

Unfortunately, early melanoma development is accompanied by impaired immune effector functions in the initial tumor-draining lymph node, the sentinel lymph node (SLN) and this may facilitate early metastatic events. Immunopotentiality in these early stages may therefore be a valuable adjuvant treatment option. We recently demonstrated that intradermal injections of granulocyte/macrophage colony-stimulating factor (GM-CSF) around the excision site of primary melanoma increase the number and activation state of dendritic cells (DC) in SLN and hypothesized that this may be more conducive to the generation of T cell-mediated anti-tumor immunity. The aim of this study was to investigate the frequency of tumor-specific T cells in the SLN and blood of stage I melanoma patients and the effect of locally administered GM-CSF or saline.

Material and methods: Twelve stage I melanoma patients were randomly assigned to preoperative local administration of either recombinant human GM-CSF or saline. SLN-DC were phenotypically and morphologically characterized by flowcytometry and immunocytochemistry. From both the SLN and peripheral blood CD8+ T cells were isolated and investigated for tumor antigen specificity with IFN- γ ELISPOT-assay and tetramer staining.

Results: Primed tumor-specific T cells can be found as early as stage I melanoma patients. Overall tumor-specific T cell response rates in the SLN were 1/6 for the control group and 4/6 for the GM-CSF-administered group, only one patient had tumor-specific CD8+ T cells in the peripheral blood. All patients with detectable tumor-specific CD8+ T cells had a percentage of SLN-DC above median (0.33%). The association between the percentage of SLN-DC and tumor-specific CD8+ T cells was significant in a two-sided Fisher's Exact Test ($p = 0.015$).

Conclusions: Even in these early stages of melanoma development anti-tumor T cell responses are present and correlate to the myeloid DC content of the SLN, which can be enhanced by GM-CSF. More robust melanoma-specific CTL reactivity was consistently found in the SLN than in peripheral blood. This is consistent with local priming of tumor-specific CTL in the tumor-draining SLN.

Publication

Melanoma and sarcoma

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PUBLICATION

Risk factors for the squamous cell carcinoma developing on burn scar

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Background: Squamous cell carcinoma is malignancy of epidermal keratinocytes. After basal cell carcinoma, is the most frequently encountered malignant neoplasm of the skin. The aim of this study was to demonstrate the squamous cell carcinoma (SCC) rate and risk factors for developing on burn scar.

Methods: Retrospectively were followed data of 241 patients with SCC diagnosed in Dermatologic clinic Nis during the 5 years period. Rate of SCC developing on burn scars, risk factors and latent period between burn and carcinoma were evaluated.

Results: The number of SCC that developing on burn scar was 19(7.88%). Seventy-one per cent were male and 29% were female with a mean age of 34.5 years. The most common localization of SCC developing on burn scar was lower extremities 11(57.89%). The period between burn and carcinoma is 8 to 45 years. Cox multivariate analysis of risk factors for the squamous cell carcinoma developing on burn scar showed that degree of burn HR 3.69 (1.50 to 11.72) and localization HR 2.18 (0.90 to 8.26) had statistically significant effect on malignant transformation.

Conclusion: SCC developing on burn scar is seen at early age and more frequently localized on lower extremities. Degree of burn and scar localization were the most important prognostic factors for malignant transformation.

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PUBLICATION

A novel method of eye immobilisation and treatment delivery for photon beam irradiation of ocular melanoma

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Introduction: Photon beam radiotherapy using a relocatable stereotactic frame has been described for treatment of ocular melanoma. The relocatable frame must be modified to achieve eye immobilisation. We use a soft-contact lens attached to a rod to provide eye immobilisation in the treatment of retinoblastoma. We have developed an apparatus

that combines the Gill-Thomas-Cosman frame with the lens-rod set-up for treatment of adults with ocular melanoma.

Methods: An in-house designed and built lens-rod system is attached to the GTC frame. The position of the lens over the iris is recorded with measurements and a photo. A small amount of pressure is applied to the eye by downward displacement of the rod before fixing the rod position. This limits movement of the eye and gives the patient a physical guide as to the correct position of the eye. It is not necessary for the eye to have vision for the system to work. A horizontal line engraved on the rod is the reference point for treatment set-up. It lies a fixed distance from the cornea and a known distance from the treatment isocentre so stereotactic coordinates are not required. Multiple small fixed photon fields using a multi-leaf collimator with 5 mm wide leaves are used instead of circular collimators. Correction factors for small photon fields have been generated.

Results: The lens-rod system provides a closed system of eye immobilisation and treatment set-up. The position of the treatment volume relative to the globe is not affected by movement of the eye as the set-up point moves with the eye. The GTC frame allows a wide range of beam angles to be used. The technique requires the presence of the treating radiation oncologist for approximately 10 minutes before each treatment fraction. Verification of the lens position over the iris is all that is required for daily treatment verification. The apparatus has been used to treat 5 patients up until now and has been well tolerated. All patients reported that the main discomfort was pressure on the face from the GTC frame. Mild to moderate watering of the eye occurred as the lens was placed on the eye. Acute toxicities are reported in detail.

Conclusion: This hybrid lens-rod-GTC apparatus provides excellent and reproducible eye immobilisation. It enables the delivery of fractionated small-field radiation to the posterior eye.

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PUBLICATION

The modified St. Jude hospital protocol in adult Ewing Sarcoma cases

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Background: To test the effectiveness of intensive chemotherapy regimen in adult Ewing sarcoma cases.

Material and methods: 23 patients (22 men, 1 woman) with Ewing sarcoma were administered modified St. Jude hospital protocol for a period of 41 weeks. The chemotherapy protocol was as follows: Induction chemotherapy from week 0 to the end of week 6 [Ifosfamide 2 g/m²/day on days 1-3; etoposide 150 mg/m²/day on days 1-3; cyclophosphamide 1.5 g/m² on 5th day and doxorubicin 45 mg/m² on 5th day]; followed by surgical excision with or without radiotherapy on week 9; then, consolidation chemotherapy were given between weeks 11 to 17 [Vincristin 1.5 mg/m², Dactinomycin 1.5 mg/m²]; and finally, maintenance chemotherapy from week 20 to the end of week 41 [Ifosfamide 2 g/m²/day on days 1-5, Etoposide 150 mg/m²/day on days 1-5, Cyclophosphamide 1 g/m²/day on days 1 and 2, Doxorubicin 60 mg/m² given as 24 hours-continuous infusion; with two drugs in combination]. All chemotherapies were given every three weeks.

Results: The median age of patients was 21 (range: 20-55). Initial stage at diagnosis was stage II in 17 patients and Stage IV in 6 patients. Eleven patients were treated by radiotherapy, 3 patients by surgery and 8 patients by combination of surgery and radiotherapy. The other one patient has not reached at the 9th week of treatment, yet. Total therapy duration was 9.08 months (median). Two patients with initial Stage II have relapsed during the administration of the protocol or after the completion of chemotherapy. The median time to disease relapse after the completion of chemotherapy was 129.3 days (median). Ten patients had complete response, 5 had partial response, while 8 patients progressed. All progressed patients have died. Myelotoxicity was the most common side-effect (35%). Transfusion was done in 30% of patients and growth factor was used in 22% of patients, totally. Two patients showed transient nephrotoxicity and neurotoxicity and one patient had transient hepatotoxicity. The median follow-up period was 20.57 months (2.1-57.8). The median survival was 28.8 months. The 36-month overall and disease-free survival rates were 41% and 26%, respectively.

Conclusion: This protocol is tolerable with non-serious side-effects. The prolonged follow-up period of non-metastatic and metastatic cases is henceforth required to see if survival benefit may be procured by this treatment approach.