

# Primary Melanoma of Skin of the Breast Region

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Primary melanoma of skin of the breast region accounted for less than 5% of all malignant melanomas. During a two-year period, 12 patients were seen with these unique lesions. It appears that wide excision and prophylactic lymphadenectomy, including radical mastectomy, gave the best long-term local and regional control. Dissection of the internal mammary nodes did not seem to be beneficial. Pertinent literatures emphasizing several important pathological factors which correlate with higher incidence of metastases to the regional lymph nodes are reviewed. A rational therapeutic approach, synthesizing above information and incorporating postoperative adjuvant immunotherapy, is suggested.

**M**ALIGNANT melanoma of the breast should be divided into two categories: Metastatic and primary lesions. In addition to cutaneous metastases, melanoma can spread to the breast parenchyma. Hadju and Urban<sup>21</sup> described 14 such cases among 51 patients with metastatic cancer in the breast. Pressman<sup>42</sup> summarized another 7 cases, and Silverman and Oberman<sup>45</sup> added 6 more patients. Hyman and Abellera<sup>26</sup> noted metastatic melanoma in an intramammary lymph node.

Primary melanoma can arise in the skin or glandular tissue of the breast. The latter condition is very rare and there are only two such cases reported in the literature.<sup>15,48</sup> Melanoma of the skin overlying the breast is much more common. Statistically, approximately 25% of all malignant melanomas are located on the trunk (Table 1). Most such lesions are found in the pectoral or scapular regions and only 5% occur in the anterior chest wall.<sup>28</sup> In contrast to the preponderance of females

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among patients with malignant melanoma of the lower extremity,<sup>3</sup> melanoma of the trunk appears less often in females (the women to men ratio = 1:1.5).<sup>29,39</sup>

The treatment for malignant melanoma usually involves wide local excision of the primary tumor down to or including the underlying fascia in order to prevent local recurrence.<sup>1</sup> In keeping with these procedures, a partial or simple mastectomy would be necessary for melanoma of the breast. However, none of the articles written about melanoma of the trunk deal specifically with melanoma of the breast nor do they discuss whether a mastectomy influences the natural course of the disease.

The rarity of this clinical problem and the complex decisions that may face other surgeons managing such cases prompted us to review our clinical experiences. We have seen 12 cases of primary melanoma of the breast region among 186 patients with melanoma of various sites during a two-year period. The clinical courses of these 12 patients are presented and the pros and cons of the surgical management of melanoma of the breast as reported in the literature are discussed.

## Material

We reviewed 186 patients with biopsy-proven melanoma referred to the Division of Surgical Oncology, at the University of California at Los Angeles (UCLA) from August, 1971 thru September, 1973. All the patients were referred to the senior author (D.L.M.) for possible immunotherapy, and a significant number of the patients had complicated histories and required special management. Many of the details of the initial surgical therapy

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TABLE 1. Reported Frequency of Melanoma of the Trunk with Survival Rates

Reference	Year	Total cases	% Trunk	5-Year Survival Rate	
				All cases	Trunk melanoma
Pack et al. <sup>40</sup>	1952	1,190	24.2	21.4%	13.7%
Fortner et al. <sup>14</sup>	1965	804	24.0	—	35.2
Mundith et al. <sup>39</sup>	1965	427	24.0	43.0	29.0
Cochran <sup>7</sup>	1969	165	15.0	50.0	36.0
Knutson et al. <sup>28</sup>	1971	230	19.6	30.0	16.0
Shah & Goldsmith <sup>44</sup>	1972	1,552	27.0	53.0	40.0
Conrad <sup>8</sup>	1972	640	37.5	{ 72.0 44.0	{ 58.0 (histologically negative node) 49.0 (histologically positive node)
Overall		5,008	15.0–37.5%	21.4–72.0%	13.7–58%

and pathological specimens were not available, thus we cannot correlate the width of normal tissue excised, diameter and thickness of the primary, the depth of invasion, etc., with the frequency of local or regional recurrences.

Among the 186 patients, we found 12 patients with primary melanoma located in the breast region. Breast region is defined according to Hicken<sup>25</sup> who showed that the lactiferous ducts spread widely over the anterolateral chest wall. The boundaries of the breast region are the clavicle, sternum, costal margin and anterior axillary line.

Five of these 12 patients were free of disease after surgical therapy. One patient had a 3 cm re-excision of a superficial spreading melanoma. Another patient died of a second cancer, adenocarcinoma of the jejunum, 81 months following excision and nodal dissection for the melanoma. The other three patients, all treated at UCLA Medical Center, had wide excision and prophylactic dissection of the axillary lymph nodes. They have been followed for 18, 20, and 26 months without recurrence of disease. One patient with a Clark's level IV lesion received post-surgical adjuvant immunotherapy.

Seven patients had recurrent disease after initial therapy (sites of recurrence and treatments are presented in Table 2). Two of the 7 patients (J.A., J.W.) had wide excision and radical mastectomy as initial therapy and had no recurrence of local or regional disease. Distant visceral metastases appeared 70 and 92 months later.

The initial treatment of the other five patients consisted of wide excisions of the melanoma only. Two patients (A.F., H.K.) had recurrence near the original scars at 12 and 24 months, followed by dissection of subsequent axillary metastases at 48 months. A third patient, the only female (J.V.) had a radical mastectomy when melanoma recurred near the old scar over her breast 58 months after initial excision. A fourth patient (S.N.) needed axillary dissection 81 months after initial therapy. This procedure delayed the reappearance of melanoma for about 40 months. The fifth patient (H.T.) had recurrence in two subcutaneous lymph nodes of the breast 18

months after excision of a melanoma in the medial breast, one lateral to the nipple and one adjacent to the lower axilla. These probably are the prepectoral and adventitious mammary lymph nodes described by Haagenensen.<sup>20</sup> He encountered them only occasionally in his personal series of over 1,000 mastectomies. Such irregular nodal tissues can be found in subcutaneous tissue in the breast parenchyma or upon the fascia covering the pectoralis major muscle.<sup>26</sup>

Only one (H.T.) of these 7 patients had dissection of the internal mammary lymphatic tissues. Since none of the 7 patients had recurrent disease in the internal mammary nodal chain even with medial or centrally located lesions, it would seem that internal mammary node dissection neither improves the regional control nor influences the distant dissemination. Six of the 7 patients received some form of immunotherapy. Treatment details and preliminary results of immunotherapy for malignant melanoma have been reported by us elsewhere.<sup>12,38</sup>

The 12 patients with melanoma of skin of the breast could be divided into three groups by their initial therapy: 1) Of six patients who had wide excision only, 5 had recurrence either near the scars or in the axilla at 12, 18, 24, 58 and 81 months that required further surgical intervention. All five had lymphadenectomy for clinically positive lymph nodes at 18, 48, 48, 81 and 98 months, followed by systemic dissemination of disease; 2) Of four patients who had wide excision and prophylactic dissection of the axillary lymph nodes, three were free of disease for 18, 20 and 26 months. The fourth patient died of an unrelated jejunal adenocarcinoma 81 months later; 3) Two patients who had wide excision and radical mastectomy had no recurrence of local or regional disease but did have distant metastases at 70 and 92 months after initial therapy.

This, it appears that wide excision of melanoma of the breast region alone is often followed by recurrence either near the scar or in the axilla and that wide excision and prophylactic axillary lymphadenectomy gave the best long-term local and regional control. Dissection of the internal mammary nodes did not seem to alter the results.

TABLE 2. Seven Patients Who had Recurrent Disease

Patient (Sex, Age)	Location of Lesion	Initial Therapy	Re-current Interval	Recurrent Site	Treatment for Recurrent Disease	Condition at Last Follow-up																																																													
J. A. (M, 24)	One inch below nipple	Wide excision & radical mastectomy	70 mon	Lung	Thoracotomy, resection of lung and mediastinal nodes, systemic immunotherapy Chemotherapy	80 mon, died with disease																																																													
			75 mon	Brain			J. W. (M, 45)	One inch medial to nipple	Wide excision & radical mastectomy	92 mon	Disseminated	Chemotherapy	95 mon, died with disease	A. F. (M, 69)	Areola	Wide excision	12 mon	Near scar	Wide excision Axillary node dissection, systemic immunotherapy Axilla re-dissection, radiotherapy	72 mon, alive and well	48 mon	Axilla	57 mon	Axilla	H. K. (M, 69)	Near nipple	Wide excision	24 mon	Near scar	Wide excision Axillary node dissection Radical neck dissection, systemic immunotherapy Chemotherapy, radiotherapy	79 mon, died with disease	48 mon	Axilla	52 mon	Low neck	66 mon	Disseminated	J. V. (F, 36)	Lower	Wide excision	58 mon	Near scar	Radical mastectomy Radiotherapy, excision and chemotherapy Forequarter amputation Intralesional BCG and systemic immunotherapy Chemotherapy	152 mon, died with disease	98 mon	Axilla	124 mon	Shoulder	134 mon	Satellois	141 mon	Disseminated	S. N. (M, 34)	Breast	Wide excision	81 mon	Axilla	Axillary node dissection Intralesional BCG Chemotherapy	143 mon, Cutaneous nodules all gone, alive and well	124 mon	Satellois	126 mon	Disseminated	H. T. (M, 53)	Medial lower	Wide excision	18 mon
J. W. (M, 45)	One inch medial to nipple	Wide excision & radical mastectomy	92 mon	Disseminated	Chemotherapy	95 mon, died with disease																																																													
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H. T. (M, 53)	Medial lower	Wide excision	18 mon	Lateral to nipple (Subcutaneous nodules)	Wide excision, total mastectomy, axillary and internal mammary node dissection, systemic immunotherapy Chemotherapy	22 mon, died with disease																																																													
			21 mon	Disseminated																																																															

We saw two patients treated with radical mastectomy. This approach could have prevented the recurrent lesions in prepectoral and axillary lymph nodes seen in another patient (H.T.).

### Discussion

In general, melanoma of the trunk has the lowest survival rate (Table 1). Cochran<sup>7</sup> hypothesized that melanoma of the trunk probably related to endogenous rather than exogenous carcinogens. His data showed that the prognosis for patients with melanoma of the exposed surfaces was better than that for melanoma of the covered areas (5-year survival rates: 58% vs 35%). Pack et al.<sup>40</sup> reasoned that patients with melanoma of the trunk had a lower survival rate because the lymphatic drainage from the trunk was potentially unpredictable. For example, the metastases from melanoma of the abdomen may spread to either groin, either axilla, either side of the neck or to all 6 regions.

McNeer and Das Gupta<sup>35</sup> showed that the prognosis for trunk melanoma could be similar to that for lesions of the extremities or head and neck, if the disease

was treated before involvement of the regional nodes. In their discussion of therapeutic approaches, McNeer and Das Gupta<sup>34</sup> listed four principles: 1) Radical neck dissection should be considered in melanoma of the infraclavicular region; 2) Bilateral dissection of the axillary or groin lymph nodes should be carried out for melanoma located at the midline dependent upon the anatomic location; 3) In melanoma of the lateral trunk, the level of the eighth rib seemed to define the direction of lymphatic spread, i.e., below this level, lymphatic drainage was primarily toward the ipsilateral groin, whereas melanoma above this line generally metastasized to the ipsilateral axilla; 4) Melanoma of the suprapubic area was prone to metastasize bilaterally to lymph nodes of the groins. There was no specific mention of unusual treatment for melanoma of skin of the breast in these discussions.

Attie and Khafif<sup>2</sup> commented that lesions located over the breast or on one side of the anterior chest wall were treated best by radical mastectomy with or without a skin graft. No clinical data or long-term results from this treatment approach were presented. Ketcham<sup>27</sup> reported that he usually performs a complete

dissection of internal mammary nodes for melanoma of the anterior chest wall unless the lesion overlies the sternum and is deeply invasive and/or ulcerating. However, he added that internal mammary nodes were seldom involved with tumor even at autopsy. Lise et al.<sup>29</sup> reported a series of 20 patients who had prophylactic internal mammary node dissection for melanoma located between the nipple lines and only one patient had metastatic disease. Thus, dissection of this nodal basin did not improve survival rate.

One wonders if prophylactic dissection of axillary lymph nodes should be carried out for melanoma of the breast region. There are as many answers and as much controversy over this question as there are to surgical treatment of early adenocarcinoma of the breast. Historically, prophylactic dissection of regional lymph nodes as an adjuvant to surgery for malignant melanoma was first proposed by Handley in 1907.<sup>22</sup> Knutson et al.<sup>28</sup> summarized 8 reports in the literature and showed that from 13 to 50% of clinically non-involved regional lymph nodes contained metastases by histological examination. The survival rate in patients with pathologically positive lymph nodes is definitely lower than for those who had no metastases to nodes (5-year survival rate, 30% vs 80%, and 15-year, 15% vs 53%).<sup>16</sup> Unlike carcinoma of the breast where the mortality rate rose sharply when four or more nodes were involved, melanoma patient survival curves are quite similar whether two nodes or multiple nodes are involved.<sup>5,18</sup>

The proponents of prophylactic node dissection point to a 10 to 20% improvement in survival when lymphadenectomy is done routinely for stage I melanoma.<sup>10,16,17,43</sup> Patients who had prophylactic lymphadenectomy had fewer problems with local recurrence and regional node metastases (9% vs 40%).<sup>17</sup> In patients with clinical stage I disease, the removal of normal regional nodes does not appear to affect the host-tumor balance because the incidence of local failure after removal of uninvolved lymph nodes was similar to that of patients who did not have lymphadenectomy.<sup>33</sup>

Skeptics of prophylactic lymphadenectomy emphasize that the difference in survival rates of incidence of recurrence between patients treated with wide resection alone and those who had added lymphadenectomy is not statistically significant.<sup>9,28,47</sup> However, even skeptics<sup>28</sup> recommend elective dissection of the regional nodes for melanoma of the head, neck, or upper extremities, when the lesion extends below the level of papillary dermis. For lower extremity lesions, they would not routinely remove the ilio-inguinal nodes except when groin dissection could be performed in continuity with the primary tumor. Improved operative techniques using separate abdominal and inguinal incisions,<sup>8</sup> and

better postoperative care<sup>30</sup> have decreased the incidence of postoperative complications.

Using a mathematical model, Polk et al.<sup>41</sup> showed that the probability for benefit from prophylactic removal of the regional nodes might outweigh the "harm" when the chance of metastases to the lymph nodes was 20% or greater. Spratt et al.<sup>46</sup> concluded that unless a cancer, including melanoma, demonstrated at least an 18% likelihood of metastases to the inguinal lymph nodes, prophylactic groin dissection could not be justified.

What are the characteristics that clinicians can use to predict the likelihood of lymph node metastases of malignant melanotic lesions? Several important prognostic factors include depth of invasion,<sup>6,37</sup> thickness of the lesion,<sup>4</sup> degree of lymphocyte infiltration,<sup>13,23</sup> mitotic rate,<sup>5,32</sup> gross diameter<sup>5</sup> and appearance.<sup>31,37</sup> The first two appear to have the most influence on the natural history of melanoma and correlate best with results of therapy, although most of the factors are interrelated.

Donnellan et al.<sup>11</sup> studied 119 cases of melanoma of the head and neck region and Wanebo et al.<sup>49</sup> studied 151 patients with melanoma of the extremity. There was a striking correlation between the depth of dermal invasion according to Clark's classification<sup>6</sup> and the incidence of eventual lymph node metastases. Mehnert and Heard<sup>36</sup> showed that wide excision and prophylactic node dissection had a 20% better 5-year survival rate over those without node dissection for intradermal lesions (Clark's level III and IV). Wanebo et al.<sup>49</sup> showed that patients with level III lesions do significantly better when they have prophylactic node dissection. Thus, many surgeons recommend elective lymph node dissection for level III or deeper lesions.<sup>19,24</sup>

Breslow<sup>4</sup> found that simultaneous evaluation of tumor thickness, as measured with an ocular micrometer, and level of invasion was of greater value in assessing prognosis than either alone. For melanoma invading 1.5 mm or deeper, Wanebo et al.<sup>49</sup> showed patients who had wide excision and node dissection had definite improvement in survival. Hansen and McCarten<sup>23</sup> also found that the addition of elective node dissection offered significantly improved survival for such lesions, especially in cases with minimal lymphocytic infiltration.

Cady et al.<sup>5</sup> found that location, gross diameter, mitotic rate and depth of invasion were all useful criteria. Elective nodal dissection benefited only 10% of the patients whose melanoma occurred on the arm, head and neck, and those with combinations of low mitotic rate, maximal diameter less than 1.5 cm or level II depth of invasion. On the other hand, all nodular melanoma and deeper lesions of the leg and trunk had more than 30% risk of regional nodal disease, and prophylactic nodal resection was indicated.

In our institution, many of the patients with stage II (positive metastases to the regional nodes) and stage III (metastases at distant sites) malignant melanoma received post-resectional adjuvant BCG immunotherapy. The long-term survival and apparent cure of patients A.F. and S.N. could be related to the immunotherapy they received. The background, rationale, treatment details and end results have been reported elsewhere.<sup>12,38</sup> Essentially, systemic BCG immunotherapy with or without additional tumor cell vaccine was only partially effective following surgical resection of tumor bulk in patients with stage III disease. However, early results using BCG immunotherapy as an adjuvant to primary surgical therapy of stage II lesions were most encouraging. At two years, the incidence of recurrence rate in BCG-treated patients was half that of the control group. BCG was more effective in patients with a smaller tumor burden at the time of initial surgical treatment.

### Conclusion

About 5% of primary malignant melanoma of the skin is located in the breast region. It appears that there is no standard surgical approach for treatment of this unique lesion. After reviewing our own clinical data (12 patients seen over two years), and the current literature, we would recommend the following therapeutic approach. The primary lesion should be treated by a wide three dimensional excision. In certain female patients, when cosmetic results are important, the major part of the breast may be saved. However, the patient should be warned that the local recurrence rate is higher after limited resection and that melanoma can metastasize to lymph nodes located in breast tissue.

Acknowledging several important pathological factors which correlate with higher incidence of metastases to the regional lymph nodes, an elective axillary dissection is recommended for all melanomas invading papillary dermis or deeper (Clark's level III or more) and/or with a maximal thickness of 1.5 mm or more as measured with a micrometer. When the regional lymph nodes are clinically positive for melanoma, a therapeutic dissection is mandatory. An internal mammary node dissection does not improve local or regional control. In our institution, when the axillary lymph nodes contain metastases on histological examination, a randomized clinical trial is underway to compare no additional therapy with postoperative adjuvant immunotherapy using BCG alone or BCG with allogeneic tumor cell vaccine.

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