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Assessment and Treatment Outcomes of Persistent Radiation-Induced Alopecia in Patients With Cancer

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IMPORTANCE Persistent radiation-induced alopecia (pRIA) and its management have not been systematically described.

OBJECTIVE To characterize pRIA in patients with primary central nervous system (CNS) tumors or head and neck sarcoma.

DESIGN, SETTING, AND PARTICIPANTS A retrospective cohort study of patients from January 1, 2011, to January 30, 2019, was conducted at 2 large tertiary care hospitals and comprehensive cancer centers. Seventy-one children and adults diagnosed with primary CNS tumors or head and neck sarcomas were evaluated for pRIA.

MAIN OUTCOMES AND MEASURES The clinical and trichoscopic features, scalp radiation dose-response relationship, and response to topical minoxidil were assessed using standardized clinical photographs of the scalp, trichoscopic images, and radiotherapy treatment plans.

RESULTS Of the 71 patients included (median [range] age, 27 [4-75] years; 51 female [72%]), 64 (90%) had a CNS tumor and 7 (10%) had head and neck sarcoma. Alopecia severity was grade 1 in 40 of 70 patients (56%), with localized (29 of 54 [54%]), diffuse (13 of 54 [24%]), or mixed (12 of 54 [22%]) patterns. The median (range) estimated scalp radiation dose was 39.6 (15.1-50.0) Gy; higher dose (odds ratio [OR], 1.15; 95% CI, 1.04-1.28) and proton irradiation (OR, 5.7; 95% CI, 1.05-30.8) were associated with greater alopecia severity ($P < .001$), and the dose at which 50% of patients were estimated to have severe (grade 2) alopecia was 36.1 Gy (95% CI, 33.7-39.6 Gy). Predominant trichoscopic features included white patches (16 of 28 [57%]); in 15 patients, hair-shaft caliber negatively correlated with scalp dose (correlation coefficient, −0.624; $P = .01$). The association between hair density and scalp radiation dose was not statistically significant (−0.381; $P = .16$). Twenty-eight of 34 patients (82%) responded to topical minoxidil, 5% (median follow-up, 61 [interquartile range, 21-105] weeks); 4 of 25 (16%) topical minoxidil recipients with clinical images improved in severity grade. Two patients responded to hair transplantation and 1 patient responded to plastic surgical reconstruction.

CONCLUSIONS AND RELEVANCE Persistent radiation-induced alopecia among patients with primary CNS tumors or head and neck sarcomas represents a dose-dependent phenomenon that has distinctive clinical and trichoscopic features. The findings of this study suggest that topical minoxidil and procedural interventions may have benefit in the treatment of pRIA.

Supplemental content

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Approximately 80 000 primary central nervous system (CNS) tumors and 1500 head and neck sarcomas are diagnosed annually,[1,2] with 5-year survival reaching 33% of adults and 75% of children with CNS tumors and 66% of adults and 73% of children with head and neck sarcomas.[3,4] Sixty percent of CNS cancer survivors and 30% of patients with head and neck sarcoma will undergo cranial radiotherapy (CRT), frequently as part of multimodality therapy including surgery and chemotherapy.[3,5]

The risk of acute alopecia is well recognized by clinicians and patients alike, with 75% to 100% of CRT recipients having noticeable hair loss of the scalp at single-fraction radiation doses greater than 2 Gy, with the hair usually growing back within 2 to 4 months. *Persistent radiation-induced alopecia* (pRIA), defined as incomplete hair regrowth 6 months following radiotherapy completion, affects approximately 60% of CRT recipients and has longer-lasting effects on psychosocial functioning and quality of life (QoL).[6-8]

Hair is integral to identity, social interactions, and self-image,[9,10] and pathologic loss of hair can result in psychological distress.[11,12] Alopecia is frequently cited as one of the most distressing adverse events of cancer therapy including CRT.[13-15] Persistent alopecia has been self-reported by 14% of childhood cancer survivors overall and was associated with CRT and an increased risk of anxiety, somatization, and depression.[16,17]

Despite its high incidence among CRT recipients and significant QoL burden, to our knowledge, the clinical and trichoscopic phenotype and response to dermatologic therapy of pRIA have not been systematically described. Thus, we sought to characterize pRIA in patients with primary CNS cancer or head and neck sarcoma.

Key Points

Question What are the clinical features, associated factors, and treatment response of persistent radiation-induced alopecia in patients with cancer?

Findings In this cohort study of 71 children and adults with cancer who underwent cranial radiotherapy, alopecia had localized, diffuse, or mixed localized plus diffuse patterns with frequent white patches on trichoscopy; severe alopecia was associated with greater scalp radiation dose and proton irradiation. Alopecia improvement was observed in 82% of patients treated with topical minoxidil, 5%, solution and 100% of patients treated surgically.

Meaning The findings of this study suggest that topical minoxidil may improve alopecia observed in persistent radiation-induced alopecia, and surgical procedures may be effective in nonresponders.

Methods

Patients

Seventy-one patients diagnosed with a primary CNS tumor or head and neck sarcoma and with pRIA between January 1, 2011, and January 30, 2019, were identified retrospectively at Memorial Sloan Kettering Cancer Center, New York, New York, and St Jude Children's Research Hospital, Memphis, Tennessee, using institutional data management systems and a medical imaging software archive (Mirror, Canfield Scientific Inc).

This study was approved by institutional review boards at each site. Written informed consent was obtained from adults and parents or guardians of minors, and informed assent was obtained from children and adolescents before questionnaire completion. Participants did not receive financial compensation. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Alopecia Assessment and Therapy

Standardized clinical photographs of the vertex, frontal, lateral, and occipital views of the scalp with the hair parted and combed in the center, as well as overt patches of alopecia, were examined (n = 57). Clinical photographs were evaluated with the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0, where grade 1 alopecia is defined as hair loss less than 50% of normal, which does not require camouflage, and grade 2 is hair loss greater than or equal to 50% of normal, which requires camouflage or is associated with psychosocial impact, as stated in the CTCAE.[18] Alopecia distribution was categorized into localized, diffuse, or mixed localized plus diffuse patterns; alopecia attribution was determined based on clinical history and photographs.

Trichoscopy images were evaluated in 28 patients and obtained using a camera-based trichoscope (Folliscope 2.8, Anagen Corp). Trichoscopic images at ×50 magnification were obtained in a standardized fashion of the frontal scalp, occipital scalp, or other areas of alopecia. Trichoscopic images were analyzed for relevant trichoscopic features by a blinded observer (G.S.P.).

Among patients prescribed topical minoxidil, 5%, solution twice daily with baseline and follow-up clinical images (n = 25), longitudinal evaluation of hair growth was assessed using a 4-point scale comparing baseline with follow-up photographs by a single-blind investigator (M.E.L.): complete response was considered a reduction in alopecia severity by 1 or more CTCAE grades; partial response, improved scalp coverage without a change in CTCAE grade; stable disease, no change in scalp coverage; and progression of disease, worsening alopecia.

The Hairdex Questionnaire, a validated 48-item, alopecia-specific QoL tool,[19] was used to assess hair-related QoL among 13 participants. Total and subscale scores are scaled from 0 to 100 points, with higher scores indicating worse QoL.

A blinded observer (M.E.F.) retrospectively estimated maximum scalp radiation dose based on isodose curves corresponding to approximately 5 mm deep to the outer surface of the skin (n = 35 photon therapy, n = 2 proton therapy). The radiotherapy treatment planning systems, Eclipse (Varian Medical Systems) and Top Module (Memorial Sloan Kettering Cancer Center), calculate doses via an anisotropic analytical algorithm and pencil beam convolution, respectively.

Statistical Analysis

Descriptive statistics were used to describe patient and alopecia characteristics. Univariate and multivariate binary logistic regressions were performed to assess the association between estimated scalp radiation dose as a continuous variable and alopecia severity, with grade 1 alopecia as the reference group; a separate regression was performed to analyze the association of proton vs photon therapy with alopecia severity owing to the limited availability of proton therapy treatment plans. A 2-sided *P* value <.05 was considered statistically significant. eFigure 1 in the Supplement further depicts the analytical subsets and specific statistical tests performed. Statistical analyses were performed using Excel (Microsoft) and SPSS Statistics, version 26 (IBM Corp).

Results

Clinical, Trichoscopic, and QoL Characteristics of pRIA

A total of 71 patients with pRIA were included (median age, 27 years; 95% CI, 22-37 years [range, 4-75 years]). The most common brain tumors were medulloblastoma (22 [31%]) and glioblastoma multiforme (18 [25%]); rhabdomyosarcoma constituted 5 of 7 head and neck sarcomas (71%). Most patients underwent surgery (64 [90%]) and chemotherapy (68 [96%]) in addition to radiotherapy (**Table**). Median duration between radiotherapy and pRIA evaluation was 100 (95% CI, 67-227) weeks (interquartile range [IQR], 58-405 weeks).

Severity was grade 1 in 40 of 70 patients (56%) and grade 2 in 30 patients (43%). Median cumulative scalp radiation dose was 39.6 (95% CI, 30-42; range, 15.1-50.0) Gy and dose per fraction was 1.3 (95% CI, 1.0-1.4; range, 0.54-1.79) Gy among 37 patients with evaluated radiotherapy treatment plans. Median scalp dose was higher for patients with grade 2 alopecia vs grade 1 alopecia: 31.9 vs 41.5 Gy (*P* = .001). On univariate analysis, pRIA severity was significantly associated with maximum estimated scalp radiation dose and receipt of proton compared with photon therapy (eTable 1 and eTable 2 in the Supplement). The odds ratio (OR) for grade 2 alopecia for every 1-unit increase in radiation dose was 1.15 (95% CI, 1.04-1.28), and the OR for grade 2 alopecia with proton irradiation was 5.7 (95% CI, 1.05-30.8). On multivariate analyses controlling for sex, age at radiotherapy administration, and concurrent chemotherapy, the scalp dose and proton vs photon therapy remained statistically significant factors associated with alopecia severity (eTable 3 and eTable 4 in the Supplement); the odds of grade 2 alopecia increased by 16% for every 1-Gy increase in scalp dose (OR, 1.16; 95% CI, 1.03-1.29), and the dose at which the probability of grade 2 alopecia is 50% was 36.1 Gy (95% CI, 33.7-39.6 Gy) (**Figure 1**).

Among 54 patients with clinical images available, pRIA distribution was localized (29 [54%]), diffuse (13 [24%]), or mixed (12 [22%]); pRIA was attributed to radiotherapy alone (40 [74%]) or radiotherapy plus chemotherapy (14 [26%]). Alopecia distribution was associated with age, cancer type, radiotherapy field, and attribution (*P* < .001) (**Figure 2**). In a multivariate model, diffuse irradiation (eg, whole brain or craniospinal irradiation) was associated with diffuse alopecia

Table. Patient and Alopecia Characteristics

Patients	No. (%)
No.	71
Age at radiotherapy, median (IQR), y	21 (8-44)
Age at pRIA evaluation, median (IQR), y	27 (20-45)
Sex	
Female	51 (72)
Male	20 (28)
Race	
White	58 (82)
Asian	7 (10)
Black	3 (4)
Other/not specified	3 (4)
Cancer type	
Medulloblastoma	22 (31)
Glioblastoma multiforme	18 (25)
Other glioma[a]	16 (23)
Pineal germ cell tumor	3 (4)
PCNSL	3 (4)
Pineoblastoma	1 (1)
Craniopharyngioma	1 (1)
Head and neck sarcoma[b]	7 (10)
Primary tumor site	
Supratentorium	38 (54)
Infratentorium	25 (35)
Nasopharynx/skull base	6 (9)
Leptomeningeal	1 (1)
Scalp	1 (1)
Cancer therapy	
Surgery	64 (90)
Autologous hematopoietic stem cell transplant	6 (9)
Chemotherapy	68 (96)
Cytotoxic	43 (61)
Combination cytotoxic plus targeted	24 (34)
None	3 (4)
Targeted	1 (1)
No. chemotherapeutic agents, median (IQR)	3 (2-5)
Radiotherapy field	
Focal	41 (58)
Diffuse	3 (4)
Focal and diffuse	27 (38)
Prescribed cumulative radiotherapy dose, Gy, median (IQR)	55.8 (54-60)
Prescribed dose per fraction, Gy, median (IQR)	1.8 (1.8-2.0)
Radiotherapy modality (n = 52)	
Photon	42 (81)
Proton	10 (19)
Alopecia characteristic	
Severity (n = 70)	
Grade 1	40 (57)
Grade 2	30 (43)
Distribution (n = 54)	
Localized	29 (54)
Diffuse	13 (24)
Mixed localized and diffuse	12 (22)
Attribution (n = 54)	
Radiotherapy	40 (74)
Radiotherapy plus chemotherapy	14 (26)

(continued)

Table. Patient and Alopecia Characteristics (continued)

Patients	No. (%)
Response to minoxidil, 5% (n = 25)	
Complete	4 (16)
Partial	13 (52)
Stable	7 (28)
Progression	1 (4)

Abbreviations: IQR, interquartile range; PCNSL, primary central nervous system lymphoma; pRIA, persistent radiation-induced alopecia.

[a] Other glioma includes astrocytoma, oligodendroglioma, ependymoma, and mixed glioma.

[b] Head and neck sarcoma includes rhabdomyosarcoma, Ewing sarcoma, and chondrosarcoma.

(reference category, localized alopecia: OR, 341; 95% CI, 1.59-73 089; P = .03), attribution to radiotherapy plus chemotherapy vs radiotherapy alone was associated with diffuse alopecia (reference category, localized alopecia: OR, 165; 95% CI, 2.64-10 262; P = .02), and attribution to radiotherapy plus chemotherapy was associated with mixed distribution alopecia (reference category, localized alopecia: OR, 112; 95% CI, 1.87-6738; P = .02) (eTable 5 in the Supplement).

Trichoscopic findings were analyzed in 28 of 71 patients (39%). At pRIA diagnosis, median hair shaft density at a representative area of alopecia was 96 hairs/cm^2 (95% CI, 84-144; IQR, 78-166 hairs/cm^2), corresponding to a terminal hair density of 90 hairs/cm^2 (95% CI, 74-129; IQR, 50-153 hairs/cm^2) and vellus hair density of 12 hairs/cm^2 (95% CI, 5-17; IQR, 3-20 hairs/cm^2). Median hair shaft diameter was 46.7 µm (95% CI, 42.2-56.0; IQR, 40.3-58.3 µm). Most follicular units consisted of a single hair shaft (median proportion, 93%; 95% CI, 84%-100%; IQR, 82%-100%), with few containing 2 shafts per follicular unit (7%; 95% CI, 0%-16%; IQR, 0%-18%); all but 2 patients had zero follicular units containing 3 shafts. Predominant trichoscopic features included white patches (57%), thin arborizing vessels (36%), and milky red areas (32%) (eTable 6 in the Supplement). Hair caliber negatively correlated with estimated scalp radiation dose in 15 patients with trichoscopy and radiotherapy treatment plans (Spearman correlation coefficient ρ = −0.624, P = .01). The association between hair density and scalp radiation dose was not statistically significant (ρ = −0.381, P = .16) (**Figure 3**). Concurrent chemotherapy recipients had lower median hair density (n = 28, 168 vs 93 hairs/cm^2, P = .04). Diffuse-field radiotherapy was associated with smaller hair diameter (n = 28, 42.4 vs 57.2 µm, P = .003).

Alopecia-related QoL was analyzed in 13 (2 children and 11 adults) of 71 patients (18%). The median overall Hairdex Questionnaire score was 26.6 (95% CI, 12.2-34.9; IQR, 11.8-35.7), which included emotions (33.3; 95% CI, 15.0-48.3; IQR, 14.2-50.8), self-confidence (21.4; 95% CI, 17.9-35.7; IQR, 17.9-35.7), functioning (13.6; 95% CI, 4.5-27.3; IQR, 3.4-27.3), stigmatization (6.3; 95% CI, 0-31.3; IQR, 0-32.8), and symptoms (10.7; 95% CI, 3.6-21.4; IQR, 1.8-23.2) subscales (eFigure 2 in the Supplement). The QoL burden was worse in the emotions subscale compared with functioning, stigmatization, and symptoms subscales (P < .04).

Topical minoxidil, 5%, solution was prescribed to 53 patients (75%). Twenty-eight of 34 evaluable patients (82%) responded to minoxidil, 5%, treatment with a median follow-up time of 61 weeks (95% CI, 41-97; IQR, 21-105; range, 7-226 weeks). Among 25 minoxidil, 5%, recipients with clinical images, complete response occurred in 4 patients (16%) (**Figure 4**A), partial response in 13 patients (52%), stable alopecia in 7 patients (28%), and progression of alopecia in 1 patient (4%). Change in grade was not appreciably dependent on pRIA severity (4 of 13 patients [31%] with grade 1 alopecia underwent a reduction in severity grade vs 0 of 12 [0%] grade 2 cases; P = .10). Three patients (4%) underwent a procedural intervention for pRIA; of these, 2 patients received hair transplantation with partial and complete responses (Figure 4B) and 1 patient underwent scalp expansion and plastic surgical reconstruction with a complete response.

Discussion

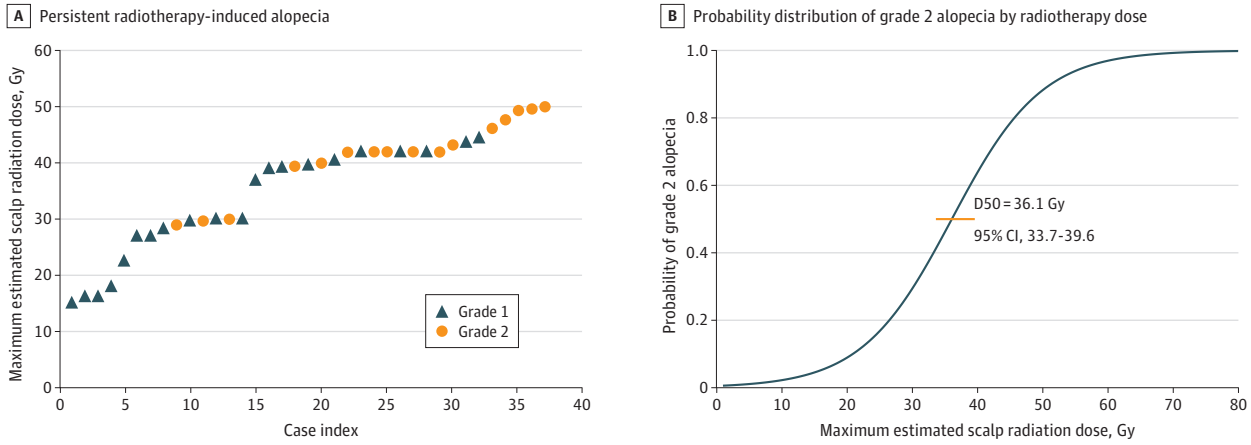
pRIA Clinical Characteristics

We characterized a cohort of patients with primary CNS tumors and head and neck sarcomas with pRIA based on clinical history, standardized photographic evaluation, and trichoscopic evaluation and summarized the outcomes of topical minoxidil, 5%, therapy and procedural interventions in these patients. Clinically, we observed that alopecia presented in 3 variants: localized, diffuse, and mixed patterns, which were informed by demographic and disease factors that determined cancer therapies (surgery, radiotherapy, and chemotherapy) and subsequent attribution. The clinical picture was consistent with documented cases of pRIA.[7,20-22]

Although mechanisms of pRIA are not well understood, substantive genotoxic insults from radiotherapy or cytotoxic chemotherapy can damage epithelial hair follicle stem cells in the bulge region in addition to the rapidly dividing hair matrix cells in the hair follicle bulb, preferentially causing an anagen effluvium that is histologically consistent with nonspecific scarring alopecia.[7,8,21,23-28] Hair follicle radiosensitivity is also dependent on hair cycle stage: anagen matrix cells are more radiosensitive than telogen matrix cells owing to relative differences in proliferation rates.[8,29] While the dose threshold for transient epilation is low (0.75-2 Gy)[30-32] and the single-fraction lethal dose for a hair follicle was historically considered to be 7 to 16 Gy,[7,33,34] the risk factors and dose thresholds for pRIA in patients with cancer receiving modern fractionated CRT are less clear.

Hence, we identified a dose-response association between estimated scalp radiation dose and pRIA severity by CTCAE grade. The dose at which half of patients would be expected to have severe alopecia was 36 Gy, which is lower than reported in 26 adults with brain tumors who received CRT (43 Gy; 95% CI, 33-52 Gy)[35] and higher than the pRIA threshold reported in 12 pediatric patients with medulloblastoma who received proton craniospinal radiotherapy plus posterior fossa boost therapy (21 Gy with high-dose chemotherapy, 30 Gy with conventional chemotherapy).[21] However, the latter report excluded boost doses from the calculations, which, from our

Figure 1. Scalp Radiation Dose-Response Association With Alopecia Clinical Severity



A, Persistent radiation-induced alopecia cases. B, Probability distribution of severe (grade 2) alopecia by scalp radiation dose. D50 indicates the dose at which 50% of patients might incur grade 2 over grade 1 alopecia.

experience, might lead to threshold underestimation since the boost dose tends to evoke the most dramatic patch of alopecia.[21] In addition, the former study used scalp areas as the unit of analysis,[35] whereas our grading relied on the global clinical picture. Given that our cohort consisted of both child and adult brain tumor survivors of various tumoral types, it is possible that our estimated dose would lie between the 2 aforementioned reports.

Furthermore, proton beam therapy conferred greater odds of grade 2 alopecia. Although proton therapy has a dosimetric advantage with conventional and intensity-modulated photon therapy in terms of sparing nontumor structures, proton radiation is not known to show a skin-sparing advantage over photons for CRT, likely owing to an added range uncertainty margin with proton dosing, thereby augmenting the exit skin dose, and the lack of build-up effects resulting in higher skin surface doses for targets located near the surface.[21,36]

Although the association between radiotherapy fractionation and normal tissue responses to radiation is well established,[37] we did not find an association between number of radiotherapy fractions and pRIA severity, possibly owing to the homogeneity of fractionation schemes. Similarly, higher-energy photons tend to have skin-sparing properties[21]; however, all but 1 of our photon cases used 6-MV beams, so this association could not be adequately assessed. Our estimation of maximum scalp dose was limited in part because it did not directly consider the radiation field volume and involved scalp surface area; however, point approximation of scalp surface dose may be a convenient metric for use during treatment planning.

Newer treatment-planning modalities (eg, intensity-modulated radiotherapy, volumetric-modulated arc therapy) are preferable to traditional radiotherapy delivery modalities in terms of off-target dose delivery (eg, hair-sparing properties).[30,38,39] Other tactics with uncertain utility in decreasing skin dose include margin adjustment, blocking devices, limiting the use of fixation materials, scalp cooling, and topical agents, including nitroxide compounds (eg, tempol).[21,35,40-43] Patients should be counseled on discussing the risks of RIA and pRIA with their radiation oncologist, keeping their specific radiotherapy treatment planning dosing scheme in mind. Further research is required to substantiate supportive measures for pRIA prevention, and as radiation delivery technologies continue to evolve, it is necessary to consider potential scalp dose to limit iatrogenic alopecia.

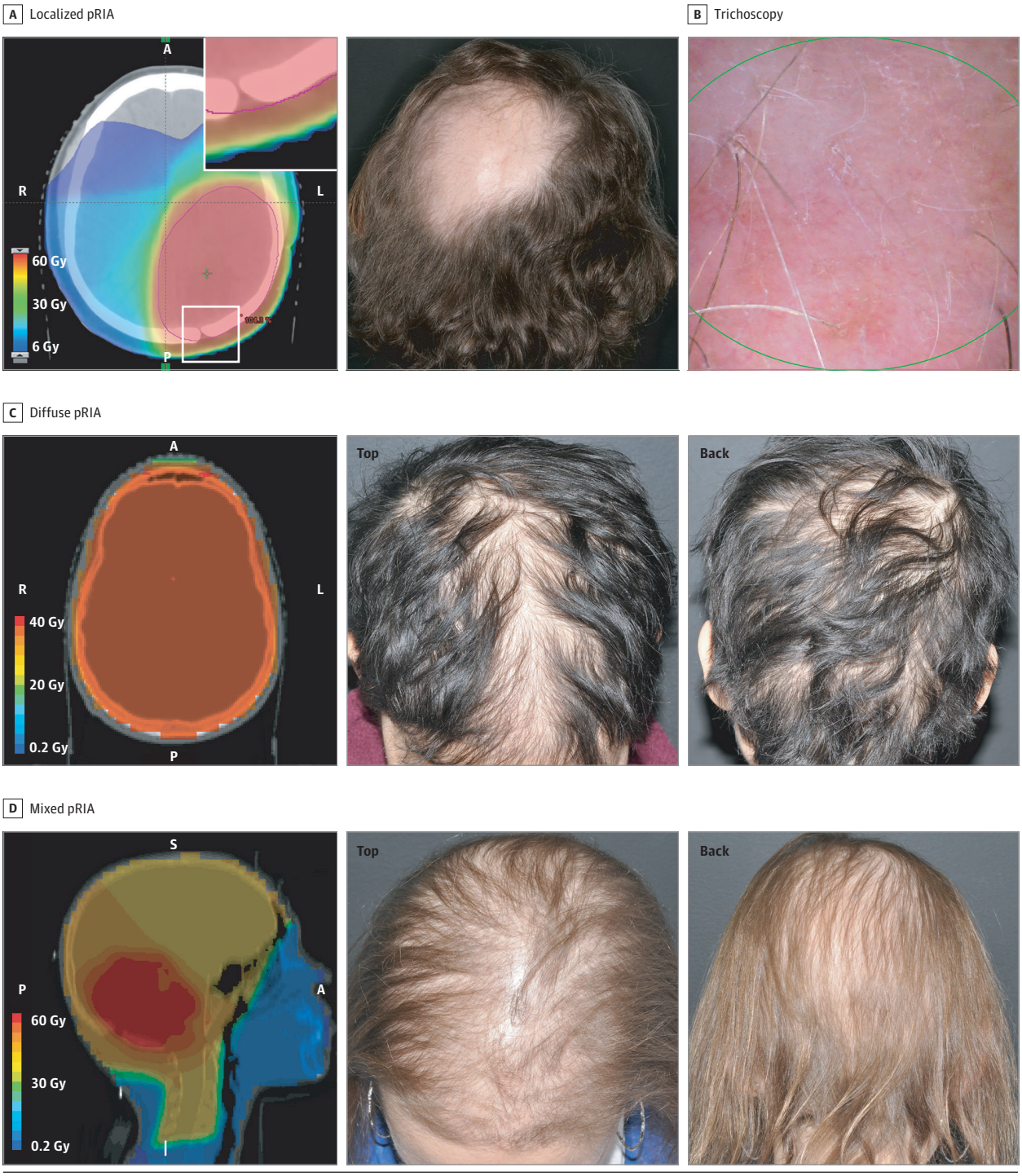
Trichoscopic Findings and QoL

Scarring alopecias are characterized by decreased hair density and whitish, pale areas (white patches) with variable degrees of absence of follicular openings.[44-49] White patches were most prevalent among the pRIA cohort, corroborating a scarring process in the pathogenesis of pRIA. Yellow and black dots were identified in a few cases, which have been reported in association with RIA from endoscopic fluoroscopy procedures.[50] We hypothesized that white patches would portend a worse prognosis with regard to response to minoxidil, 5%; yet, no appreciable association was observed between subjective response measures and white patches, possibly owing to small sample size and lack of objective response measures. Larger, prospective studies would be better suited to deciphering the potential relevance of trichoscopy to pRIA prognosis and treatment allocation.

To assess the association between dose and alopecia on the microscopic level, we correlated maximum scalp dose with trichoscopic findings, noting that scalp radiation dose negatively correlated with hair diameter. We offer our retrospective analysis as a proof of concept that trichoscopic metrics can be correlated with radiotherapy dose, which, with the development of reliable dose-response models, would be of use to dosimetrists and radiation oncologists during treatment planning and pretherapy counseling.

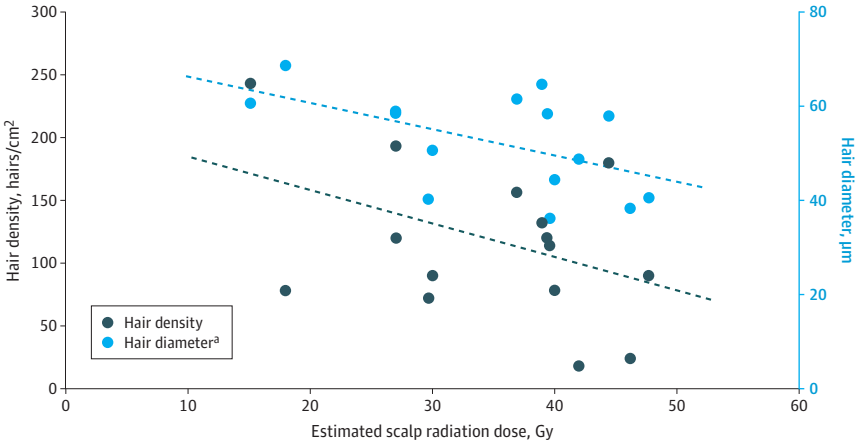
Hair-related QoL among 13 female survivors with pRIA evidenced a high emotional burden of pRIA, which is comparable to results in women with endocrine therapy–induced

Figure 2. Radiotherapy, Clinical, and Trichoscopic Correlation of Persistent Radiation-Induced Alopecia (pRIA)



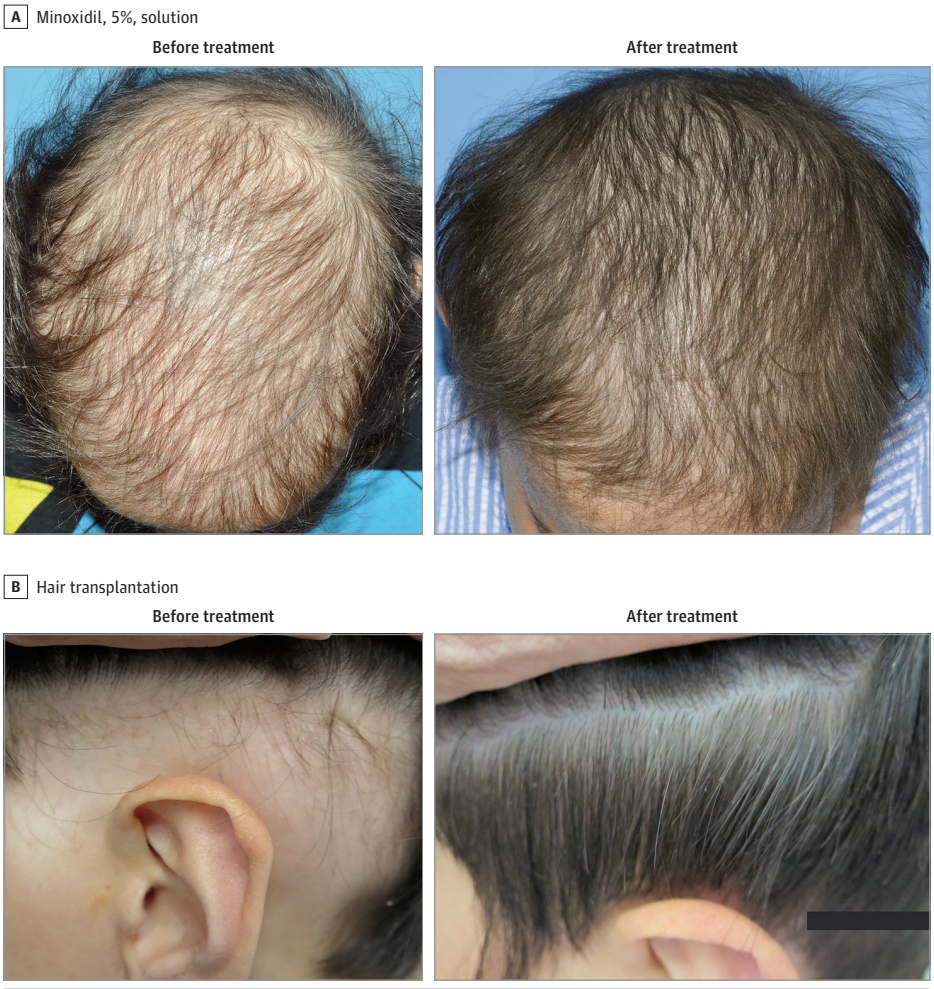
A, Axial computed tomographic (CT) scan of the head with overlying color wash of planned radiation dose distribution and corresponding localized pRIA following 59.4-Gy photon intensity-modulated radiotherapy; inset shows enlarged image of the scalp and cranium at an area of high radiation dose, outlined by the white box. B, Trichoscopy findings showing decreased hair follicle density and diameter, vellus hairs, white patches, dotted and thin arborizing vessels, and mild scaling. C, Axial CT scan of the head with overlying color wash of planned radiation dose distribution and corresponding diffuse pRIA following 36-Gy craniospinal irradiation (CSI) plus 18-Gy pineal boost. D, Sagittal CT scan of the head with overlying color wash of planned radiation dose distribution and corresponding mixed pRIA following 39.6-Gy CSI plus 16.2-Gy posterior fossa boost. A indicates anterior; I, inferior; L, left; P, posterior; R, right; and S, superior.

Figure 3. Baseline Trichoscopic Parameters Plotted According to Estimated Scalp Radiation Dose



[a] Significant correlation between radiation dose and hair diameter was found. Spearman correlation coefficients: hair density, −0.381, $P = .16$; hair diameter, −0.624, $P = .01$.

Figure 4. Persistent Radiation-Induced Alopecia Clinical Response



A, Response to topical minoxidil, 5%, solution. B, Response to hair transplantation.

alopecia, persistent chemotherapy-induced alopecia, and endocrine therapy–induced alopecia after chemotherapy (mean overall Hairdex score, 26-30 vs our cohort, 23).[51,52]

Therapeutic Interventions and Outcomes

Thought to promote hair growth through local vasodilation via adenosine triphosphate–dependent potassium channel acti-

vation and/or stimulation of hair follicles into the anagen phase via growth factor and antiandrogenic signaling,[53-63] topical minoxidil, 5%, solution twice daily produced a subjective response in 28 survivors (82%) with pRIA. To our knowledge, minoxidil efficacy for pRIA has been hitherto unreported, with minoxidil ineffective in a case of RIA.[20] In studies examining the use of minoxidil, 5%, moderate to significant improvement was seen in 54 cases (67%) of persistent chemotherapy-induced alopecia, 42 cases (76%) of endocrine therapy-induced alopecia after chemotherapy, and 46 cases (80%) of endocrine therapy–induced alopecia in patients with cancer or survivors.[51,52] Conversely, a 3-month course of topical minoxidil, 2% to 5%, in 14 patients with persistent chemotherapy-induced alopecia was deemed unsuccessful.[64-66]

These findings suggest that topical minoxidil could have benefit in pRIA and that clinical trials are warranted to determine efficacy and tolerability for pRIA in cancer survivors. Our reported response rate is encouraging; however, few survivors (4 [16%]) achieved a complete response in their alopecia to topical minoxidil, 5%, suggesting that effect size may limit the clinical significance of topical minoxidil for treatment of pRIA. In addition, the possibility of spontaneous hair regrowth irrespective of minoxidil use in these patients cannot be excluded. Hence, the use of validated QoL and objective measures as part of controlled clinical trials for pRIA would be essential to capture the true clinical significance of alopecia and its interventions, which have predominantly psychosocial implications.

Procedural specialists and surgeons have traditionally been wary of intervening at sites of previous radiotherapy, with concerns of increased healing time, wound dehiscence, and infection.[67-69] However, success has been reported with reconstructive procedures in both recently and formerly irradiated body sites including the scalp.[7,70-75] We present 3 cases of procedural interventions for pRIA that had no complications despite targeting a sequela of radiotherapy. In addition to improved cosmesis, these procedures have the potential for beneficial implications for long-term well-being and social functioning, especially among survivors of childhood cancer. However, further research is needed to stratify individuals with pRIA unlikely to respond to other therapies as procedural candidates.

Limitations

The retrospective study design and limited availability and analysis of radiotherapy treatment plans, standardized clinical photographs, and trichoscopy images represent study limitations. To inform the reader of the limitations to sampling associated with lack of data availability, eTable 7 in the Supplement compares demographics and alopecia severity between patients with these data available and those without data available. Furthermore, scalp dose estimates were approximated with point estimates using treatment planning systems, which have their own limitations with dose estimation, especially at the skin, where the build-up phenomenon is most prominent. In addition, since scalp tattoos were not implementable to verify trichoscopy follow-up localization, objective measurements of treatment response were not included. Also, the Hairdex Questionnaire is an in-house translation of the original German Hairdex—to our knowledge, its validity in English-speaking patients has not been formally established.

Conclusions

Persistent radiation-induced alopecia among patients with primary CNS or head and neck sarcomas represents a dose-dependent phenomenon that is tractable in clinical severity evaluation, clinical photographs, and trichoscopic images. In this study, we present evidence for the potential utility of topical minoxidil, hair transplantation, and plastic surgical reconstruction for pRIA. These findings may inform pretherapy counseling and efforts to identify preventive and therapeutic strategies, including randomized clinical trials in cancer survivors, for this burdensome sequela of a principal axis of cancer therapy.

ARTICLE INFORMATION

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