

Controversies on cosmetic outcomes in black women after breast conservation therapy: hyperperception or hyperpigmentation?

Sophia M Edwards-Bennett¹
Carol L Brown²

¹Department of Radiation Oncology, Moffitt Cancer Center, Tampa, FL; ²Department of Gynecologic Oncology and Surgery, Memorial Sloan Kettering Cancer Center, NY, USA

Abstract: Multiple studies have reported inferior cosmetic outcomes after breast conservation surgery and adjuvant radiation therapy in black women. However, cosmetic analysis scales contemporarily utilized in the field of radiation oncology rely largely on subjective visual and tactile perception. These methods are undeniably fraught with intraobserver and interobserver variability. Herein, we uncover how and why these methods may unwittingly and disparately misjudge cosmetic outcomes in black women, and the clinical ramifications thereof. In addition, we highlight more objective cosmetic outcomes assessment programs that promise to yield more reproducible and unbiased results.

Keywords: cosmetic outcomes, black women, breast conservation

Introduction

Breast conservation therapy, a treatment algorithm comprised of breast conservation surgery and radiation, has been established as standard of care for early-stage breast cancer, because it yields survival outcomes equivalent to mastectomy.^{1,2} The former approach affords breast preservation which is cosmetically appealing to women. In the realm of breast conservation, there has been increasing focus on breast cosmesis over the past two decades. As such, there has been a plethora of studies published on cosmetic outcomes following breast conservation therapy. However, very few studies have reported on the cosmetic outcomes in African American women after breast conservation therapy. Those that have, consistently report inferior outcomes in black women.

Tuamokumo et al reported their results of a matched-pairs analysis of 20 white and 20 black women with early-stage breast cancer who underwent breast conservation therapy.³ In this small study, the authors concluded that black women had worse cosmetic outcomes than white women. Deutsch and Flickinger⁴ and Taylor et al⁵ also reported significantly better cosmetic outcomes among white women than in black women. A more recent study by Vicini et al also reported that black women experienced less favorable cosmetic outcomes than white women after breast conservation therapy.⁶

In the aforementioned studies, conventional standard fractionation (using 22–25 fractions of 200 cGy each) was employed. If the consensus is that black women reap inferior cosmetic benefits after breast conservation followed by standard fractionated radiation, radiobiological principles indicate that unconventional hypofractionated regimens using larger doses per fraction should yield worse cosmetic outcomes.⁷ On this premise, Canadian fractionation⁸ and accelerated partial breast irradiation,⁹ which prescribe larger doses per fraction (16 fractions of 265 cGy and 10 fractions of 385 cGy, respectively), would result in worse cosmesis in black women. Radiation oncologists

Correspondence: Sophia Edwards-Bennett
Department of Radiation Oncology,
Moffitt Cancer Center, 12902 Magnolia
Drive, Tampa, FL 33612, USA
Tel +1 813 745 1075
Fax +1 813 745 7231
Email sophia.edwardsbennett@moffitt.org

may therefore be reluctant to offer these options to black women. Such a de facto practice could have far reaching consequences.

Multiple studies have shown that underuse of and noncompliance with adjuvant radiation is a grave problem in black women, contributing to inferior treatment outcomes in this patient population.^{10–12} Some have cited the commitment to a 5–6-week course of radiation as one of the reasons for underutilization of radiation therapy.^{12,13} Therefore, the option of a shortened course of radiation, such as Canadian fractionation (given over three weeks) or partial breast irradiation therapy (delivered over five days), when clinically appropriate, may be pivotal to improving underutilization of and noncompliance with adjuvant breast radiation in black women.

In the research to date, as in the majority of breast conservation therapy studies, cosmetic outcomes and skin toxicities were largely determined by subjective methods. The Harvard National Surgical Adjuvant Breast and Bowel Project/Radiation Therapy Oncology Group breast cosmesis grading scale is widely used in the assessment of cosmesis after breast conservation therapy.¹⁴ This instrument incorporates symmetry between breasts, skin pigmentation changes, scar appearance, and fibrosis. The extent of each feature is determined, and a cosmetic grade is assigned (Grade I excellent, Grade II good, Grade III fair, Grade IV poor). According to this scale, obvious skin color changes are assigned Grade IV. This method is entirely subjective because it relies on the evaluator to determine the severity of each cosmetic parameter by visualization only. In addition, the evaluator may be different between patients and between consecutive assessments of the same patient. This introduces considerable interobserver, interpatient, and inpatient variability, rendering the current visual methods poorly reproducible.

Hyperperception or hyperpigmentation?

As mentioned, pigmentation change is one of the parameters used to measure cosmetic outcomes after breast conservation therapy in the Harvard National Surgical Adjuvant Breast/Bowel Project and Radiation Therapy Oncology Group cosmetic analysis tool.¹⁴ Skin pigmentation is mainly determined by two skin chromophores, ie, melanin and hemoglobin (oxygenated and deoxygenated).¹⁵ Melanin, produced by melanocytes, is present in the basal layer of the epidermis. Hemoglobin is transported by blood vessels, which are abundant in the dermis. The number of melanocytes is not different between patients. However, darker-skinned indi-

viduals produce more melanin at baseline. Thus, in darker skin, the melanin pigment in the epidermis dominates, while in lighter skin, the pinkish color is a reflection of blood in the dermis.¹⁵

Oxyhemoglobin and deoxyhemoglobin absorb in the visible wavelength range of 520–610 nm and the near-infrared wavelength range of 740–820 nm. Erythema is visualized as the sum of increased light absorption in the green (520–580 nm) and decreased light absorption in the red (600–700 nm) part of the spectrum. Melanin also absorbs strongly in the visible spectrum, and pigmentation is perceived as the increasing slope toward shorter wavelengths in the 620–700 nm region.¹⁶

Because of this overlap in absorption spectra, a distinct contribution from each chromophore is difficult to distinguish with the naked eye. For example, Matas et al found that erythema was not accurately perceived by visual techniques in dark-skinned individuals, leading to incorrect determination of the blanch response used in the early detection and diagnosis of pressure ulcers.¹⁷ Also, recent studies have shown that visual perception of erythema and pigmentation does not correlate with more quantitative measures.¹⁸

Because the visual perception of skin color is the cumulative result of contributions of all three optically active species, it should be possible to determine quantitatively the relative contributions of each chromophore, to quantify change in chromophore directly induced by radiation, and to determine the differences in radiation-induced change in pigmentation as a function of skin color.

One heavily explored method is analysis of the remittance spectra of skin tissue utilizing diffuse reflectance spectroscopy.¹⁹ With this technique, apparent concentrations of melanin, oxyhemoglobin, and deoxyhemoglobin can be extracted from absorption spectra, thus separating changes in erythema and pigmentation, and dissecting out the relative chromophoric contributors to each skin reaction.

Although the field of dermatology has utilized these objective skin color measures for decades, radiation oncology has been slower to adopt such techniques. Currently, the existing cosmetic assessment tools depend solely on visual cues to determine changes in skin pigmentation during radiation. With such a model, there may be a hyperbolic perception of pigmentation in darker-skinned women.

Objective methods for skin and cosmetic analysis

The last few years have heralded the advent of novel objective methods to measure skin pigmentation and cosmesis.

For example, skin analysis software developed by Konica Minolta for quantitative evaluation and analysis of skin color and pigmentation allows accurate measurements by separately calculating the melanin index, hemoglobin index, and hemoglobin oxygen saturation index.²⁰ This instrument uses diffuse spectroscopic reflectance as described earlier. One could envisage this program being used to assess changes in radiation-induced skin pigmentation objectively. A more comprehensive program, BCCT (Breast Cancer Conservative Treatment) core program described by Carduso et al incorporates several parameters related to asymmetry, color differences, and scar appearance, to quantify cosmetic outcomes according to changes in pigmentation and breast symmetry.²¹ It is clear that these methods will be able to determine cosmetic outcomes after breast conservation therapy more objectively, concretely, and accurately.

As mentioned in the introduction to this commentary, there may be more than cosmesis at stake. Rather than propagating inferences based on subjective methods, it may be constructive to embrace more objective methods to better assess cosmetic outcomes, inform our clinical practice, and “diversify” our treatment recommendations.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*. 2002;347:1233–1241.
2. Van Dongen JA, Voogd AC, Fentman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst*. 2000;92:1143–1150.
3. Tuamokumo NL, Haffty BG. Clinical outcome and cosmesis in African-American patients treated with conservative surgery and radiation therapy. *Cancer J*. 2003;9:313–320.
4. Deutsch M, Flickinger JC. Patient characteristics and treatment factors affecting cosmesis following lumpectomy and breast irradiation. *Am J Clin Oncol*. 2003;26:350–353.
5. Taylor ME, Perez CA, Halverson KJ, et al. Factors influencing cosmetic results after conservation therapy for breast cancer. *Int J Radiat Oncol Biol Phys*. 1995;31:753–764.
6. Vicini F, Jones P, Rivers A, et al. Differences in disease presentation, management techniques, treatment outcome, and toxicities in African-American women with early stage breast cancer treated with breast-conserving therapy. *Cancer*. 2010;116:3485–3492.
7. Peters IJ, Withers HR. Applying radiobiological principles to combined modality treatment of head and neck cancer – the time factor. *Int J Radiat Oncol Biol Phys*. 1997;39:831–836.
8. Whelan TJ, Pignol JP, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med*. 2010;362:513–520.
9. Vicini FA, Chen P, Wallace M, et al. Interim cosmetic results and toxicity using 3D conformal external beam radiotherapy to deliver accelerated partial breast irradiation in patients with early-stage breast cancer treated with breast-conserving therapy. *Int J Radiat Oncol Biol Phys*. 2007;15:1124–1130.
10. Du XL, Gor BL. Racial disparities and trends in radiation therapy after breast-conserving surgery for early stage breast cancer in women, 1992 to 2002. *Ethn Dis*. 2007;17:122–128.
11. Hershman DL, Unger JM, Barlow WE, et al. Treatment quality and outcomes of African Americans versus white breast cancer patients: Retrospective analysis of Southwest Oncology Studies S8814/S8897. *J Clin Oncol*. 2009;27:2157–2162.
12. Bickell NA, Wang JJ, Wang SO. Missed opportunities: Racial disparities in adjuvant in adjuvant breast cancer treatment. *J Clin Oncol*. 2006; 24:1357–1362.
13. Bickell NA, Weidmann J. Underuse of breast cancer adjuvant treatment: Patient knowledge, beliefs and mistrust. *J Clin Oncol*. 2009;27: 5160–5167.
14. National Surgical Adjuvant Breast and Bowel Project protocol B-39 (Radiation Therapy Oncology Group protocol 0413): A randomized Phase III study of conventional whole breast irradiation (WBI) versus partial breast irradiation (PBI) for women with stage 0, I, or II breast cancer. Available at: <http://www.rtog.org/members/protocols/0413/0413.pdf>. Accessed on February 11, 2011.
15. Parrish JA, Jaenicke KF, Anderson RR. Erythema and melanogenesis action spectra of normal human skin. *Photochem Photobiol*. 1982;36: 187–191.
16. Feather JW, Elli DJ, Leslie G. A portable reflectometer for the rapid quantification of cutaneous hemoglobin and melanin. *Phys Med Biol*. 1988;33:711–722.
17. Matas A, Sowa MG, Taylor V, et al. Eliminating the issue of skin color in assessment of the blanch response. *Adv Skin Wound Care*. 2001;14: 180–188.
18. Takiwaki H, Miyaoka Y, Skrebova K, et al. Skin reflectance-spectra and color-value dependence in ordinary reflectance spectrophotometer and tristimulus colourimetry. *Skin Res Technol*. 2002;8:78–83.
19. Zonios G, Bykowski J, Kollias N. Skin melanin, hemoglobin, and light scattering properties can be quantitatively assessed *in vivo* using diffuse reflectance spectroscopy. *J Invest Dermatol*. 2001;117:1452–1457.
20. Daniel LC, Heckman CJ, Kloss JD, et al. Comparing alternative methods of measuring skin color and damage. *Cancer Causes Control*. 2009; 20:313–321.
21. Cardoso MJ, Cardoso J, Amaral N, et al. Turning subjective into objective: The BCCT core software for evaluation of cosmetic results in breast cancer conservative treatment. *Breast*. 2007;16:456–461.

Clinical, Cosmetic and Investigational Dermatology

Publish your work in this journal

Clinical, Cosmetic and Investigational Dermatology is an international, peer-reviewed, open access, online journal that focuses on the latest clinical and experimental research in all aspects of skin disease and cosmetic interventions. All areas of dermatology will be covered; contributions will be welcomed from all clinicians and

Submit your manuscript here: <http://www.dovepress.com/clinical-cosmetic-and-investigational-dermatology-journal>

basic science researchers globally. This journal is indexed on CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.