

# HYPERTHERMIC PERFUSION IN CLINICAL PRACTICE: ISOLATED LIMB PERFUSION

## Melanoma and soft tissue sarcomas of the limb

Melanoma and soft tissue sarcomas are malignant tumors originating from the skin and from the soft connective tissues. Hyperthermic Isolated Limb Perfusion (ILP) with chemotherapy drugs is an accepted treatment modality that achieves regional control in advanced stage melanoma of the extremities or tumor recurrency after excisional surgery [1]. In advanced stage melanomas of the limb in which malignant cells have migrated to the surrounding tissues and/or to regional lymph nodes, i.e. in-transit metastases, ILP is the most efficacious procedure to obtain local control and to achieve the limb salvage [2]. Similar results are obtained for non-resectable soft tissue sarcoma of the limb [3].

## Isolated limb perfusion (ILP)

Perfusion of an isolated limb is achieved by surgical cannulation of the two main blood vessels, an artery and vein, after complete vascular exclusion of all of the collateral vessels and positioning of an hemostatic tourniquet at the limb root. After having reached a complete vascular isolation, the limb perfusion is selectively achieved with only minimal blood leakage to the systemic circulation. Vascular isolation of the limb could be obtained by interventional radiology, with the use of special balloon catheters. After surgical or radiological vascular isolation, the limb perfusion is performed by recirculating the blood, previously oxygenated and heated at 39-42° C, by the use of a special device for extracorporeal circulation. Chemotherapy drugs and/or cytokines are eventually added to the blood during the hyperthermic recirculating phase, that usually lasts 60 minutes [3].

## Advantages of ILP

The advantages of ILP, compared to systemic chemotherapy (be it neo-adjuvant or adjuvant) are the following:

1. the possibility to use much higher, and therefore much more effective, concentrations of the cytotoxic chemotherapy drugs;
2. the reduced systemic adsorption of the cytotoxic drug (through the vascular isolation and selective perfusion of the limb), resulting in reduced systemic toxicity;
3. the possibility to clear, at the end of the procedure, the drug not adsorbed from the limb;
4. the possibility of regionally administering the drug at a high temperature, increasing both its cytotoxic activity and its penetration into the tumor bulk.

## Cytotoxic drugs used in ILP

The drugs commonly used in ILP are Melphalan and/ or Doxorubicin [4]. Due to its systemic toxicity, the additional injection of Tumor Necrosis Factor- $\alpha$  (TNF-  $\alpha$ ) in ILP must be done only after complete vascular isolation of the limb and blood leakage monitoring. Blood leakage from the isolated limb is monitored after injection of radio-labeled albumin and only a detection of less that 10% of radioactivity in the systemic circulation is considered safe for the Patient [1, 4, 6].

## Current indication for ILP

The clinical indications to the combined surgical and oncological treatment by ILP are the following [1, 2]:

1. melanoma of the limb with in-transit metastases (Stage IIIA, according to MD Anderson Cancer Center staging system);
2. melanoma of the limb with in-transit metastases to regional lymph nodes (Stage IIIB, according to MD Anderson Cancer Center staging system);
3. association of the two above mentioned stages (Stage IIIAB, according to MD Anderson Cancer Center staging system);
4. primary, locally advanced and not resectable soft tissue sarcomas of the limb.

## Bibliography

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