Registry Data Overview

Melanoma, First Course of Treatment 2001
Analytic Cases

- Surgery
- Surgery & Chemotherapy
- Surgery & Radiation
- Surgery & Immunotherapy
- No Treatment

All Cancer, First Course of Treatment 2001
Analytic Cases

- Surgery
- Chemotherapy
- Surgery & Chemotherapy
- Radiation & Chemotherapy
- All Other
- No Treatment

Melanoma Observed Survival 2001

NCDB 93-94 100 83 73 66 62 58
UCH 93-94 100 100 91 87 87 87

Observed Survival By Combined Stage Group
Five Year Observed Survival Melanoma, 1993-1994

Source: NCDB, Commission on Cancer, ACoS
At the University of Chicago Hospitals we offer a variety of different services to meet the physical and emotional needs of every patient. We understand that each patient is unique. Our goal is to provide the best care and services that we can offer.

Melanoma is a serious form of skin cancer; however, if detected early enough melanoma is often curable. In men, melanoma often develops in areas between the shoulders and hips, whereas, in women, it usually occurs on the lower legs. Although melanoma can occur in all age groups, the chances of developing the disease increases with age. In African American patients, the palms of the hands and the soles of the feet are frequent sites for melanoma.

In 2001, the American Cancer Society (ACS) predicted approximately 1,268,000 new cancer cases in the United States. In 2002, the ACS estimated that 1,284,900 new cancer cases would be diagnosed in the United States. Of these cases, approximately 53,600 cases are expected to present as melanomas. Melanomas account for roughly 2% of new cancer diagnoses. In the United States, the incidence of melanoma is rising at a rate that exceeds that of all other cancers.

Of the 2,249 total cancer cases (1,755 analytic, 494 nonanalytical) seen at the University of Chicago Hospitals in 2001, 50 cases (28 analytic, 22 nonanalytical) were diagnosed and treated for melanoma. There were over 75 new melanoma patients seen in the clinic in 2001, including patients seen for a second opinion only, and there were 49 melanoma patients who were treated by a clinical trial. See graphs below.

Although it is not the most common cancer, melanoma can significantly alter a patient’s quantity and quality of life; therefore, prevention, early diagnosis, and effective treatment are crucial components of any comprehensive approach. Any cancer can become deadly if left untreated. The cancer committee works diligently to increase awareness and involvement of all physicians to improve our cancer program.
Surgical Treatment of Melanoma

The role of the surgeon in the care of the melanoma patient is to remove cancer for cure or palliation, prevent recurrence, and provide prognostic information to be used in making decisions for further treatment. In doing so, the surgeon may address primary, recurrent, or metastatic tumors. The number of melanoma cases occurring in the U.S. has increased dramatically in the last two decades, and most patients present with early stage disease that can be definitively treated by surgery. However, advanced disease at the time of presentation, repeated recurrence of indolent disease, or rapid progression of melanoma may require surgical treatment in conjunction with other systemic treatment modalities.

The surgical treatment of cutaneous melanoma has evolved steadily based upon studies evaluating the necessary extent of surgical resection, and upon the identification of factors that predict an increased risk for aggressive disease. Primary melanomas are excised with a surrounding area of normal tissue. This treatment strategy prevents local recurrences from microscopic satellite nests of tumor cells that are near to, but not contiguous with the primary lesion. The amount of normal tissue that must be removed to assure a low risk of recurrence is based on several factors, the most important of which is the thickness of the primary melanoma. An accurate measurement of tumor thickness is necessary in order to plan appropriate definitive surgery. Therefore, a biopsy of any suspicious pigmented lesion should encompass its entire depth.

Once a diagnosis of melanoma is made, initial staging is determined by pathology review of the tumor biopsy and additional radiological studies in high-risk patients. Melanoma staging was revised in 2002 to reflect newly identified prognostic factors, with changes incorporated in the classification of the primary tumor lesion (T), lymph node metastatic disease (N), and systemic metastatic disease (M). The primary determinant of T stage continues to be tumor thickness, while recent revisions incorporate the histologic level of invasion into the staging of thin (≤ 1 mm thick) melanomas. In addition, ulceration of the primary lesion is a poor prognostic factor and increases the T stage for tumors of any thickness. For lymph node metastases, the number of metastatic nodes determines the N stage, although sub-stages have now been designated based on the lymph node tumor burden. Finally, systemic metastases are now stratified by site and the serum level of the chemical marker LDH. Although these changes have made the stage grouping for melanoma increasingly complex, they may one day help to identify high-risk patients who will benefit from aggressive therapies.

After any necessary pre-operative staging, surgical removal of the primary melanoma is indicated for patients without advanced metastatic disease. Historically, melanoma was excised with a margin of normal skin 3 to 5 cm in all directions from the tumor. Excisions of this extent often required skin grafting for closure and healing of the wound. From the 1970s to the 1990s, randomized studies were performed examining the excision margin necessary for invasive melanomas. In a study conducted by the World Health Organization, over 600 patients with melanomas up to 2.0 mm thick were treated by excision with narrow (1 cm) margins or wide (3 cm) margins. No increased rate of tumor recurrence or death was seen in the group who received excisions with narrow margins. However, within this group, the local recurrence rate for patients with tumors less than 1.0 mm thick was 1%, versus 6% for patients with tumors 1.0 to 2.0 mm thick. A second study conducted by the U.S. Intergroup Melanoma Committee evaluated the efficacy of 2 cm margins versus 4 cm margins for patients with intermediate thickness (1.0 to 4.0 mm) melanomas. In this trial, no significant differences in the recurrence rates or survival were seen between the two treatment groups. Based on the results of these two trials, invasive melanomas less than 1.0 mm thick are commonly excised with a 1 cm margin of surrounding normal tissue, and those 1.0 to 4.0 mm thick are excised with a 2 cm margin. No controlled studies of thick melanomas (> 4 mm) have been performed, and there are no retrospective data suggesting that margins greater than 2 cm are beneficial. In situ melanomas are adequately treated by complete excision.

At the time of melanoma excision, the surgeon will also perform dissection of the regional lymph node bed if metastatic nodal disease is clinically apparent. Prior to the era of sentinel lymph node biopsy, elective removal of the regional lymph nodes for patients with intermediate thickness melanomas (1.0 to 4.0 mm) was advocated by some surgeons in order to increase the likelihood of complete tumor removal and cure. The potential benefits of
elective node dissection for any patient must be weighed against the risk of symptomatic lymphedema following major lymph node dissection, which may occur in up to 50% of cases. Three worldwide, randomized, multi-institutional trials conducted before 1995 did not show a survival or recurrence benefit to elective lymph node dissection in patients with intermediate thickness melanomas. However, advocates for elective node dissection noted that retrospective subgroup analyses in these studies suggested a benefit for certain patients defined by tumor thickness, tumor location, gender, or age.

Sentinel lymph node biopsy has diminished the clinical significance of the elective node dissection controversy. During this procedure, the injection of colored and / or radioactive tracer at the site of a melanoma is used to define the lymphatic drainage pathways and remove the potential first site of lymph node metastases without the morbidity of a major lymph node dissection. In experienced hands, the information gained from the examination of the sentinel node or nodes is equivalent to that gained by elective node dissection in 98% of cases. For patients with > 1.0 mm thick melanomas, sentinel lymph node biopsy is indicated if the diagnosis of nodal metastases would lead to further surgical or medical therapy. Ongoing and future studies will determine whether patients with sentinel lymph node disease that is detected only by microscopic examination of specially stained tissue or by laboratory DNA analysis derive benefit from any additional treatment.

For patients who develop symptomatic systemic metastases from melanoma, surgery is often the most effective means to achieve palliation. There are no controlled data regarding which, if any, asymptomatic patients should undergo surgery for metastatic disease. Therefore, the history and pattern of metastatic disease must be considered for each case individually. Prolonged survival after removal of metastases has been demonstrated in patients with a long interval before the development of metastatic disease, and in patients with only one metastatic tumor. However, it must be noted that at large cancer centers, the two-year survival rate of patients carefully selected to undergo these procedures is only 15-30%.

Patients with multiple cutaneous or subcutaneous metastases of an extremity and no evidence of systemic disease are suitable candidates for isolated limb perfusion. Isolated limb perfusion is a highly specialized surgical procedure during which the blood flow to an arm or leg is intra-operatively sequestered from the rest of the body. The isolated circulatory circuit is then used to deliver chemotherapy for a brief period of time at doses that would be toxic if delivered systemically. Complete response rates of 60-80% are reported at specialty centers, although most of these patients will eventually recur.
The Role of the Hematologist/Oncologist in Treating Melanoma

The Melanoma Program in Hematology/Oncology is responsible for administering systemic therapy for patients with locally advanced or metastatic disease, and is the driving force for the scientific development of new therapeutic approaches.

Adjuvant therapy: Patients with thin (<1.00 mm) cutaneous melanomas are treated successfully with surgery alone. If the skin lesion is 1.00 mm or deeper, then a sentinel lymph node biopsy is performed by our surgical oncology colleagues. If the regional lymph nodes are involved with either microscopic or macroscopic disease, then a complete lymph node dissection is performed and the patient is considered for adjuvant therapy. Until recently, there was no adjuvant therapy that reduced the recurrence rate and improved the survival for patients with resected stage III melanoma. However, immunotherapy with interferon-2b has been shown to improve disease-free survival from 26% to 37%, making it the standard treatment in this setting.

Although adjuvant treatment with interferon-2b is effective, it is accompanied by significant side effects, which has motivated investigation into new therapies that may be at least as effective but better tolerated. Melanoma is a tumor type that is responsive to interventions that boost the body’s immune response against the cancer, so immunotherapy remains a focus of therapeutic development. Our center has recently completed a phase I study of a monoclonal antibody against CTLA-4, an inhibitory receptor expressed on activated T lymphocytes, to augment the function of tumor-reactive T cells. We are currently carrying out a multicenter trial of a melanoma vaccine with or without another immunomodulatory factor, GM-CSF, in the post-surgical adjuvant setting. It is hope that these and other studies will lead to the establishment of improved standard adjuvant therapies for patients with melanoma.

Metastatic disease: The overall survival for patients with metastatic melanoma is 6-9 months despite current treatment approaches. Clearly, new strategies are needed to combat this disease. Chemotherapy alone causes tumor shrinkage in only around 15% of patients and only rarely is a patient cured. However, immunologic therapies are proving to be more interesting, leading to durable complete responses in a significant minority of patients. We recently developed in our own laboratory and tested in pilot clinical trials a novel melanoma vaccine. Of 20 patients treated, 10% had a complete response, other patients had lesser clinical responses, and the median survival was over 12 months. Monitoring of the immune response in treated patients showed a significant increase in melanoma-specific T cells. Follow-up vaccine trials aiming to build upon this approach are underway.

Another strategy being investigated involves combining chemotherapy with immune-stimulating cytokines. The underlying premise is that chemotherapy agents will induce some tumor cell death, generating antigens that will be picked up by cells of the immune system. The cytokines will then boost the resulting immune response and promote further tumor cell death. In a recent phase II trial our outpatient chemoinmunotherapy regimen has given response rates of 23-43% and a median overall survival of over 15 months. Testing of this approach in a larger cohort of patients is being planned.

Finally, the modest clinical responses seen with standard therapies in advanced melanoma have motivated the exploration of new agents in this disease. Blood vessel-stopping anti-angiogenic drugs, novel chemotherapeutics, and molecularly targeted signal transduction inhibitors are all being studied in phase II clinical trials. We will continue to investigate new drugs and integrate those that are most successful to build effective combination therapies in the future.
The Role of Radiation Therapy in Malignant Melanoma

While radiation therapy (RT) occupies an important role in the treatment of skin cancers per se, its role in the treatment of malignant melanoma is more limited. RT is occasionally used in the treatment of primary melanoma tumors, particularly unresectable or incompletely resected lesions. RT is also indicated in select patients with regional nodal disease and those with tumors in "special sites", e.g. posterior uveal tumors. Its primary role, however, is the treatment of metastatic lesions, particularly central nervous system (CNS) metastases.

While cutaneous melanomas are typically treated with surgical excision, several sites are instead treated with definitive RT. Posterior uveal tumors receive a specialized type of RT known as plaque brachytherapy. Plaque brachytherapy involves a radiation implant placed surgically on the sclera directly over an intraocular tumor. While first introduced in the late 1920s using a cobalt-60 implant, plaque brachytherapy is performed most commonly today with Iodine-125. This approach is associated with excellent tumor control rates and visual preservation in the majority of patients with small diameter lesions away from the fovea. Large lesions are unlikely to be controlled with plaque brachytherapy. Another site commonly treated with definitive RT is the vagina. Unfortunately, many vaginal melanoma patients present with locally advanced disease and are poorly controlled despite high doses of external RT and intracavitary brachytherapy.

The most important use of RT today, however, in patients with malignant melanoma is in the treatment of metastatic lesions, particularly CNS metastases. Patients with multiple CNS metastases respond well to whole brain RT. Patients with limited volume disease, however, are candidates for stereotactic radiosurgery (SRS). SRS is an outpatient procedure and involves the delivery of high radiation doses to a small intracranial volume with high precision. SRS is performed with either a Gamma Knife or a modified linear accelerator. At the University of Chicago, the SRS program is under the joint direction of Drs. R. Loch Macdonald (Neurosurgery) and Arno J. Mundt (Radiation Oncology). Between 7/94 and 7/01, 85 patients with CNS metastases were treated with SRS, of which 11 had malignant melanoma. Overall, <2% of patients developed a significant RT-related sequelae supporting the continued routine uses of SRS in these patients.

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The Role of Dermatology in Diagnosing and Treating Melanoma

Cutaneous melanoma is becoming a health problem of epidemic proportions. Apart from being the skin cancer with highest overall mortality, it tends to affect patients at a younger age than most basal cell or squamous cell carcinomas. This results in a relatively great number of years of potential life lost to this cancer, and a proportionately high social impact. The incidence of reported melanoma cases has risen strikingly in recent decades, at a rate of increase that exceeds that of any other human cancer. Although part of this increment may be due to increased awareness or changes in diagnostic criteria, there also seems to be a real increase in incidence. Since there is still no reliable cure for advanced disease, it is crucial to detect melanoma in its early, potentially curable stages. Here dermatology can play a vital role.

Many factors are associated with the risk of developing melanoma. Among them, exposure to ultraviolet radiation, particularly in childhood and in intense bursts causing severe sunburns, appears to be of great significance. Patient with certain rare syndromes associated with decreased capacity for DNA repair (such as xeroderma pigmentosum) have increased rates of melanoma. Immunosuppression and personal or family history of melanoma are also associated with higher risk. Of note, several important risk factors are gross phenotypes such as fair skin, blue or green eyes, red hair, and the number of typical acquired, congenital, or atypical (dysplastic) nevi, and of freckles. Because of their ability to monitor and evaluate the latter phenotypic associations, dermatologists are ideally placed to identify patients at risk, including those patients who come to clinical attention because of other concerns such as warts or acne. For this reason, most dermatologists strongly recommend that patients with skin complaints receive a complete skin examination, at least at their initial visit.

One focus of such comprehensive dermatologic examinations is the detection of potential precursor lesions to melanoma. Large (> 20 cm) congenital nevi have a 10% or more lifetime risk of developing melanoma. The terms atypical mole or dysplastic nevus denote an acquired melanocytic nevus that resembles melanoma, clinically and histologically. Points of clinical similarity include large size (generally over 5 mm), poor circumscription, border irregularity, a play of colors, and asymmetry. The first clinical challenge confronting the dermatologist is to discriminate an atypical nevus from melanoma, so that needlessly wide excisions are avoided.

Rapidly evolving techniques, such as dermoscopy (magnifying lens directly applied to the skin surface), telespectrophotometry (analysis of color variation), ultrasonic imaging, and macroscopic spectral imaging may help dermatologists to make this distinction. Systematic use of digitally stored clinical photographs (“mole mapping”) permits reliable detection of changing nevi, themselves a strong risk factor for melanoma. Atypical nevi, whether occurring sporadically or in the context of a melanoma-prone familial predisposition, are proven to be an independent risk factor for development of melanoma. As such, atypical nevi can function both as markers of a melanoma risk and as actual precursors for melanoma. However, it is also true that the vast majority of nevi never undergo malignant transformation. Moreover, nevi are not an obligatory step in development of melanoma, most of which apparently arise from epidermal melanocytes. Thus dermatologists must view every pigmented lesion individually and assess its melanoma risk by carefully evaluating its gross characteristics.

Another key goal of comprehensive dermatologic examinations is to detect melanoma at an early stage, at which cure is most likely. This represents a great opportunity for the dermatologist, because melanoma is one of the few
cancers to arise on a readily visible body surface, and to have a pigmented pattern that often correlates with its pathologic changes. Patients with thin melanomas (with Breslow thickness <1 mm) have an overall five-year survival of greater than 90%. The main features correlating with worse prognosis in thin melanomas are higher Breslow thickness, ulceration, vascular invasion, vertical growth phase, regression, and microscopic satellitosis (nests of melanoma cells separate from the main lesion).

Dermatologists, as the acknowledged experts on management of skin lesions, play a crucial role in combating the melanoma epidemic. Over the course of three years of specialized residency training, dermatologists learn to recognize those gross characteristics that point to a diagnosis of melanoma or to its potential precursors such as atypical melanocytic nevi and congenital nevi. They also learn how to distinguish these dangerous lesions from harmless growths such as common acquired nevi, seborrheic keratoses, and dermatofibromas. The dermatologic consultant can accurately and rapidly screen most lesions, equipped only with a bright light and a low-power magnifying lens. Accordingly, dermatologists perform highly cost-effective management of pigmented lesions, offering welcome reassurance to many patients and potentially life-saving interventions to a few.

In addition to their bedside diagnostic skills, dermatologists are also intensively trained in the diagnostic histopathology of melanocytic lesions, and how to correlate the gross and microscopic appearance of such neoplasms. In fact, dermatology residents typically spend much more time studying the histopathology of skin lesions than pathology residents do. In this way dermatologists come to incorporate histologic thinking into their understanding of tumor pathophysiology in a way that very few other clinical specialties equal.

Finally, dermatologists are highly trained in the surgical management of primary melanoma of the skin, and this expertise is gaining in emphasis with each passing year. The combination of a deep, histopathology-based knowledge about skin lesions, together with expert surgical skills, permits dermatologists to perform surgical procedures in ways that are most likely to yield the most efficient diagnostic and therapeutic results. In certain medically advanced countries, including Japan and Germany, dermatologists perform not only the primary excisions of melanoma but also lymphadenectomies. In the United States, this training is not emphasized, and the role of dermatologists is rather to complement their colleagues in surgery and medical oncology, using a team approach in order to achieve the best outcome for patients with melanoma.

Because patients who have had one melanoma are at increased risk of developing a second one, dermatologists have an ongoing role in patients’ care long after the primary cancer has been excised. In fact, most melanoma patients should probably receive comprehensive skin examinations at least yearly for the rest of their lives. Furthermore, examination of first-degree blood relatives of melanoma patients is also recommended, as not infrequently such relatives are found to have suspicious pigmented lesions that warrant biopsy or clinical follow-up.
The Role of Plastic Surgery in the Treatment of Melanoma

Plastic surgery has traditionally held a prominent role in the multidisciplinary approach to the treatment of melanoma. Specifically, the role of the plastic surgeon is threefold. First, the diagnosis, ablative treatment and aesthetic reconstruction of melanomas of the head and neck region have been performed by plastic surgeons. Critical to the management of melanomas in the head and neck region are the crucial structures of the face, forehead, ears, and scalp that are often involved with melanoma. Tumors involving, abutting and encompassing these crucial structures must be managed by carefully planned ablative surgical operations that will ultimately provide the patient not only with an effective oncologic treatment but also with the restoration of form, function and aesthetics. Total or partial eyelid, nose, ear and forehead reconstructions are examples.

Secondly, plastic surgery is integral in the management of trunk and extremity melanoma. Ablative operations for melanoma in the trunk and extremity can often times leave large tissue and structural defects that the plastic surgeon can restore with local, regional and distant flaps of skin, muscle or composite tissues. Structural restoration and composite tissue reconstruction can afford the patient a faster recovery than traditional methods of direct wound closure. Total or partial thumb, foot and trunk reconstructions are examples.

Finally, the most important and effective role that plastic surgeons play in the treatment of melanoma is that of surveillance and early detection. Plastic surgeons are often frontline physicians that examine and diagnose changing pigmented lesion of the skin especially in the head and neck regions. With early detection and treatment, less radical surgical treatment is possible and overall survival benefit can be given.
The Role of Nursing in Melanoma Cancer

Nursing care in the patient diagnosed with melanoma can be very challenging. Whether the patient is newly diagnosed with a very thin melanoma or with distant metastatic disease, the patient needs support, education, and prompt care. Our patient population has an age range from mid teens to late 80s; we are therefore meeting a variety of people bringing different life experiences with them. Our role is crucial in the emotional support of the patient and the family. Some patients had been given a diagnosis years ago of a stage I or II melanoma that carries anywhere from 50% to a 95% survival rate and are returning with distant metastatic disease looking at a survival rate of less than a year. Such patients are dealing with the shock and anger that accompany disease recurrence. We are also a key figure in the education of the patient. We teach them about the biology of their disease, the therapy they are about to receive, and the side effects they can expect and how to manage them. And since time is of the essence, it is important that we start treatment as quickly as possible, working together with the physicians, surgeons, and radiation oncologists to treat the patient in a collaborative effort. The role of the research nurse is to identify, screen and enroll patients onto clinical trials. After enrollment, we monitor and report toxicities associated with the treatment plan. The melanoma research nurse acts as the central liaison for the patients, from answering questions to coordinating treatment plans to facilitating medical attention in emergency situations. This is all done in an effort to give the best possible care to the patient and their families.