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The role of full thickness scalp resection for management of primary scalp melanoma

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Abstract

BACKGROUND—Scalp melanoma is aggressive and has a proclivity for regional metastasis. We hypothesize that subperiosteal scalp melanoma resection reduces in-transit/satellite recurrence, when compared to subgaleal resection.

METHODS—We identified patients with intermediate to deep, primary scalp melanoma referred to head/neck surgery over an eight-year period. Patients were compared based on scalp resection depth, including subperiosteal (resection to the level of calvarium) and subgaleal (resection including skin, subcutaneous tissue, and galea). The dependent variables were in-transit/satellite recurrence and time to in-transit/satellite recurrence.

RESULTS—Among 48 identified patients, the in-transit/satellite recurrence rate was 16.7%. Subgaleal resection patients had higher in-transit/satellite recurrence rates than subperiosteal resection patients (24.0% vs. 8.7%, $p=0.155$). Among node-negative patients, subgaleal resection had significantly higher in-transit/satellite metastasis rates when compared to subperiosteal resection (26.3% vs. 0%, $p=0.047$).

CONCLUSION—For node-negative, primary scalp melanoma, subperiosteal resection significantly decreases in-transit/satellite recurrence when compared to subgaleal resection. Given our small sample size, further studies are necessary to confirm these results.

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Keywords

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INTRODUCTION

Scalp melanoma is an aggressive disease with a proclivity for regional metastasis¹. Aggressive resection creates considerable reconstructive challenges, particularly when defects include large areas of exposed calvarium. For intermediate to deep Breslow depth tumors, the literature contains no generally accepted guideline for depth of surgical resection.

The traditional approach to scalp melanoma excision preserves calvarial periosteum. This structure supports skin graft survival securing a straightforward reconstructive option. Conversely, when periosteum is excised with the tumor (i.e. a subperiosteal resection), a skin graft placed directly on exposed calvarium will not survive. In the past, large local rotational flaps or free tissue transfer were required to close full-thickness scalp defects resulting from subperiosteal resection²⁻⁴.

We have previously reported that INTEGRA® Dermal Regeneration Template (Integra Life Sciences, Plainsboro New Jersey), a dermal collagen matt, can be used to reconstruct full-thickness scalp defects in a staged procedure. The dermal collagen matt was applied to exposed calvarium after tumor extirpation. After vascular ingrowth for four weeks, the neodermis served as a reliable recipient bed for split thickness skin grafting⁵. This technique allowed assurance of a clear deep margin prior to definitive reconstruction, assuming no bony invasion had occurred. The dermal matt confers distinct advantages over flap alternatives for full-thickness scalp defects. These include ease of use, shorter operative times, and decreased donor site morbidity^{2, 6}.

In this series, we report the University of Michigan Cancer Center experience with scalp melanoma over an eight-year period. We contend that subperiosteal scalp melanoma resection reduces in-transit/satellite recurrence when compared to subgaleal scalp melanoma resection that leaves scalp periosteum *in situ*. This is of particular relevance given the simplified means by which full-thickness scalp defects can be closed with a dermal collagen matt (INTEGRA®).

METHODS

The University of Michigan maintains a prospective registry of all melanoma patients. The Melanoma Registry was used to all identify patients referred to our multi-disciplinary melanoma program for scalp melanoma management between 2001 and 2009. The scalp was defined as the hair-bearing area extending from the supraorbital ridges anteriorly to the superior nuchal line posteriorly and the mastoid and zygoma laterally.

Study inclusion criteria were the following: 1) primary subperiosteal scalp melanoma resection (full thickness scalp resection to the level of calvarium) or subgaleal scalp

melanoma resection (scalp resection which included skin, subcutaneous tissue, and galea) performed at the University of Michigan by a head and neck surgeon (CRB or RSR), 2) operative and surgical pathology documentation inclusive of all independent variables below, and 3) physician follow-up greater than 6 months. Because tumor involvement of periosteum is a clear indication for subperiosteal resection, we excluded patients with histologic evidence of periosteal invasion. This allowed us to compare those patients for whom subperiosteal resection was not clearly indicated. Resection depth was determined by surgeon preference.

Independent variables included age, Breslow depth, surgical margin size, depth of resection, nodal status, and length of follow-up. Nodal status was tracked as a dichotomous (positive versus negative) variable. Lymph node involvement was determined at the time of primary melanoma extirpation. This was accomplished by clinical documentation and results of sentinel lymph node (SLN) biopsy when performed. All variables were extracted using retrospective medical record review.

An attempt was made to contact all patients by telephone. Patients were not screened for recurrence using the telephone. Rather, they were asked 1) how recently a physician had examined their scalp and 2) how recently a physician had told the patient there was no evidence of disease. Length of follow-up for this study was defined as the time between initial surgical resection and the last physician examination of the scalp.

Dependent variables included recurrence and time to recurrence. We examined the data set using the in-transit and satellite recurrence definition as outlined in the 2010 AJCC Guidelines, specifically “in-transit/satellite recurrence, i.e. grossly visible cutaneous and/or subcutaneous metastasis occurring within (satellite) or greater than (in-transit) 2 cm of the primary melanoma and the first echelon of regional lymph nodes”⁸. Determination of in-transit or satellite metastasis was based on review of available clinical and pathologic documentation by a board-certified dermatologist with extensive experience in head and neck melanoma (TMJ).

Bivariate statistics were generated using the chi-squared test or Fisher’s exact test for dichotomous variables and two-tailed Student’s t-test for continuous variables. Stratified analysis was performed for patients with and without nodal disease. We planned to perform multivariable logistic regression to examine the association between scalp resection depth and recurrence when controlling for other independent variables. However, a paucity of outcome events made statistically rigorous use of multivariable regression impossible.

This study was approved by the University of Michigan Institutional Review Board.

RESULTS

The University of Michigan Melanoma Registry was queried for the time period of 2001–2009. The Registry contained 51 patients meeting our inclusion criteria (Figure 1). Three patients were excluded for histologic involvement of the periosteum, leaving 48 patients for our analysis.

We attempted to contact all patients by telephone to identify their last scalp examination by a physician. Among those able to be contacted, phone screen did not identify any cases of recurrent scalp melanoma that had been managed at another institution.

Our data set was comprised of patients with intermediate to deep scalp melanoma. The average Breslow depth was 3.93mm (range 0.2mm to 9.0mm).

Twenty-five patients (52%) underwent subgaleal resection and 23 patients (48%) underwent subperiosteal resection. There was no significant difference in Breslow depth, mean surgical margin, mean age, sentinel lymph node status, or mean length of follow-up between the subgaleal and subperiosteal resection groups. When SLN biopsy was not indicated, operative time for subperiosteal resection with INTEGRA® reconstruction was significantly shorter than subgaleal resection with skin graft (25 vs. 52 minutes, $p=0.016$). When SLN was performed, there was no significant difference in operative time between subperiosteal and subgaleal resection (86 vs. 131 minutes, $p=0.123$) (Table 1).

There were no significant differences in mean percentage of skin graft adherence between patients who had subgaleal versus subperiosteal resection (96% vs. 97%, $p=0.81$). One patient in the subgaleal resection group had 50% skin graft loss that required a second operation. No skin graft losses that required a second operation were seen in the subperiosteal group. Prior to skin grafting, four patients in the subperiosteal group required an additional operation for exposed calvarium due to incomplete Integra adherence. Each patient subsequently had complete wound closure with a skin graft. One patient in each group had cellulitis at the skin graft donor site that required treatment with oral antibiotics.

The overall rate of in-transit/satellite recurrence was 16.7% (8 of 48 patients). Patients who had subgaleal resection were more likely to have in-transit/satellite recurrence than patients whose melanoma resection included the periosteum (24.0% vs. 8.7%, $p=0.155$). This difference was not significant.

Effect of sentinel lymph node status on in-transit/satellite recurrence

Patients with a positive SLN clearly have disease within the lymphatic system and therefore represent a distinct population. To control for this confounder, patients were stratified based on positive or negative SLN at time of the original scalp surgery. Thirty-six patients had no clinical or pathologic evidence of nodal disease. Of those patients with negative SLN, there were no significant differences in mean age, gender, mean Breslow depth, mean surgical margin size, or mean length of follow-up between subgaleal and subperiosteal resection groups (Table 2).

Among node-negative patients, 13.9% (5 of 36 patients) had in-transit/satellite metastases. Node-negative patients who had subgaleal resection were significantly more likely to have in-transit/satellite metastases when compared to patients who had subperiosteal resection (26.3% vs. 0%, $p=0.047$) (Figure 2). Among node-negative patients with recurrence, the average time to in-transit/satellite recurrence was 10.4 months. Logistic regression could not be performed as there were no recurrences in the node-negative, subperiosteal resection group.

Of patients with positive SLN, 25% (3 of 12 patients) developed in-transit/satellite metastases. Among the node-positive patients, in-transit/satellite metastasis rates were not significantly different between patients who had subgaleal versus subperiosteal resection (33% vs. 66%, $p=1.00$).

Representative patient photos for subgaleal and subperiosteal resection are shown in Figure 3.

DISCUSSION

Intermediate to deep Breslow depth scalp melanoma is an aggressive disease with a proclivity for local, in-transit/satellite and regional metastasis¹. Our data set contained patients who underwent subperiosteal or subgaleal scalp melanoma resection. With an average Breslow depth of 3.93mm, this series represents a population with advanced disease. The overall rate of in-transit/satellite recurrence was 16.7%. These intralymphatic manifestations of melanoma constitute considerable risk for additional locoregional and distant metastasis⁷.

Resection depth appeared to influence in-transit/satellite recurrence in this population. Among patients without regional nodal disease, those undergoing subperiosteal scalp melanoma resection were significantly less likely to experience in-transit/satellite recurrence than those patients who had subgaleal resection that left calvarial periosteum *in situ* (0 vs. 26.3%). Interestingly, there were no instances of recurrence within the node-negative subperiosteal resection group.

Dermal collagen matt (INTEGRA®) can be used to close full-thickness scalp defects devoid of periosteum in a straightforward fashion⁵. Through our adoption of INTEGRA®, we have added reconstructive options for scalp melanoma at our institution.

INTEGRA® is an FDA approved bilaminate bovine collagen construct that provides a scaffold for dermal regeneration. Its two layers are 1) a porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan (chondroitin-6-sulfate) manufactured with a controlled porosity and 2) a temporary silicone epidermal substitute. The collagen dermal replacement layer serves as a matrix for the infiltration of fibroblasts, macrophages, lymphocytes, and capillaries derived from the wound bed⁸. Routine burring of the calvarium is not performed and vascularization is assumed to occur via infiltration of cells from the wound periphery^{6,9}. A skin graft can then be placed over the collagen matt in a second procedure. Survival of skin grafts placed on INTEGRA® derived neodermis are reported to be between 90–95%^{10,11}.

Use of INTEGRA® for reconstruction of full-thickness scalp defects was first reported in 2005^{5,12}. Since then, several other groups have published on the utility of this technique^{6,9}. INTEGRA® allows uncomplicated repair of full thickness scalp defects and has distinct advantages over flap coverage. These advantages include not burying residual tumor under rotation or advancement flaps, ease of use, shorter operative times, and decreased donor site morbidity^{2,6}. The major disadvantage of INTEGRA® is that a second operation for skin grafting is required.

Our finding that removal of periosteum decreases in-transit/satellite recurrence is compelling within the current understanding of scalp lymphatics. Anatomic studies have shown the galea to contain large caliber lymphatic vessels in free communication with subcutaneous and dermal networks via pre-collecting ducts¹³. These vertically connected networks span the scalp and serve as potential conduits for in-transit/satellite and primary nodal metastasis. To our knowledge, anatomic studies that examine lymphatic drainage pathways within the periosteum, or assess for communications between the lymphatic structures in the galea and periosteum, have not been performed. If such communications exist, it is plausible that microscopic disease could remain within the scalp's vertical lymphatic network when anything less than subperiosteal resection is employed.

Limitations

Our study has several limitations. Most notably, our retrospective study is prone to both chronology and selection bias¹⁴. The study spanned an eight-year period and is thus prone to chronology bias, where secular trends in the medical system change how diseases are diagnosed and treated. At our institution, patients treated more recently were more likely to have full thickness resection with INTEGRA® reconstruction. The potential for selection bias also existed in our study. Specifically, one surgeon had a uniform change in practice after 2005. All primary scalp melanoma patients treated by this surgeon had full-thickness scalp resection and Integra® reconstruction unless medically unfit for a staged procedure. However, a second surgeon did not uniformly change practice; rather, they continued to perform a mixture of subgaleal and subperiosteal primary scalp melanoma resections. Subperiosteal resection was reserved for more aggressive tumors, however the specific criteria under which resection depth was chosen were unclear. Thus, although our patient populations were similar among identified confounders (Table 1 and Table 2), an occult channeling bias and/or confounding by unrecognized factors may still be present. Presence of multiple sources of bias, which are inherent to retrospective studies, has led us to temper our recommendations for use of subperiosteal resection (see *Clinical Implications* and *Conclusion* sections), although statistical significance was present.

Positive SLN was identified as a notable confounder in our data set. We performed a stratified analysis to control for this factor. However, this resulted in a small sample size for the positive sentinel lymph node group (N=12). Our data for this subgroup are likely underpowered to identify a difference if one is truly present. A larger sample size of patients with positive SLN would be necessary to appropriately perform this analysis. This study was designed to analyze only patients with primary scalp melanoma. Thus, the results cannot necessarily be generalized to patients being treated for recurrent disease. Our study population was comprised of patients with intermediate to deep scalp melanoma who required either subperiosteal or subgaleal resection. As a result, our conclusions are not applicable to patients with thin scalp melanoma, such as those treated in the outpatient dermatology setting. Further prospective analysis could elucidate the Breslow depth at which subperiosteal resection becomes clinically beneficial.

Clinical Implications

In patients with intermediate to deep, node-negative primary scalp melanoma, subperiosteal resection appears to be associated with a significantly decreased rate of in-transit/satellite recurrence. Subperiosteal scalp resection typically requires at least two operations and thus is appropriate only for patients who can safely tolerate an additional operation. Although we demonstrate a statistically significant difference between the two treatment strategies, several sources of bias are present within our study. Thus, the potential for a type I error remains notable and we cannot recommend a global change in practice based solely on our results.

CONCLUSION

Our retrospective cohort study demonstrates that patients with intermediate to deep, node-negative, primary scalp melanoma have significantly decreased in-transit/satellite recurrence rates with subperiosteal scalp resection, when compared to subgaleal resection. However, with a small sample size and potential sources for bias which remain uncontrolled, we cannot recommend a change in practice based solely on our data. Further research using rigorous, prospectively established protocols is required to examine the validity of this potential high impact finding.

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Figure 1.
Scalp melanoma exclusion criteria

Figure 2.
In-transit/satellite recurrence rates stratified by depth of resection

Figure 3.

Representative patient photos. Patient 1 (Figures 3a and 3b) had a subgaleal resection with immediate skin graft placement to periosteum. She had an intransit/satellite recurrence that required re-resection to periosteum and skin grafting. Photos were taken 48 months after initial surgery. Patient 2 (Figures 3c and 3d) had a subperiosteal resection with Integra placement and skin grafting at a second operation. He had multiple in-transit/satellite recurrences that required re-resection to bone and skin grafting. Photos were taken 30 months after initial surgery.

Table 1

Patient demographics stratified by depth of resection (N=48)

	Resection Depth		p value
	Subgaleal	Subperiosteal	
Number of patients	25	23	--
Age, mean	67	66	0.796
Male, %	68%	61%	0.606
Breslow depth (mm), mean	3.54	4.33	0.312
Operative time (minutes), mean			
Resection, no SLN	52	25	0.016
Resection, with SLN	131	86	0.123
Surgical margin (cm), mean	1.83	1.90	0.551
Positive SLN, %	24%	26%	0.868
Length of followup (months), mean	33	23	0.176

Table 2

Demographics of patients with negative sentinel lymph node stratified by depth of resection (N=36)

	Resection Depth		p value
	Subgaleal	Subperiosteal	
Number of patients	19	17	--
Age, mean	71	65	0.289
Male, %	63%	58%	0.790
Breslow depth (mm), mean	3.62	3.81	0.837
Surgical margin (cm), mean	1.87	1.89	0.890
Length of followup (months), mean	28	27	0.824