

Melanoma: Isolated Limb Perfusion

What We Know

- › Although integumentary involvement accounts for 95% of melanoma cases, melanoma occurs in other sites, including the lymph nodes, GI system, genitourinary tract, eyes, and leptomeninges (i.e., the arachnoid and pia mater)
 - Almost half of all primary cutaneous (i.e., skin) melanoma lesions occur on the extremities (i.e., arms or legs). For women melanoma most commonly shows up on the lower legs and for men it appears more often on the head or trunk. As many as 85% of patients who have primary melanoma lesions on an extremity develop locoregional (i.e., local or regional and in the vicinity of the original/primary site) recurrence or metastases throughout the extremity (called in-transit metastases), including in the lymph system of the extremity^(4,5)
 - Although in-transit metastases are a strong predictor of concurrent or subsequent distant metastasis, treatment of the affected limb is important because, if left untreated, the lesions are associated with increased mortality and can cause significant morbidity such as bleeding, ulceration, pain, infection, edema, and impaired function⁽⁸⁾
- › Treatment of extremity recurrence or metastasis depends on the size and number of melanoma lesions
 - One or a few small melanoma lesions can typically be treated by simple surgical excision⁽⁴⁾
 - Treatment options for patients with multiple and/or large melanoma lesions include radiation therapy, laser ablation, and intralesional injections with anticancer agents⁽⁶⁾
 - The use of systemic chemotherapy, which can include single or combination infusions of antineoplastic, immunotherapeutic, or biologic agents, for treatment of extremity recurrence or metastasis may cause toxicity or other side effects associated with systemic chemotherapy.
 - Isolated limb perfusion (ILP; i.e., a type of regional high-dose chemotherapy or radiation therapy in which the agent is delivered intra-arterially and circulated and absorbed in the extremity only) has been used to treat extremity recurrence and metastasis of melanoma in clinical trials and at technologically advanced treatment centers since the late 1950s⁽⁶⁾
 - Treatment of in-transit melanoma (ITM) may require a combination of systemic and localized therapies, such as ILP⁽⁷⁾
 - Isolated Limb Infusion (ILI) is a recently developed treatment as a less invasive alternative to ILP which involves the infusion of chemotherapy to the affected limb⁽⁶⁾
 - Amputation may be indicated for aggressive disease in some instances; however, it is associated with severe disability and poor quality of life⁽⁶⁾
- › ILP is the recommended treatment for multiple and/or large recurrent melanoma lesions and for metastatic melanoma lesions that are confined to an extremity^(2,6)
 - The extremity is isolated from the rest of the body's circulatory system using bypass technology similar to that used in cardiopulmonary bypass surgery⁽⁷⁾
 - Isolation of the limb's circulation is achieved by clamping and cannulating the major arteries and veins, connecting the patient to an oxygenated extracorporeal circuit, ligating collateral vessels, and applying a tourniquet proximal to the site of perfusion⁽⁷⁾

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Authors

Teresa-Lynn Spears, RN, MSN
Cinahl Information Systems, Glendale, CA

Nathalie Smith, RN, MSN, CNP
Cinahl Information Systems, Glendale, CA

Reviewers

Darlene Strayer, RN, MBA
Cinahl Information Systems, Glendale, CA

Lee Allen, RN, MS
Glendale Adventist Medical Center,
Glendale, CA

Nursing Executive Practice Council
Glendale Adventist Medical Center,
Glendale, CA

Editor

Diane Hanson, MM, BSN, RN, FNAP

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- Creating two circulation systems—one within the extremity and the other throughout the rest of the body—is beneficial because it greatly reduces the risk for severe systemic toxicity and enables focused drug therapy in concentrations that are 10 times higher than those possible with systemic treatment using the same drug
- The temperature of the extremity is increased to 101.3–103.1°F (38.5–39.5°C)⁽³⁾
 - Increasing the extremity temperature improves the physiologic response by causing vasodilation in the subdermal and dermal tissue which improves local delivery of the therapeutic agent⁽³⁾
 - Extreme hyperthermia is avoided; tissue temperatures of 106.7–109.4°F (41.5–43°C) can yield a high response rate but are associated with increased risk for major adverse effects
- The treatment agent is administered into the arterial circulation of the extremity while the rest of the body’s circulation system is bypassed⁽⁶⁾
 - Melphalan (Alkeran), an antineoplastic alkylating agent, with actinomycin D is considered the gold standard for ILP treatment of melanoma lesions in the extremity⁽²⁾
 - Effective treatment requires circulation of the drug(s) at an elevated temperature for 60–90 minutes
 - Continuous monitoring for systemic drug leakage, flow balance, appropriate hyperthermia levels in the extremity, and pressures (e.g., central pressure and extremity venous and arterial pressure) is important
 - When drug perfusion is completed, the extremity’s circulation is “washed out” (i.e., rinsed or cleansed) with an electrolyte rinse solution
- ILP is indicated for therapeutic use but not for prophylactic use⁽⁶⁾
- Evidence shows that ILP has a higher response rate than ILI; however, ILP has a higher risk of toxicity and more rare complications such as compartment syndrome or amputation⁽⁸⁾
- › ILP is associated with acute and long-term adverse effects^(2,5). ILP is, however, typically well-tolerated by most patients with minimal regional toxicity⁽⁸⁾
 - Potential acute adverse effects of ILP include edema with blistering, erythema, and damage to deep tissue by the development of compartment syndrome⁽²⁾
 - Amputation is indicated in rare cases of ILP-related adverse effects⁽⁸⁾
 - ILP is associated with the potential for long-term impairment in limb function⁽⁵⁾
 - Impaired limb function is caused by persistent swelling of the limb as a result of lymphedema and localized toxicity in articular ligaments and capsules⁽⁵⁾
 - Common long-term adverse effects of ILP include joint stiffness and muscle atrophy, and transient neuropathy reported by 40-60% of patients⁽⁶⁾
 - About 20 years after undergoing ILP, 33% of patients report having difficulty with moderately strenuous/difficult tasks, and 67% report not having any or having only slight impairment in performance of daily activities⁽⁵⁾
- › Investigators evaluating health-related quality of life (HRQoL) among patients who have in-transit melanoma metastases treated with ILP concluded that, aside from potential transient diminishment of HRQoL related to local toxicity, patients with complete treatment response typically returned to baseline HRQoL within 1 year of treatment. The researchers concluded that ILP can be a useful palliative treatment for patients with in-transit melanoma⁽⁶⁾
- › In a systematic review investigators found that ILP had an objective response rate of 77% and ILI had an objective response rate of 62% but far fewer complications⁽⁶⁾

What We Can Do

- › Learn about the use of ILP in treatment of melanoma so you can accurately assess your patients’ personal characteristics and health education needs; share this information with your colleagues
- › Assess your patients for extremity lesions and encourage them to become familiar with their skin by performing routine self-examination
 - If appropriate, encourage your patients to talk with their primary, dermatology, or oncology clinician if they are concerned about symptoms or other personal risk factors
 - Encourage patients being treated with ILP to discuss the treatment so you can provide supportive educational information
- › Educate your patients regarding the importance of following a total sun avoidance program, including the regular use of sunscreen (for more information, see *Evidence-Based Care Sheet: Melanoma: Sunscreen Use*)

- › Provide emotional support for your patients who have melanoma and encourage them to ask their oncology clinician for a referral to a clergy person or a mental health clinician, if appropriate, for counseling on coping strategies, palliative care, and if appropriate, hospice. (for details, see *Evidence-Based Care Sheet: Melanoma: Assessment for Psychological Adjustment* ; *Evidence-Based Care Sheet: Melanoma: Coping Strategies* ; *Evidence-Based Care Sheet: Melanoma: Coping Through Spiritual and Religious Beliefs* ; and *Evidence-Based Care Sheet: Melanoma: Psychological Adjustment by Disease Stage*)
- › Assist patients to focus on health rather than illness by providing them with correct information and emotional support to meet their activities of daily living. A recent study evaluated patient experiences with ILP and found that patients reported needing more nursing support to focus on health and assistance with dealing with the negative side effects of the treatment (1)
- › Collaborate with your hospital's medical education department to provide education for clinicians of all specialties regarding ILP treatment of melanoma

Coding Matrix

References are rated using the following codes, listed in order of strength:

M Published meta-analysis	RV Published review of the literature	PP Policies, procedures, protocols
SR Published systematic or integrative literature review	RU Published research utilization report	X Practice exemplars, stories, opinions
RCT Published research (randomized controlled trial)	QI Published quality improvement report	GI General or background information/texts/reports
R Published research (not randomized controlled trial)	L Legislation	U Unpublished research, reviews, poster presentations or other such materials
C Case histories, case studies	PGR Published government report	CP Conference proceedings, abstracts, presentation
G Published guidelines	PFR Published funded report	

References

1. Ekenberg, M., Wesslau, H., Bagge, R.O., & Engström, M. (2019). Patient experiences with isolated limb perfusion for malignant melanoma – A qualitative study. *Eur J Oncol Nurs*, 43. doi:10.1016/j.ejon.2019.101672 **(R)**
2. Falk Delgado, A., Zommodi, S., & Falk Delgado, A. (2019). Sentinel Lymph Node Biopsy and Complete Lymph Node Dissection for Melanoma. *Curr Oncol*, 21(6), 54. doi:10.1007/s11912-019-0798-y **(RV)**
3. Grünhagen, D. J., Verhoef, C., & Tyler, D. S. (2016). Isolated limb perfusion for stage III melanoma: Does it still have a role in the present era of effective systemic therapy?.includes discussion. *Oncology (08909091)*, 30(12), 1045-1052. **(GI)**
4. Harding, M.H. (2020). Integumentary Problems. In J. Kwong, D. Roberts, D. Hagler, & C Reinisch (Eds.), *Lewis's Medical-Surgical Nursing: Assessment and Management of Clinical Problems* (pp. 413-415). St.Louis, MO: Elsevier. **(GI)**
5. Knorr, C., Melling, N., Goehl, J., Drachsler, T., Hohenberger, W., & Meyer, T. (2008). Long-term functional outcome after hyperthermic isolated limb perfusion (HILP). *International Journal of Hyperthermia*, 24(5), 409-414. doi:10.1080/0265673080 **(R)**
6. Read, T., Lonne, M., ... Sparks, D.S. (2019). A systematic review and meta-analysis of locoregional treatments for in-transit melanoma. *J Surg Oncol*, 119(7), 887-896. doi:10.1002/jso.25400 **(M)**
7. Read, R.L., & Thompson, J.F. (2019). Managing in-transit melanoma metastases in the new era of effective systemic therapies for melanoma. *Expert Rev Clin Pharmacol*, 12(12), 1107-1119. doi:10.1080/17512433.2019.1689121 **(RV)**
8. Wright, F.C., Kellett, S., ... Hong, N.J.L. (2020). Locoregional management of in-transit metastasis in melanoma: an Ontario Health (Cancer Care Ontario) clinical practice guideline. *Curr Oncol*, 27(3), e318-e325. doi:10.3747/co.27.6523 **(G)**