Validating a Novel Device to Improve Skin Color Matching for Face Transplants

Jordan Gornitsky, MD
Eli Saleh, MD, MSc
Gabriel Bouhadana, MD
Daniel E. Borsuk, MD, MBA

Introduction: Facial vascularized composite allotransplantation (VCA) offers an added layer of complexity when compared to solid organ transplantation. VCAs must account for aesthetic variables such as skin tone and color. The goal of this study is to validate the Nix Color Sensor as a novel tool to be added to the plastic surgeon’s armamentarium for evaluating skin color match of the donor and recipient.

Methods: A prospective study of 100 individuals was conducted. All participants were photographed and scanned with the Nix Color Sensor. Sixty pairwise comparisons were randomly generated. Skin color analysis was performed using photographs and the Nix Color Sensor. Delta E2000 values were compared to mean evaluator ratings using a Spearman correlation analysis.

Results: One hundred patients were included. A Spearman’s correlation demonstrated a strong inverse correlation between Delta E2000 values and the mean evaluator ratings. The higher the mean evaluator rating for likeness, the lower the delta. A correlation coefficient of −0.850 demonstrates a statistically significant relationship (P < 0.01).

Conclusions: When the Delta E2000 rises above 5 there is a significant drop in the mean evaluator ratings. As mean evaluator ratings of 5 and above would be considered adequate for face transplant amongst most plastic surgeons, an E2000 value of 5 or lower should be targeted when matching donors with recipients for face transplant. The Nix Color Sensor positively correlates to the plastic surgeon’s perception of skin color and can serve as an adjunct in donor selection for facial VCAs.

(Plast Reconstr Surg Glob Open 2022;10:e4649; doi: 10.1097/GOX.0000000000004649; Published online 18 November 2022.)

INTRODUCTION

Vascularized composite allotransplantation (VCA) is the transplantation of vascularized composite allografts, a single functional unit consisting of multiple tissue types (skin, fat, muscle, bone, nerve, vessels). Since the first successful face transplantation in 2005, the field of VCA transplantation has expanded worldwide.1–3 Although similar to solid organ transplantation in that donor and recipient must be compatible for ABO blood types, VCAs have an added layer of complexity by also needing to account for aesthetic variables. Factors such as age, gender, ethnicity, bone structure, and tone and color must all be considered to ensure cosmetic success. Although most donor/recipient variables can be matched using quantitative methods such as blood tests and CT scans, others remain subjective. Currently, there are no universal protocols or guidelines for skin color matching in the context of VCAs. Photographs of the donor and recipient, combined with cardboard paint color palettes, are the gold standard for attempting to match skin tone and color for skin-containing VCAs. Initial assessment is carried out by the organ procurement organization, followed by an in-person and photographic assessment by the treating surgeon.4

The Nix Color Sensor (Nix Sensor Ltd., Hamilton, Canada) is a compact portable scanner capable of accurately scanning a multitude of objects, textures, and surfaces. It has an associated mobile application allowing for easy quantitative color analysis. It has been used in both the medical and cosmetic fields for color analysis, and is relatively affordable.3

Although a multitude of studies have reported on optimizing VCAs, none have focused on quantitative analysis of skin color matching between donors and recipients. In addition, skin color matching has been found to be
suboptimal in VCAs that have been carried out to date, indicating a clinical necessity for an improvement in this domain. In fact, the degree of skin tone matching for the face has been shown to be highly subjective, and significantly different between laypeople and plastic surgeons. Therefore, the goal of this study is to validate the Nix Color Sensor as a novel tool to be added to the plastic surgeon’s armamentarium in skin-containing VCA planning. The authors hope this new device can be used as an adjunct to help reduce the degree of skin color mismatch in VCAs.

MATERIALS AND METHODS

Ethics approval of this prospective cohort study was granted by the institutional review board at Maisonneuve-Rosemont Hospital. The authors recruited 100 individuals at random from an outpatient plastic surgery clinic waiting room over two consecutive days. Participants were selected regardless of age, gender or ethnicity. Exclusion criteria consisted of presence of craniofacial deformities, facial scarring (surgical or traumatic), makeup, and those refusing both facial skin color scanning and photographs.

Written consent was obtained from the included individuals (n = 100). Demographic information such as age, gender, and ethnicity was documented (Table 1). Participant photographs were taken in a standardized fashion in a controlled environment. Lighting, distance, and type of camera used remained constant. Skin color was scanned using the Nix Color Sensor (Nix Sensor Ltd.) on the anterolateral right cheek. This anatomic region was selected as it is typically included in a Le Fort osteotomy (or type 2, type 3) pattern for facial VCA. The Nix Flat Adapter was utilized to create a uniformed surface to provide a more accurate scan.

To make the comparisons clinically relevant, participants were assigned a Fitzpatrick skin type (I–VI) by two independent observers, and further categorized into three subgroups: group 1 (Fitzpatrick I–II), group 2 (Fitzpatrick III–IV), and group 3 (Fitzpatrick V–VI) (Table 1). This grouping allowed for pairwise comparisons that would be more clinically relevant by comparing patients that would, at the first glance, potentially be considered a suitable match. Sixty pairwise comparisons, matched by gender, were then randomly generated. Ten comparisons were performed within groups 1, 2, and 3, respectively. Ten intergroup comparisons were also performed between groups 1 and 2, groups 1 and 3, and groups 2 and 3, respectively.

Skin color analysis was performed in two phases. First, an online questionnaire was created, consisting of the 60 pairs of de-identified photographs. The questionnaire was distributed to plastic surgery residents and attending surgeons. Evaluators were instructed to rate the skin color similarity between each pair using a 10-point Likert scale (1 = not at all similar, 10 = identical). In addition, color analysis was performed objectively using the Nix Color Sensor mobile application. The application compares the Delta E2000 as defined by the International Commission on Illumination (CIE), which allows for the algorithmic measure of change in the visual perception of two given colors. The smaller the Delta E2000 value, the more alike the two color tones.

Following data extraction, descriptive statistics were performed. Delta E2000 values were then compared to mean evaluator ratings using a Spearman correlation analysis. The Spearman’s rank-order correlation calculates a coefficient which is a measure of the strength and direction of the relationship between two continuous or ordinal variables. All statistical tests were carried out using SPSS v.25 (IBM Corp, Armonk, N.Y.), with statistical significance set at a P value less than < 0.05.

RESULTS

A total of 100 patients were included with a mean age of 38.3 years and a female:male ratio of 1.3:1 (Table 1). Sixty pairwise comparisons, matched by gender, were randomly generated. Ten comparisons were performed within groups 1, 2, and 3, respectively. Ten intergroup comparisons were also performed between groups 1 and 2, groups 1 and 3, and groups 2 and 3, respectively (Figs. 1 and 2). In the study, Delta E2000 values ranged from 1.1 to 22.2, with a mean of 8.6 and a standard deviation of 5.8. The mean evaluator ratings across all groups was 4.5 with a standard deviation of 2.2 (Table 2).

Spearman’s rank-order correlation was run to assess the relationship between the E2000 values and the mean evaluator ratings. The analysis showed the relationship to be monotonic as assessed by visual inspection of a

Table 1. Patient Demographics and Breakdown of Fitzpatrick Groupings

|       | No. Patients | Mean Age | 1     | 2     | 3     |
|-------|--------------|----------|-------|-------|-------|
| Male  | 43           | 35.5     | 60.5  | 28.9  | 10.5  |
| Female| 57           | 40.6     | 68.4  | 24.6  | 7.0   |

Fitzpatrick types I–II, III–IV, and V–VI corresponded to groups 1, 2, and 3, respectively.
scatterplot. Based on the 60 pairwise comparisons, the analysis showed evidence of a strong inverse correlation between E2000 values and the mean evaluator ratings. As expected, the higher the mean evaluator rating for likeness, the lower the delta. A correlation coefficient of $-0.850$ demonstrates this statistically significant relationship ($P < 0.01$) (Table 3).

On closer analysis of the scatter plot (Fig. 3), when the Delta E2000 rises above 5, there is a significant drop in the mean evaluator ratings. As mean evaluator ratings of 5 and above would be considered adequate for face transplant amongst most plastic surgeons, similar to the color match acceptability threshold of greater than 50$\%$, a Delta E2000 value of 5 or lower should be aimed for when identifying donors and recipients for face transplant.

**DISCUSSION**

Although still in its relative infancy, the field of vascularized composite allotransplantation has expanded exponentially over the past decade. Increased experience as well as technologic advancements in virtual surgical planning have aided in the feasibility and refinement of the technique. As the indications for facial VCA continue to evolve, it is likely this will be considered as a viable primary reconstructive option. This possibility places
Significance

Table 3. Spearman’s Correlation Coefficient and 2-tailed considerations that must be accounted for. 12,14 Despite further layer of complexity due to the numerous aesthetic immunologic criteria required, facial VCAs offer an ever, that given the restricted donor pool and the many recipient skin match in VCA. It is important to note, however, that given the restricted donor pool and the many other critical factors associated with skin-containing VCAs, a less-than-perfect skin color match may be deemed acceptable. Nonetheless, having a practical, evidence-based and objective tool to aid surgeons in this endeavor may facilitate the overall process and contribute to a more patient-centered approach. The impact of color mismatch from other surgical procedures in the face may be a useful correlate into the importance of such among VCA recipients. For example, a few studies in the literature have looked into color mismatch following free flaps on the face, given this region’s sensitive nature in day-to-day interactions for our patients. 24,29,30 Patient satisfaction seems to increase following refinement procedures for color mismatch on the face, either through overgrafting with skin grafts from the scalp or cosmetic tattooing, indicating the importance of trying to avoid such a mismatch in any type of facial surgery. 24,30,31

The Nix Color Sensor mobile application allows for direct comparison of scanned skin color from two individuals and computes a Delta E2000. The Delta E2000 is currently the most sophisticated algorithm used to analyze the difference between two colors by taking into account factors such as lightness, chroma, and hue. 29 Values range from 1 to 100, with a Delta of 1 equivalent to a “just noticeable difference.” 29,30 In the current study, E2000 values ranged from 1.1 to 22.2, with a mean of 8.6. When selecting donors for face transplant, we are more likely to prioritize patients within similar Fitzpatrick groupings. As can be expected, Delta E2000 values were lower when comparing skin color of individuals within the same Fitzpatrick groupings, and higher for those from different groupings. To validate this device, it was compared to the current gold standard of skin color matching, photograph comparisons as judged by trained plastic surgeons and residents. Mean evaluator ratings were 4.4 of a maximum of 10 across all sixty photograph comparisons, with a range of 1–8.1. Mean evaluator ratings were higher for individuals within the same Fitzpatrick groupings, and dropped significantly when compared across different groupings. Intergroup comparisons, groups 1 and 3 and 2 and 3, demonstrated a greater than three-fold Delta value as compared to intragroup comparisons. However, the intergroup comparison of groups 1 and 2 more closely resembled that of the intragroup ones. The lower mean Delta value of the intergroup comparisons of groups 1 and 2 (Delta E2000 = 6.3) could be due to the randomly sampled individuals corresponding to the upper extreme of group 1, and lower extreme of group 2. This is also reflected in the mean evaluator score (5.5), which also more closely resembled the intragroup comparison values.

When plotting mean evaluator ratings versus mean Delta E2000 values, an inverse relationship was observed such that higher mean evaluator scores corresponded to lower Delta E2000 values. Spearman’s correlation coefficient of -0.850 represented a statistically significant correlation between both sets of values. When attempting to identify suitable matches for facial VCA, mean evaluator ratings greater than 5 would generally be considered adequate with regards to skin color likeness. A similar value was utilized in the study by Hoffman et al in which a color match acceptability threshold of 50% was considered.

Table 2. Group Statistics Showing Means Delta E2000 and Evaluator Ratings

|               | DeltaE2000(+/- SD) | Mean Evaluator Ratings(+/- SD) |
|---------------|-------------------|-------------------------------|
| Group 1       | 6.0 (2.4)         | 5.9 (1.8)                     |
| Group 2       | 5.1 (1.9)         | 5.5 (1.3)                     |
| Group 3       | 3.0 (1.3)         | 5.8 (1.3)                     |
| Groups 1 and 2| 6.3 (3.9)         | 5.5 (1.5)                     |
| Groups 1 and 3| 16.0 (3.9)        | 1.6 (0.4)                     |
| Groups 2 and 3| 15.0 (5.6)        | 2.5 (0.6)                     |
| All groups    | 8.6 (5.8)         | 4.4 (2.2)                     |

Delta E2000 values range from 0 to 100 (the lower the value the closer the color match). Mean evaluator ratings are scaled from 1 to 10, the higher the value the closer the color match.

Table 3. Spearman’s Correlation Coefficient and 2-tailed Significance

| Spearman’s Test | Correlation Coefficient | Sig (2-tailed) |
|-----------------|-------------------------|---------------|
|                 | -0.850                  | <0.001        |

Further emphasis on the added complexity of donor and recipient matching, as well as the current shortage of organ donors. 2,18,20 Recent studies have estimated that only 10% of the worldwide organ donation needs are met annually. 2,19–21 Considering that only a fraction of organ donors agree to donate their tissue as part of VCAs, this shortage is further emphasized. 21 In addition to the rigorous immunologic criteria required, facial VCAs offer an added layer of complexity due to the numerous aesthetic considerations that must be accounted for. 21,22 Despite further restricting the potential donor pool, avoiding skin color mismatch is an integral component of a successful VCA, especially for partial face transplants (FTs), allowing patients to seamlessly reintegrate into society. This was clearly demonstrated by the recent FT performed by the team at Brigham and Women’s, where a full rather than partial FT was performed due to concerns for skin color mismatching in the literature, Park et al have suggested that color matching in partial FTs carried out to date have not been any formal reports of complete skin color mismatching in the literature, Park et al have suggested that color matching in partial FTs carried out to date have been suboptimal from the perspective of both the general public and healthcare professionals.

Much of the previously developed electronic instruments used to quantify skin color have been critiqued for being inaccessible and impractical. 22,23,24 For example, the group at NYU has thus studied and then resorted to the use of a handheld color palette. 1 It comes to no surprise, however, that given the rapidly evolving technological landscape, a device such as the Nix Color Sensor has been developed. Its relatively cheap cost, small shape, and ease of accessibility may preclude the previous limitations attributed to such devices. It may, therefore, expedite and better objectify the process of evaluating potential donor-recipient skin match in VCA. It is important to note, however, that given the restricted donor pool and the many other critical factors associated with skin-containing VCAs,
acceptable for skin tone swatches using the Pantone SkinTone Guide. As observed on the scatter plot (Fig. 1), when mean evaluator scores dropped below 5, a significant rise in Delta E2000 values occurred. In fact, Delta E2000 values greater than or equal to 5 corresponded to observer scores below 5. It can therefore be extrapolated that individuals with Delta E2000 values less than 5 would generally be considered suitable matches for facial VCA based on skin color alone.

This study is not without its limitations. Despite attempting to standardize and control for all variables when photographing the participants, differing facial morphology can result in uncontrollable shadowing, which in turn can alter the perceived skin color, impacting the evaluator score. Although assigning Fitzpatrick skin type has some inherent subjectivity, and skin color represents a range rather than six concrete colors, the overall trends and relationships between observer evaluation and Nix Color Sensor values remain unaffected. This seems to be a more objective method than what has been previously described in the literature, where ethnicity has been used as a correlate for skin color. The major limitation in studying VCA is its relatively small sample size. This makes studying the impact of a mismatch and the potential to avoid it a difficult task, due to the lack of procedures performed and of available donors. It is worthy to note that, although there has not been any formal assessment of skin changes in VCA posttransplantation, a lack of stability in skin color and pigmentary changes might affect the applicability of our study. Skin color changes have, however, been of concern in the context of acute graft rejection and have been of interest in the literature. It would be interesting to study the applicability of the Nix Color Sensor for detecting such skin reactions and its correlation with the biopsy gold standard. To take this one step further, future studies should look into the true impact of VCA color mismatch on patient satisfaction, namely into any potential limitations it may pose regarding integration of their ADLs.

**CONCLUSIONS**

In the attempt to improve VCA outcomes, new technologies have been instrumental in our ability to plan osteotomies, match immunity and blood, and monitor outcomes. The ability to objectively analyze skin color, in an easily reproduced way, will help to further advance the field of VCA. To date, no other studies have attempted to determine what constitutes an ideal skin color match in the setting of VCA, and therefore, no objective measurements exist in clinical practice. Although not expected to replace the plastic surgeon’s judgement, experience or keen critical eye, this study demonstrates the reliability of the Nix Color Sensor when applied to skin color. It positively correlates to the plastic surgeon's perception of skin color and can serve as an adjunct in donor selection for VCA. The authors suggest that suitable skin color matches can be expected for individuals with a Delta E2000 less than 5.

Daniel E. Borsuk, MD, MBA
Division of Plastic and Reconstructive Surgery
Université de Montréal, CHU Sainte-Justine
3175 Chemin de la Côte-Sainte-Catherine, Montreal
QB H3T 1C4, Canada
E-mail: dborsuk@gmail.com

**PATIENT CONSENT**

Patients provided written consent for the use of their images.

**REFERENCES**

1. Dubernard JM, Lengelé B, Morelon E, et al. Outcomes 18 months after the first human partial face transplantation. *N Engl J Med.* 2007;357:2451–2460.

2. Siemionow M. The decade of face transplant outcomes. *J Mater Sci Mater Med.* 2017;28:64.
3. Mendenhall SD, Ginnetti MT, Sawyer JD, et al. Prevalence and distribution of potential vascularized composite allograft donors, implications for optimizing the donor-recipient match. Plast Reconstr Surg Glob Open. 2018;6:e1833.

4. Hoffman AF, Park JJ, Berman ZP, et al. Establishing a clinically applicable methodology for skin color matching in vascularized composite allograft transplantation. Plast Reconstr Surg Glob Open. 2020;8:e2655.

5. Nix Color Sensor. 2002. Available at https://www.nixsensor.com/industry-medical-and-lifesciences/. Accessed February 5, 2022.

6. Park JJ, Diep GK, Alfonso AR, et al. Have we achieved optimal skin color matching in partial facial transplantation? A survey study of the general public and medical professionals. J Craniofac Surg. 2020;31:2213–2216.

7. Yesancharao PS, Lopez J, Reategui A, et al. Combined symphyseal and condylar fractures: considerations for treatment in growing pediatric patients. Plast Reconstr Surg. 2021;148:51e–62e.

8. Mohan R, Borsuk DE, Dorafshar AH, et al. Aesthetic and functional facial transplantation: a classification system and treatment algorithm. Plast Reconstr Surg. 2014;133:386–397.

9. Sharma G, Wu W, Dalal EN. The CIEDE2000 color-difference formula: implementation notes, supplementary test data, and mathematical observations. Color Res Appl. 2005;30:21–30.

10. Luo M, Cui G, Rigg B. The development of the CIE 2000 colour difference formula: CIEDE2000. Color Res Appl. 2001;26:340–350.

11. Ramly EP, Kantar RS, Díaz-Siso JR, et al. Computerized approach to facial transplantation: evolution and application in 5 consecutive face transplants. Plast Reconstr Surg Glob Open. 2019;7:e2379.

12. Kantar RS, Alfonso AR, Diep GK, et al. Facial transplantation: principles and evolving concepts. Plast Reconstr Surg. 2021;147:1022e–1038e.

13. Kantar RS, Plana NM, Díaz-Siso JR, et al. Facial transplantation for an irreparable central and lower face injury: a modernized approach to a classic challenge. Plast Reconstr Surg. 2019;144:256e–283e.

14. Rifkin WJ, David JA, Plana NM, et al. Achievements and challenges in facial transplantation. Ann Surg. 2018;268:260–270.

15. Cammarata MJ, Wake N, Kantar RS, et al. Three-dimensional analysis of donor masks for facial transplantation. Plast Reconstr Surg. 2019;143:1290e–1297e.

16. Brown EN, Dorafshar AH, Bojovic B, et al. Total face, double jaw, and tongue transplant simulation: a cadaveric study using computer-assisted techniques. Plast Reconstr Surg. 2012;130:815–823.

17. Maciejewski A, Krakowczyk L, Szmyczk C, et al. The first immediate face transplant in the world. Ann Surg. 2016;263:e36–e39.

18. Mills E, Felsenheld JH, Berman ZP, et al. Guiding strategies for the future of vascularized composite allograft transplantation: a systematic review of organ donation campaigns. Plast Reconstr Surg. 2020;146:922–934.

19. Kiwunaka H, Avcart MA, Bueno EM, et al. Patient recruitment and referral patterns in face transplantation: a single center’s experience. Plast Reconstr Surg. 2016;138:224–231.

20. Manyalich M, Nelson H, Delmonico FL. The need and opportunity for donation after circulatory death worldwide. Curr Opin Organ Transplant. 2018;23:136–141.

21. Plana NM, Kimberly LL, Parent B, et al. The public face of transplantation: the potential of education to expand the face donor pool. Plast Reconstr Surg. 2018;141:176–185.

22. Kauke M, Panayi AC, Tchiloemb B, et al. Face transplantation in a black patient - Racial considerations and early outcomes. N Engl J Med. 2021;384:1075–1076.

23. Rodríguez-Lorenzo A, Audolfsen T, Wong C, et al. Vascular perfusion of the facial skin: implications in allotransplantation of facial aesthetic subunits. Plast Reconstr Surg. 2016;138:1073–1079.

24. Lannon DA, Nowak CB, Neligan PC. Resurfacing of colour-mismatched free flaps on the face with split-thickness skin grafts from the scalp. J Plast Reconstr Aesthet Surg. 2009;62:1363–1366.

25. Everett JS, Budescu M, Sommers MS. Making sense of skin color in clinical care. Clin Nurs Res. 2012;21:495–516.

26. Piérard GE. EEMCO guidance for the assessment of skin colour. J Eur Acad Dermatol Venereol. 1998;10:1–11.

27. Roberts WE. Skin type classification systems old and new. Dermatol Clin. 2009;27:529–533, viii.

28. Taylor S, Westerhof W, Im S, et al. Noninvasive techniques for the evaluation of skin color. J Am Acad Dermatol. 2006;54:8282–8290.

29. van Driel AA, Mureau MAM, Goldstein DP, et al. Aesthetic and oncologic outcome after microsurgical reconstruction of complex scalp and forehead defects after malignant tumor resection: an algorithm for treatment. Plast Reconstr Surg. 2010;126:460–470.

30. Barstow MD, Fox CM, Dingley ME, et al. Cosmetic tattooing of free flaps following head and neck reconstruction. Cranio-maxillofac Trauma Reconstr. 2013;6:61–64.

31. Walton RL, Cohn AB, Beahm EK. Epidermal overgrafting improves coloration in remote flaps and grafts applied to the face for reconstruction. Plast Reconstr Surg. 2008;121:1606–1613.

32. Dorante MI, Kollar B, Bittner M, et al. Software-based detection of acute rejection changes in face transplant. J Reconstr Microsurg. 2022;38:420–428.