of financial toxicity experienced by African-Americans receiving conventional versus hypofractionated RT.

A culturally sensitive survey developed in cooperation with the Walking Forward program [36] will provide documentation of barriers (both real and perceived) of African-American breast cancer patients to patient navigation and results will be objectively quantified. Subsequently, the impact of patient navigation on RT access will be collated and analyzed from survey results pre-RT versus post-RT as well as for patients with versus without receipt of patient navigation. Finally, the validated COST-Functional Assessment of Chronic Illness

Therapy score will be distributed to patients following completion of RT [37] to compare financial toxicity after hypofractionation versus standard fractionated RT financial toxicity for patients with early-stage breast cancer who have received lumpectomy.

These findings from NAVAH will provide important insights into objectively quantified barriers faced by African-American breast cancer patients in receiving RT, the impact of patient navigation on these barriers, and the financial toxicity of standard versus hypofractionated RT. The natural progression of this work will be to expand this model to include additional breast cancer populations most vulnerable to suffering RT access disparities within the United States (Native American, Hispanic American, Appalachian) previously described [38–40], and eventually other common malignancies, such as prostate cancer, another common cancer where evidence to support hypofractionated regimens has been accumulating and disparities in outcomes remain substantial. Further progression will involve formal clinical trial investigation towards actively addressing barriers in receipt of RT.

Conflicts of Interest: Dr. McClelland has received travel funding from GT Medical Technologies, Inc. Dr. Harris has received an honorarium from Physician Education Resource as a speaker for the School of Breast Oncology. Dr. Spratt receives research funding from the National Institutes of Health and the Prostate Cancer Foundation and personal fees from AstraZeneca, Bayer, Blue Earth, Boston Scientific, GT Medical Technologies Inc., Janssen, Novartis, and Varian. Dr. Jagsi has stock options as compensation for her advisory board role in Equity Quotient, a company that evaluates culture in health care companies; she has received personal fees from the National Institutes of Health as a special government employee (in her role as a member of the Advisory Committee for Research on Women's Health), the Greenwall Foundation, and the Doris Duke Charitable Foundation. She has received grants for unrelated work from the National Institutes of Health, the Doris Duke Foundation, the Greenwall Foundation, the Komen Foundation, and Blue Cross Blue Shield of Michigan for the Michigan Radiation Oncology Quality Consortium. She had a contract to conduct an investigator initiated study with Genentech. She has served as an expert witness for Sherinian and Hasso, Dressman Benzinger LaVelle, and Kleinbard LLC. Dr. Petereit is the president emeritus of the American Brachytherapy Society and receives research funding from Bristol Meyers Squibb Foundation, Polo Ralph Lauren, the Irving A Hansen Memorial Foundation, and the National Institutes of Health. No other author has any conflicts of interest.

Source of Financial Support/Funding Statement: The NAVAH program is sponsored by the University Hospitals Cleveland Medical Center Department of Radiation Oncology.

Conflict of interest

None declared.

Funding

None declared.

Acknowledgments

None declared.

Author contributions

Conception and design: McClelland, Jagsi, Petereit; manuscript writing: McClelland.
Study coordination: McClelland, Harris, Spratt, Cheatham, Petereit; final approval of manuscript: all authors.

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