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Calculating regional tissue volume for hyperthermic isolated limb perfusion: Four methods compared

D. Cecchin [a,*], A. Negri [b], A.C. Frigo [c], F. Bui [a], P. Zucchetta [a], V. Bodanza [a], M. Gregianin [d], L.G. Campana [e], C.R. Rossi [e], M. Rastrelli [e]

[a] *Nuclear Medicine Unit, Department of Medicine DIMED, University-Hospital of Padova, Italy*
[b] *Medical Physics Unit, Veneto Institute of Oncology IOV-IRCCS, Italy*
[c] *Biostatistics, Epidemiology and Public Health Unit, Department of Cardiac, Thoracic and Vascular Sciences, University-Hospital of Padova, Italy*
[d] *Radiotherapy Unit, Veneto Institute of Oncology IOV-IRCCS, Italy*
[e] *Surgical Oncology Unit, Veneto Institute of Oncology IOV-IRCCS, Italy*

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Abstract

Introduction: Hyperthermic isolated limb perfusion (HILP) can be performed as an alternative to amputation for soft tissue sarcomas and melanomas of the extremities. Melphalan and tumor necrosis factor-alpha are used at a dosage that depends on the volume of the limb. Regional tissue volume is traditionally measured for the purposes of HILP using water displacement volumetry (WDV). Although this technique is considered the gold standard, it is time-consuming and complicated to implement, especially in obese and elderly patients.
Aim: The aim of the present study was to compare the different methods described in the literature for calculating regional tissue volume in the HILP setting, and to validate an open source software.
Methods: We reviewed the charts of 22 patients (11 males and 11 females) who had non-disseminated melanoma with in-transit metastases or sarcoma of the lower limb. We calculated the volume of the limb using four different methods: WDV, tape measurements and segmentation of computed tomography images using Osirix and Oncentra Masterplan softwares.
Results and conclusion: The overall comparison provided a concordance correlation coefficient (CCC) of 0.92 for the calculations of whole limb volume. In particular, when Osirix was compared with Oncentra (validated for volume measures and used in radiotherapy), the concordance was near-perfect for the calculation of the whole limb volume (CCC = 0.99). With methods based on CT the user can choose a reliable plane for segmentation purposes. CT-based methods also provides the opportunity to separate the whole limb volume into defined tissue volumes (cortical bone, fat and water).

Keywords: PET/CT; Melanoma; Volume calculation; Hyperthermic isolated limb perfusion

Introduction

Soft tissue sarcomas (STS) form a heterogeneous group of malignant tumors accounting for approximately 1% of all cancers.[1] About 60% of sarcomas arise in the limbs, with a higher prevalence in the lower limbs.[2] In 5−10% sarcoma cannot be resected with adequate margins so these patients become candidates for amputation, although this affords no significant improvement in survival.[3,4] Hyperthermic isolated limb perfusion (HILP) offers an alternative to amputation, achieving an limb-sparing rate of 70%, and a complete tumor necrosis in 30% of cases.[5] The incidence of in-transit metastases in melanoma is 3%. Clinically, these metastases occur as single or multiple nodules located in the epidermis, dermis, or subcutaneous fat.[6] Patients with numerous nodules should receive locoregional therapies: HILP is the most effective treatment and achieves global response rates at 2 months of 80%−90%, and complete responses in around 50% of cases.[7]

* Corresponding author.
E-mail address: diego.cecchin@unipd.it (D. Cecchin).

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HILP is a surgical procedure that employs melphalan and tumor necrosis factor-alpha (TNF-α) at 38−41 °C, administered for 60 min using arterial and venous cannulation and a tourniquet on the limb to prevent systemic leakage.[8]

The melphalan dosage depends on the limb's volume (10/13 mg/L of limb with an upper limit of 120 mg), calculated on the basis of the water displaced in a tank after immersing the limb.[9] Other methods can be used, including: dosage by body weight, dosage by ideal body weight, or multiple circumference measurements.

The aim of this study was to compare the different methods used in the literature to calculate regional tissue volume for HILP, and to validate an open-source software (Osirix).

Materials and methods

Patient data

We reviewed the charts of 22 patients (11 males and 11 females) with a mean age of 63.5 years (min 40; max 76; SD 9.49) who were suffering from non-disseminated melanoma with in-transit metastases or sarcoma of the lower limb (period of recruitment from Dec/2009 to Aug/2013). The patients' body weight varied between 54 and 106 kg (mean 77.6; SD 12.3). The in-transit metastases/sarcomas involved the left lower limb in 12/22 patients and the right lower limb in 10/22. Two patients repeated the measurement (but not HILP treatment) after a period of 3 and 8 months. Before surgery, all patients underwent a complete oncological assessment, limb volume calculation, whole-body PET/CT (including the lower limbs) and regional lymph node ultrasound (in melanoma patients) to rule out dissemination and distant metastases that might contraindicate HILP. All but two of the patients underwent HILP (because PET/CT revealed distant metastases).

Surgical technique for HILP

The surgical technique involved in HILP has been described in detail elsewhere.[10] Briefly, the main artery and vein of the affected limb were isolated (femoral or iliac access) and encircled with tourniquets. After systemic heparinization, the tourniquets were tightened as arterial and venous cannulas/catheters were inserted in the vessels through a transverse incision. Then the catheters were connected to the extracorporeal circuit. An Esmarch tourniquet was placed at the root of the limb to collapse collateral vessels and prevent systemic drug leakage. 99mTc-albumin was injected into the circuit to measure systemic perfusate leakage with a gamma probe placed over the heart, and connected to a gamma counter for continuous monitoring and recording.[11,12] TNFα was injected into the arterial line, and melphalan was administered 15 min later. At the end of the HILP, the limb was washed out, the tourniquet released, the catheters removed and the vessels repaired.

PET/CT

All patients underwent whole-body 18F-FDG-PET/CT to assess distant metastases (beyond the limb) and the number and metabolic activity of limb lesions. PET/CT images were acquired 1 h after the injection of 3 MBq/kg of 18F-FDG, using a Biograph-16 from Siemens (Munich, Germany). CT (5.0 mm slice thickness) was used for correcting attenuation and locating anatomical points.

Volume calculation

Regional tissue volume is traditionally calculated for HILP using water displacement volumetry (WDV). This technique is considered the gold standard, but it is complicated − especially when dealing with obese and elderly patients − because the body should be lifted completely to enable the limb to be immersed. A considerable amount of space is needed for the procedure, it is time consuming, and it demands trained staff. In addition, the immersion stank is not disposable and the related disinfection issues further complicate the matter.

A simplified method has been proposed that relies on circumferential measurements of the extremity at preset distances (5 cm),[13] and volumes derived from CT images are sometimes used.

Other models have been developed for establishing the appropriate drug dosage for HILP (dosage by body weight[14] or by ideal body weight[15]), but they were not considered in the present study because it focused on exact limb volume calculation methods.

We therefore calculated limb volume using four methods (as discussed below) and compared the results. For safety reasons, the dosage of the drugs administered to patients was always based on the WDV technique, as usually adopted in literature. The drug dosage (mg) for the lower limbs was calculated using the formula: volume(L)*10 mg/L.

Water displacement volumetry (WDV)

The method for calculating regional tissue volume as first proposed by Wieberdink et al.[16] is implemented with the aid of a cylindrical water tank 30 and 15 cm in diameter for the legs and arms, respectively. Connections with piped water and taps are provided for filling and emptying. The transparent walls of the tank are calibrated. To obtain a reliable measure of leg volume, patients must be moved up and down while standing on a platform. The leg is placed in the empty tank, with the patient's perineum resting on the rim. Then the tank is filled to capacity. Withdrawing the limb from the tank lowers the water level proportionally with the volume of the immersed limb. A 10% correction is added for the part of the iliac perfusion region that cannot be submerged. Regional volumes are calibrated with body weight based on the assumption that the specific gravity of the tissues concerned is 1.0. The reproducibility of the method can be improved by adding small amounts of

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