

trend in our centre, NCMs does not seem to be an uncommon malignancy in India. The prognostic indicators showed inferior results in NCMs in comparison with cutaneous melanomas. The optimum management of NCMs is still not clear regarding the optimum use, doses and schedules of the treatment modalities. More prospective studies in future are required to come to any definite conclusion regarding their management.

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POSTER

# **Fluorescence diagnostics of skin tumors using 5-aminolevulinic acid and its methyl ester**

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**Background:** The incidence of malignant skin tumours is rapidly increasing. Early diagnosis, determining the margins of the tumour, is extremely important to achieve good treatment results. We investigated the fluorescence of 5-aminolevulinic acid (ALA) or its methyl ester (MAL)-induced protoporphyrin IX (PpIX) in skin carcinomas. The study aimed to compare the effectiveness of topical ALA and methyl-aminolevulinic acid in determining exact margins of skin tumours.

**Materials and Methods:** Fluorescence diagnostics measurements were performed in 132 patients with malignant, premalignant and benign skin lesions for detection of the margins of squamous cell carcinoma and basal cell carcinoma. 5-aminolevulinic acid or its methyl ester was applied to the skin lesion for 2–4h, and the evaluated PpIX fluorescence data were correlated with morphological tissue examination data. As fluorescence excitation system we used the light system based on blue light emitting diodes.

**Results:** Malignant tissue shows a specific red fluorescence when illuminated with blue-violet light, whereas no fluorescence was observed in normal skin. In 30% of cases the delineation of neoplastic lesions excited by ALA, was slightly weaker than using MAL. Sensitivity of 94.3%, specificity of 90.8% as well as positive and negative predictive values of 87.7% and 90.8%, respectively, were obtained for 342 lesions FD. The sensitivity, specificity, positive predictive value and negative predictive value for fluorescence diagnosis using MAL were 88.6; 95.4; 96.3 and 86.1, respectively, and for ALA-FD were 92.9; 85.7; 88.1 and 85.7, respectively.

**Conclusions:** Fluorescence diagnostics can be used for complete visualization of malignant skin lesions after topical 5-aminolevulinic acid or methyl aminolevulinic acid application. It has been shown to be highly effective in malignant superficial skin lesion diagnostics. This method is applicable for detecting early superficial tumours, margins of tumours and follow-up after therapy. Topical application of methyl aminolevulinic acid is slightly superior to ALA in detection of lesion margins.

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POSTER

# **Melanoma metastases to the neck nodes: role of adjuvant irradiation**

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**Background:** In melanoma, the opinion on the value of adjuvant radiotherapy (RT) following therapeutic neck surgery is not uniform. The aim of the study was to review experiences on the treatment of regionally advanced melanoma to the neck and/or parotid with the emphasis on the role of adjuvant RT.

**Patients and Methods:** Clinical and histopathological data, treatment details and outcomes of pts treated during the period 2000–2006 at the Institute of Oncology Ljubljana, Slovenia were reviewed. The sum of the risk factors present ( $\geq 3$  involved nodes, diameter of positive node  $\geq 30$  mm, extracapsular nodal spread, close/positive margins, satellitosis, disease recurrence) was termed the risk factor score.

**Results:** 40 pts with 42 dissections had surgery and 43 pts with 45 dissections had RT postoperatively to a median equivalent dose (eqTD<sub>2</sub>: 2 Gy/tx, 1 tx/d, 5 tx/wk) of 60 Gy (range, 47.8–78.8). Compared to surgical group, irradiated patients had more advanced pN-stage ( $P = 0.010$ ) and extensive surgery (involving superficial parotidectomy,  $P = 0.003$ ); higher median number of involved nodes ( $P = 0.010$ ); higher frequency of extracapsular tumor spread ( $P = 0.026$ ) and non-radical surgery ( $P = 0.059$ ) which, altogether, resulted in higher risk factor scores ( $P < 0.0001$ ). Regional control at 2 yrs after surgery was 56% (95% confidence interval [CI] 40–72%) and after postoperative RT 78% (CI 63–92%) ( $P = 0.015$ ). On multivariate analysis, postoperative RT (Yes vs. No: hazard ratio [HR] 6.3, CI 2.0–20.6) and risk factor score (HR 1.7 per score point, CI 1.2–2.6) were predictive for regional control. On logistic regression testing, the number of involved nodes was associated with the probability of distant metastases ( $P = 0.021$ ; with 10–15 involved nodes the risk was  $\geq 80\%$ ).

The incidence of late toxicity did not correlate with the mode of therapy, eqTD<sub>2</sub> or fractionation pattern.

**Conclusions:** Adjuvant RT has potential to compensate effectively for the negative impact of adverse histopathological features to disease control in a dissected nodal basin. Bearing in mind the potentially detrimental effect of high fraction doses, more conventionally fractionated RT regimens (2–2.5 Gy/tx), with cumulative eqTD<sub>2</sub>  $\geq 60$  Gy are recommended. To spare pts at significant risk of distant metastases (and of dying of disease) from potentially harmful, although effective regional therapy, the number of involved lymph nodes is proposed as an additional criterion for limiting the implementation of adjuvant RT.

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POSTER

# **Changes in metabolism and metastatic properties of melanoma cells after X-ray irradiation**

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**Background:** Malignant melanoma has the ability to form metastases at very early stages and in addition to surgical resection treatment involves immunotherapy, chemotherapy and also radiotherapy. As it is known that irradiation can influence cellular metabolism it is conceivable that it can induce metabolic changes which lead to a predisposition of certain cells to show enhanced survival, migratory activity and metastasis. The aim of this study was to investigate short term and long term irradiation effects on metabolism and proliferation of irradiated melanoma cells *in vitro* and their ability to form metastases *in vivo*.

**Material and Methods:** B16-F10 melanoma cells were irradiated with different doses of X-ray irradiation in the range of 1 to 20 Gy. One, two, and three days (short term effects) and, furthermore, 7, 14 and 21 days (long term effects) after treatment cells were analyzed concerning cell growth, viability, proliferation, cell cycle distribution, glucose and amino acid transport. Additionally, we performed *in vivo* studies in a syngeneic mouse model to analyze the capability of irradiated melanoma cells to form lung metastases.

**Results:** The analysis of short term effects showed decreased cell growth, viability and arrest in the G2/M phase of the cell cycle. Long term effects involve increase in proliferation, cell growth and glucose uptake but still decreased viability and amino acid transport. Our *in vivo* studies showed no formation of lung metastases when cells were irradiated before injection. If irradiated cells were allowed to recover for 2 weeks before injection, mice again developed lung metastases although to a lesser extent than control mice.

**Conclusions:** We conclude that melanoma cells as short term response to irradiation show cell cycle arrest and decrease in cell viability, growth and metabolic properties. One to three weeks after irradiation, the re-start of proliferation and recurrence of metabolic properties such as glucose uptake indicate that a subpopulation of surviving melanoma cells compensate for the initial irradiation-dependent damage possibly by metabolic modulations such as increase in glycolysis. Furthermore, *in vivo* studies reveal that irradiated melanoma cells are able to resume their metastatic potential within two weeks. As lung metastasis is lower when using recovered cells versus untreated cells, the role of additional mechanisms is strongly suggested.

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POSTER

# **Absence of detectable tumoral cells in the blood or bone marrow of ocular melanoma patients operated for liver metastasis**

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Disseminated tumor cells have been found in the blood and bone-marrow (BM) of many cancer patients, including those with small tumors at early stages. A few studies have found circulating tumor cells in ocular melanoma patients at the time of diagnosis of either primary tumor or liver metastasis. The presence of disseminated tumor cells in the blood/bone marrow at the time of primary treatment may be indicative of poor prognosis.

Before embarking into a prospective study to assess the prognosis value of detecting disseminated tumor cells at the time of primary treatment, we evaluated the feasibility of detecting tumor cells in the blood and BM of ocular melanoma patients with liver metastasis. Our hypothesis was most of these patients would have disseminated tumor cells in the blood, BM or both.