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# Standard & non-standard applications of sentinel node (SN) guided melanoma (MM) surgery

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**Purpose:** Identification and histology of the SN is an acceptable guide for treating Intermediate Thickness MM (ITMM). This prospective open study widens the range of applications of the SN technique.

**Methods:** 77 MM pts with either ITMM or for whom standard surgical treatment could not be offered. We used preoperative lymphoscintigraphy in 46 pts. IOLM (Intra-operative lymphatic mapping) using Patent Blue® dye and surgery were performed. We used frozen section (FS) and total node processing (TNP)+ H&E staining. Whenever SN was not identified, elective lymph node dissection (ELND) was performed. Median follow-up was 16 (2-76) months. We defined four categories of patients that may benefit from IOLM: A. ITMM, B. MM 0.75-1.5 mm + risk factors, ie; satellites, ulceration, head & neck acral, two primaries, perineal, Clark/Breslow discordance, delayed referral, C. MM around 4 mm, and D. MM of undetermined thickness, ie; regression, locally recurrent, technical pathological or surgical failure.

**Results:** IOLM successfully identified the SN in 91% of basins explored. F/S detected mets. in 8 SN. TNP added 3 metastatic SN. Twenty basins were formally dissected. A (n = 31, mean thickness 2.15 mm): Three of the 35 basins were SN+, 28 were SN-, and in 4 we failed technically. All 31 patients are NED median of 16 (3-30) months. B (n = 22, mean 1.26 mm): There were 24 SN-, and 0 SN+. Two of the 24 SN- recurred, and underwent therapeutic dissection 5 and 11 month later. All pts. are NED median of 12 (3-31) months. C (n = 9, mean 4.4 (4-6) mm): There were 4 SN+ who underwent LND, and are NED 12 to 31 months. Six SN- are NED median of 18 (5-24) months. D (n = 15): One SN+ and 14 SN- were detected, one exploration failed. All 15 pts are NED median of 14 (3-31) months.

**Conclusion:** In ITMM (A) 80% of LNDs were spared. Additionally, in thin MM with higher risk of failure (B), IOLM is advantageous in more accurate staging, patient reassurance and guidance of treatment. For MM around 4 mm (C) we achieved earlier detection of regional mets. thus avoiding early failure while on adjuvant treatment. IOLM offers the only tool to guide surgical and adjuvant treatments in undetermined thickness MM (D).

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# Hyperthermic isolated limb perfusion (HILP) - A therapeutic concept in locoregional metastasized malignant melanoma - Experiences over 20 years

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Locoregional metastasized malignant melanoma, particularly multiple in-transit metastases, is a widely accepted indication for HILP.

From 1975 to 1994 163 patients were treated with isolated perfusion in a therapeutic setting, i. e. because of manifest locoregional metastases of melanoma localized at the extremities at the Surgical Department of the University Hospital in Erlangen, Germany. The cytostatic drug used was a combination of Melphalan (L-PAM) and Actinomycin D. Simultaneously a regional lymph node dissection was performed.

The 10-year survival rate of all patients were 37%. Patients with intransit (n = 51) or lymph node metastases exclusively (n = 79) benefited mostly of the treatment with a 10-year survival rate of 41% and 40% (stage IIIA and IIIB according to M. D. Anderson classification). In case of simultaneous intransit and regional lymph node metastases (n = 33) according to stage IIIB, prognosis significantly decreased to a 10-year rate of 26%. Since 1992 a further group of 20 patients was treated with a modified perfusion technique. On the basis of experimental data, perfusion time was prolonged to 90 minutes and the drug was continuously infused over 20 minutes. Our experiences showed an increase of complete remission rate to 85% similar to that with the application of TNF $\alpha$  in HILP.

HILP apparently is a suitable tool to control local tumor growth and improve prognosis of melanoma patients with intransit metastases. With respect to the high complete remission rates, the acceptable morbidity and low mortality we continue to follow our concept of modified perfusion technique using melphalan.

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# A randomized trial of IFN $\alpha$ /IL-2 with or without CDDP in advanced melanoma: An EORTC melanoma cooperative group trial

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A randomized trial comparing immunotherapy with IFN- $\alpha$  and IL-2 versus chemo-immunotherapy with cisplatin (CDDP) and IFN- $\alpha$ /IL-2 has been performed. Treatment consisted of 10  $\times$  10<sup>6</sup> U/m<sup>2</sup>/day IFN $\alpha$  (Roferon) days 1 to 5 and high dose IL-2 (Proleukin) starting on day 3 using a decreasing regimen (1 mg/m<sup>2</sup> over 6 hours, followed by 1 mg/m<sup>2</sup> over 12 hours, 1 mg/m<sup>2</sup> over 24 hours, and a maintenance dose of 0.25 mg/m<sup>2</sup> over 24 hours for 3  $\times$  24 hours) with (arm A) or without (arm B) 100 mg/m<sup>2</sup> CDDP on day 1. Cycles were to be repeated on day 28. 138 patients with predominantly visceral metastases (86%) were randomised. Toxicity (gastrointestinal, hematologic, renal, and liver) was more pronounced in arm A. Dose modifications were necessary in only 9% of treatment cycles. The response rate was 15% without and 36% with CDDP (p = 0.01). Median response duration was 17 months without CDDP and 7 months with CDDP. Overall survival was identical in both arms.

**Conclusion:** The addition of CDDP to IFN- $\alpha$ /IL-2 is feasible, increases response rate, but does not increase survival. In a subsequent randomized trial we currently evaluate the impact of IL-2 on survival.

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# Primary anorectal melanoma: Abdominoperineal resection or local resection?

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**Purpose:** This retrospective study presents prognostic factors of primary anorectal melanoma, and proposes guidelines for surgical treatment.

**Methods:** Between 1975 and 1995, 14 women and 5 men (59.6 years) with primary anorectal melanoma were treated. Lesions ranged from 12 mm from the anal verge, mean diameter was 45.2 mm, and mean thickness was 21.6 mm. At diagnosis, 5 patients had visceral metastases, 2 had suspicious inguinal lymph nodes, and one had direct vaginal extension. Six patients had an abdominoperineal resection, and 8 had a local resection with curative intent. Two patients had a therapeutic dissection of inguinal lymph nodes. Survival analysis was calculated with Kaplan-Meier, and statistical significance between 2 proportions was calculated with the chi-square test.

**Results:** Overall five-year survival was 21%, and 2 patients were disease-free at 85 months, and at 48 months. No patients with lymph nodes invasion (pelvic or inguinal) survived longer than 24 months after diagnosis. Univariate analysis showed a significantly poorer prognosis when lymph nodes were invaded (= 0.001), when surgical margins were positive (p = 0.003), when there were metastases (p = 0.01), and when the lesion was thicker than 20 mm (p = 0.01). Prognosis was not altered by type of surgical resection.

**Conclusion:** Surgical local resection is the first choice whenever negative surgical margins are obtained. Abdominoperineal resection should be reserved for localized large tumors, not amenable to local resection. Dissection of inguinal lymph nodes should be resorted to only when therapeutically necessary.

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# Treatment of cutaneous Kaposi's sarcoma with tin ethyl etiopurpurin (SnET2) photodynamic therapy

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**Purpose:** Kaposi's Sarcoma (KS) lesions in immunocompromised individuals are often physiologically and psychologically distressing. The multifocal nature of these lesions makes local treatments (i.e. surgery, radiation) difficult and time consuming. Further, cosmetic outcomes are generally poor. Photodynamic Therapy (PDT) can overcome some of these negative outcomes in a single treatment session and as such may be of benefit to these patients.

**Methods:** SnET2 PDT was performed on 9 pts. with known KS lesions. The total number of lesions treated was 121. All patients were HIV positive.