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## **CASE REPORT: PSEUDOPROGRESSION OF METASTATIC MALIGNANT MELANOMA IN A PATIENT TREATED WITH NIVOLUMAB**

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### **BACKGROUND**

Melanoma is an aggressive disease that accounts for approximately 75% of skin cancer-related deaths. Approximately two thirds of patients who develop clinical metastases after treatment of primary cutaneous melanoma present with locoregional recurrence, with approximately 4% to 11% of all recurrences presenting as in-transit metastases.

Antiprogrammed cell death-1 (PD-1) inhibitors have been shown to significantly improve survival and to be better than ipilimumab alone in unresectable metastatic cutaneous melanoma patients.

Pseudoprogression refers to increased tumor size or even new lesions elsewhere in malignant melanoma patients receiving treatment with immune-checkpoint inhibitors.

We report a case of pseudoprogression of metastatic cutaneous melanoma treated with nivolumab.

### **CASE REPORT**

Patient, 58-years-old, female, left-sided leg melanoma in 2014 (T3N0M0), clinical stage II, submitted to resection of lesion with sentinel lymph node biopsy in 2014. Local recurrence in 2015, submitted to new resection followed by margin enlargement and sentinel lymph node biopsy. After 4 months it evolved with new relapse with transit metastases (several nodules) and pulmonary micronodules. Status BRAF mutated (V600E). She started chemotherapy until obtaining immunotherapy, because of excellent performance and no availability of the medicine at the moment. She received dacarbazine for 3 months with increased numbers of pulmonary nodules, followed by chemotherapy with carboplatin and paclitaxel for 3 months, with local progression in the left leg (increase in number and size of cutaneous nodules). Immunotherapy with anti-PD1 started (Nivolumab 3mg/kg every 2 weeks) in April/2017, when it was available. Leg disease progressed in number and size, pulmonary nodules stable and LDH increased until July/2017, when finally came back to decreased. Patient maintains stable pulmonary disease, disappearance of leg lesion and does not present immunotherapeutic toxicity until now.

### **CONCLUSION**

Solid tumors respond to immunotherapy frequently later than after chemotherapy and sometimes are preceded by progression in imaging examinations. Although pseudoprogression caused by nivolumab treatment is reported in few patients, this case shows that a new lesion may not always signify failure of treatment.

## **CASE REPORT: SUSTAINED RESPONSE TO VEMURAFENIB IN A BRAF<sup>V600E</sup>-MUTATED METASTATIC MELANOMA PATIENT**

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### **BACKGROUND**

The use of target drugs or immunotherapy has prolonged the survival of patients with unresectable or metastatic melanoma or even led to cure. Mutations in the BRAF gene are found in approximately 40 to 60% of cutaneous melanomas. Vemurafenib (Zelboraf, Hoffmann-LaRoche Inc.) demonstrated efficacy in the treatment of mutated BRAF metastatic melanoma, acting in the inhibition of BRAF serine-threonine kinase.

We report a case of mutated BRAF metastatic cutaneous melanoma with sustained response to vemurafenib.

### **CASE REPORT**

DCFR, female, 40 years, left leg melanoma, initial clinical stage II in 2016. Submitted to resection of lesion with sentinel lymph node biopsy and emptying in the same year. In 2017 recurred with ulcerated lesion in the left leg without indication of approach surgery. Started chemotherapy with dacarbazine and after 2 months, presented new local and distance progression (lung, inguinal lymph nodes and liver). The mutation search found the BRAFV600E mutated. Started vemurafenib at the dose of 960 mg twice daily. Medication acquired by own means until release of COMBO of inhibition of BRAF–MEK serine-threonine kinase (vemurafenib + cobimetinib) by judicial route. treatment was performed from June 12 to July 06/ 2017 with significant clinical improvement (reduction of ulcer area). A substantial response to vemurafenib was observed on imaging in January 2018 (7 months after vemurafenib suspension. It was used for 15 days). There was disappearance of lung lesions, reduction of lymph node and hepatic lesions. Zelboraf was reintroduced in February 2018 and MRI of the left leg of March 2018 showed complete remission of the lesion. The patient continues with good tolerance to the treatment without associated toxicities. It remains awaiting the legal release of Cobimetinib.

### **CONCLUSION**

The routine use of target therapy in patients with metastatic or unresectable disease with a BRAF V600 mutation is indicated until a finding of disease progression or limiting toxicity. However, there are cases described in the literature, such as the one presented in this report, in which the response occurs already at the beginning of the treatment and the result is maintained after its suspension. These findings are even more promising and the ideal treatment time is therefore questioned in view of the toxicities and costs involved.

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## **SUCCESSFUL TREATMENT WITH IMATINIB AFTER NILOTINIB IN PATIENT WITH ADVANCED MELANOMA – CASE REPORT**

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### **BACKGROUND**

Metastatic melanoma has a very poor prognosis. The molecular differentiation in BRAF-mutated, NRAS-mutated and C-KIT mutated melanomas led to new treatment strategies. C-KIT mutations are more common in mucosal and acral melanomas and established therapeutic target in cancers with activating mutations of KIT. Those with amplifications of KIT have typically not responded to KIT inhibitors.

We report a case of c-kit mutated metastatic acral melanoma showing impressive response to nilotinib and Imatinib.

### **CASE REPORT**

VLGGC, female, 56 years old, from Belo Horizonte (MG), with acral lentiginous melanoma in the first right podododactyl, diagnosed and undergoing exeresis in 2008. Submeted to the margin enlargement and biopsy of sentinel lymph node was negative for metastases. In 2010, it evolved with local recurrence of the lesion, being submitted to a new surgical excision and enlargement of the margins with amputation of the first right podododactyl. In 2012 it was included in a clinical research protocol with Nilotinib. He underwent treatment for 3 years, until April 2015, with complete regression of the lesion. At the end of 2016, evolved with cutaneous metastasis in the right popliteal region, and surgical excision was performed in March 2017 with free surgical margins. Mutation research conducted in June 2017 found non-mutated BRAF and c-kit mutated. PET-CT was performed, which revealed hypermetabolic cutaneous thickening in the posterior medial aspect of the middle third of the right lower limb corresponding to local recurrence of the underlying pathology. Initiated Imatinib in December 2017 due to good clinical response of the patient to previous use of nilotinib. Response evaluation tests of April 2018 showed disappearance of the lesions and clinically there was significant improvement of pain and local edema. It continues to use the medication and presents as pharmacologically controlled grade 1 nausea and vomiting.

### **CONCLUSION**

KIT inhibitors have useful clinically activity in some patients with activating mutations of the c-kit gene in small trials with agents such as imatinib. This case shows that the use of imatinib after progression upon nilotinib can be beneficial and a therapeutic option.

## **LONG-TERM SURVIVAL IN A YOUNG PATIENT WITH METASTATIC CONJUNCTIVAL MELANOMA – CASE REPORT**

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### **BACKGROUND**

Conjunctival melanoma is rare and accounts for 5% of all ocular melanomas. It usually arises from the 5th decade of life, rarely before that. presents a high mortality rate, 12 to 20% in 5 years and 30% in 10 years of pathological development. Its adequate treatment contributes to the reduction of the morbidity and mortality of this pathology.

We report a rare case of long survival in a young patient with metastatic Conjunctival Melanoma.

### **CASE REPORT**

Patient 37 years old, male, diagnosis of conjunctival melanoma in 2002, submitted of the surgical procedure. In mid-2011, presented recurrence in the nasopharynx, opted for surgical resection and chemotherapy with Dacarbazine. He received this treatment for 3 months when he was able, through expanded access, to use immunotherapy with Ipilimumab (4 cycles). Last dose in January 2012. After a new local recurrence in the nasopharynx, he underwent chemotherapy combined with Carboplatin and Paclitaxel from February to September 2012. He presented progression of the nasopharyngeal lesion with cranial base invasion. Realized local radiotherapy and it was modified the systemic treatment for Dacarbazine, Vimblastine and Cisplatin until May 2013. Still with residual nasopharyngeal lesion, radiosurgery was performed in August 2013. BRAF searched without V600E mutation. Patient since then in follow-up and without new evidence of disease.

### **CONCLUSION**

The behavior of conjunctival melanomas remains unpredictable in individual cases. To minimize local recurrence rate surgical excision should be combined with an adjunctive procedure such as irradiation, cryotherapy, or chemotherapy.

Performing rigorous follow up and early treatment of relapses with a multidisciplinary team is fundamental for favorable outcomes in the survival of young patients, as reported here.

## **DESMOPLASIC MELANOMA IN YOUNG ADULT PATIENT: CASE REPORT**

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### **BACKGROUND**

Desmoplastic melanoma is a rare variant of melanoma, corresponding to 1 to 5% of the cases, in which there is invasive injury with spindle cells and variable desmoplasia. It tends to occur in photoexposed regions such as head, neck and upper and lower back. Clinically, the diagnosis can be confused with scar, fibroma, fibromatosis or basal cell carcinoma because it typically presents as an amelanotic lesion. They are frequently locally invasive and very recurrent, but they present a better prognosis in relation to than other cutaneous melanomas in the same stage.

### **METHODS**

This case was diagnosed and treated by the melanoma and skin cancer service at Araújo Jorge Hospital in Goiânia, Goiás, Brazil, and this report is justified due to the rarity of the disease and its late diagnosis.

### **RESULTS**

Female patient, 33 years old, phototype II with a history of scalp lesion, in the right parietal region, with previous biopsy of dysplastic nevus, but continued to evolve. In the present study, the patient presented a pink lesion in the right parietal region of 2.5 x 2.0 cm and reports that it appeared 8 years ago. Six years ago the lesion increased in size during pregnancy and, after delivery, reduced its size. Four years ago she became pregnant again and the lesion increased again, but did not reduce with the end of gestation and continued to grow progressively.

An excisional biopsy with diagnosis of desmoplastic melanoma with Breslow 9.0 mm, IM = 9 / mm<sup>2</sup> and perineural invasion was performed. In the staging, PET-CT showed an image suggestive of right-sided cervical lymph node metastasis, with SUV 17.

### **CONCLUSION**

The margin of the scalp lesion was enlarged and the right cervical lymphadenectomy was performed, the patient is being followed up at the cutaneous oncology department. Desmoplastic melanoma presents as risk factors: male gender, advanced age and frequent exposure to solar rays, which were not observed in the patient of the report. Immunohistochemistry may be useful to confirm diagnosis. It is also worth noting that recurrences of desmoplastic melanoma can occur in 25 to 82% of the cases, mainly due to incomplete excision of the lesion or due to the presence of perineural involvement, demonstrating the importance of observing the appropriate surgical technique, critical analysis of the biopsy report and follow-up of the patient. Adjunctive radiotherapy is also indicated.

## **CASE REPORT: SUSTAINED RESPONSE A CTLA-4 ANTAGONIST IN METASTATIC CUTANEOUS MELANOMA**

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### **BACKGROUND**

Studies have shown that the major changes from inactive lymphocytes to effector lymphocytes, occur during the first three weeks of use of ipilimumab and the increased count of these lymphocyte subtypes is directly related to control of disease. In addition, anti-CTLA-4 therapy leads to a decrease in memory stem cells probably due to differentiation into effective memory cells. This may be one of the biological bases for sustained response to anti-CTLA-4 immunotherapy, even after short-term use.

We report a case of sustained response to ipilimumab, a CTLA-4 antagonist, after 2 cycles, in metastatic cutaneous melanoma.

### **CASE REPORT**

A 50-years-old, male, with diagnosis of Cutaneous Melanoma on the right back in February/2011 (T4N3M0), clinical stage IIIC. Submitted to radical right axillary lymph node dissection at 06th July 2001, with 7 of 15 nodes positive and skin and subcutaneous free of neoplasia. Forwarded to a research protocol at Biocancer (Belo Horizonte, MG) with interferon and adjuvant vaccine from August to November 2011. He Relapsed in the right axilla with exeresis of the lesions in November 2011. Metastatic melanoma confirmed in biopsy. Status BRAF mutated (V600E). He underwent radiotherapy followed by 6 cycles of dacarbazine (last cycle in May 2012). After 2 months, He relapsed with new cutaneous lesions, pectoralis and right arm, and had gone to a program of compassionate use of medicine at Salvador – BA. He received 2 cycles of Ipilimumab with partial local response - maintenance of small subcutaneous nodules without visceral lesions. The chest and arms hyperchromic lesion evolved with vitiligo, and biopsy confirm absence of disease, as computed tomography until today.

### **CONCLUSION**

Anti-CTLA-4 therapy has revolutionized the treatment of metastatic melanoma with a significant increase in overall survival. Some patients, as reported here, demonstrate a lasting response and long years of survival. The identification of the mechanisms involved in long-term sustained response will provide a better selection of those who will benefit from CTLA-4 alone therapy, sparing them from more toxic treatments as in the combination of immunotherapy.

## **THE IMPACT OF LATE DIAGNOSIS ON CUTANEOUS MELANOMA**

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### **BACKGROUND**

Skin cancer accounts for 30% of the malignant tumors registered in Brazil. Melanoma represents 3% in this group it is of great importance due to its severity and the possibility of metastasis.

### **CASE REPORT**

L.T.M., 54 years old, white skin. Sought medical attention in 2009 due to a speckle in right leg. The evaluation concluded that the lesion was benign without biopsy by different doctors. In 2014 was the biopsy performed. Anatomopathological Result (AP) extensive superficial melanoma level IV of Clark and with 3.5 of maximum thickness (Breslow). In 2015 was admitted in service. The conduct was to increase margin of melanoma exertion and right inguinal lymphadenectomy. Follow up exams showed lymphadenomegaly in the right external iliac chain, appearance of subcutaneous nodules. The stage became stage IV probable metastasis in CNS mutated BRAF. Patients underwent follow-up with clinical oncology and initiated target therapy, underwent immunotherapy and associated these drugs. There was an increase in lymph nodes and nodules in muscle regions, progression of the disease in lungs. In 2017 was increase of adrenal mass, was referred for radiotherapy. Disease classified as stage IV melanoma. In February secondary bone lesions and multiple lesions in the muscle-adipose plane. In November worsening of the condition and decrease in functionality. Was referral to palliative care. Received palliative care at home and died weeks later.

### **DISCUSSION**

Early diagnosis of cutaneous melanoma is related to a greater chance of cure, longer survival, lower complications and lower treatment costs. The treatment of localized neoplasia, usually detected when the diagnosis is early is surgical and with high curative potential. It is important for the non-specialist to recognize suspicious lesions and refer them to specialist centers. Decreasing the time since the first suspicion, definitive diagnosis and treatment.

### **CONCLUSION**

We emphasize the importance of continuing education so that health professionals recognize suspicious lesions.

## **IS THERE A CORRELATION BETWEEN THE PRESENCE OF NEOPLASTIC CELLS IN THE INFLAMMATORY INFILTRATE AND POOR PROGNOSIS OF PATIENTS WITH CUTANEOUS MELANOMA *IN SITU*?**

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### **BANKGROUND**

In recent years, diagnosis of cutaneous melanoma in situ (MIS), considered of excellent prognosis, have been increasingly frequent. However, some authors have reported rare cases of MIS presenting recurrence, metastasis and death. Many clinical and histological variables have been suggested, however, to date, no study has defined the causes of this unexpected behavior.

### **METHODS**

Retrospective study of lesions initially diagnosed as MIS. Immunohistochemistry with Melan-A and HMB-45 was performed, to look for melanocytes in the dermis and to measure its depth. These data were correlated with disease-free survival time (DFS).

### **RESULTS**

We identified 445 MIS in 368 patients with a mean age of 54 years old. The number of diagnosed cases has increased over the years. Brisk inflammatory infiltrate was found in 115 cases, nonbrisk in 181 and 149 cases showed no inflammatory infiltrate. We performed immunohistochemical study with Melan-A and HMB45 antibodies with satisfactory samples obtained in 421 cases and found neoplastic cells in the dermis in 53 cases. Breslow thickness of these 53 cases was from 0.09 mm to 0.88 mm (mean 0.39 mm). Nine cases had bad outcome, six with relapse and three with regional metastasis. All nine cases had inflammatory infiltrate, two with brisk type and seven with nonbrisk infiltrate. Among those, two had neoplastic cells in the dermis after immunohistochemical analysis and in one case, the sample was not satisfactory. The Mann-Whitney test indicates no statistically significant difference ( $p > 0.05$ ) between DFS for cases with and without neoplastic cells in the dermis, evaluated by. The variables that showed statistically significant correlation with poor outcome were: age, site (head and neck and lower limbs) and presence of inflammatory infiltrate (regardless of type).

### **CONCLUSION**

MIS develop recurrence or metastasis in about 2.02% of cases, usually in patients 12.7 years older than the group with good outcome. The presence of inflammatory infiltrate, shows a statistically significant correlation with the presence of neoplastic cells in the dermis, identified only by immunohistochemical study, and also with the poor outcome of patients initially diagnosed with MIS. The presence of melanocytic cells in the dermis, hidden by the inflammatory infiltrate and identified only with the immunohistochemical technique does not affect DFS, in a statistically significant way. Further studies are needed.

**CLINICAL PRESENTATION OF THE ANORECTAL MELANOMA: A CASE REPORT**

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**BACKGROUND**

The anorectal melanoma (AM) is part of a subgroup of mucous melanomas, being considered the third most prevalent within the group, followed by oral cavity melanomas and female genital melanomas. It represents about 1 to 2% of all melanomas and 16,5% of the mucous melanomas (MM). It has a higher prevalence in women, caucasian and melanodermic (2 times higher), and onsets mainly the population above 60 years of age. Rectal bleeding is considered a typical manifestation of this pathology, and is reported by 53% to 89% of the patients. There are few clinical options for the AM patients: adjuvant therapies, metastatic melanoma treatments and immunotherapies and an exact guideline hasn't been established regarding time of treatment.

**METHODS**

Evaluation of case report of a leucodermic 65-year-old female patient was diagnosed with AM in 2014, after histopathological study of a surgical specimen obtained after performance of an hemorrhoidectomy. **RESULTS** The reported case portrays the clinical progression of a patient presenting the third most frequent type of MM, the anorectal melanoma, with a presentation in the anal canal, in a patient with epidemiological characteristics that encompass the group with gender and age of higher prevalence of this disease. The clinical treatment was suggested after consideration of disease staging with the use of dacarbazine as palliative resource followed by the use of two immunotherapeutic drugs: ipilimumabe (after progression of disease under use of dacarbazine) and pembrolizumabe, until reaching control.

**CONCLUSION**

The mucous anorectal melanoma is a rare entity, with aggressive progression and bad long term prognosis. Contributing with the aggressiveness of this pathology, is its mild and unspecific manifestation that induces diagnostic confusion and long time until confirmation of disease. Late diagnosis in this case is very dangerous, because the progression of MA is linked to systemic commitment of several organs due to metastatic implants. Currently the therapeutic options are limited and with biased guidelines of administration, besides not having a confirmed effect on disease control and improvement of long term survival, causing the patients to, not so rarely, being offered only palliative focused care.

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## KNOWLEDGE TRANSFER FOR MELANOMA SCREENING WITH DEEP LEARNING

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### BACKGROUND

Literature on automated screening for melanoma exists since the early 2000's, but recent improvements brought unprecedented accuracies. Image classification learns to recognize melanoma from training images annotated by medical specialists. Deep Learning is state-of-the-art for image classification, but requires lavish amounts of annotated images. Transfer learning reuses knowledge from other domains to reduce the need for annotated skin-lesion images. In this work, previously presented at 12th Brazilian Conference of Melanoma (São Paulo, Brazil, 2017), we compare different transfer learning schemes for automated melanoma screening.

### METHODS

As baseline (0), we used Deep Learning without transfer learning. For comparison, we transferred knowledge: (1) from a large (>1 million images) training set in a generic task (ImageNet); (2) from a moderate (~100 thousand images) training set in a medical task (Kaggle Diabetic Retinopathy); (3) from both: first ImageNet, then Retinopathy. In all cases (0~3), the target task was melanoma classification trained in less than 1000 cases. The metric was the area under the receiver operating characteristic curve (AUC).

### RESULTS

Scheme 1 worked best (80.9% AUC); Scheme 2 (75.3% AUC) was slightly worse than the baseline 0 (75.7% AUC); the more complex Scheme 3 tied with the simpler Scheme 1 (80.9% AUC). The most surprising finding is the preference for a generic dataset (ImageNet) as source of knowledge, instead of another medical dataset. We expected that, although Diabetic Retinopathy presents completely different images from melanoma, it would "teach" relevant behaviors to the computer model (e.g. to pay attention to small details of the images), but that did not happen.

### CONCLUSION

The findings (A) reinforce the importance of transfer learning; (B) suggest that it is better to transfer from generic datasets instead of medical datasets from other tasks. The latter conclusion is so counterintuitive it still needs further experimental evidence, from other pairs of medical tasks. Our objective is, in the future, to automatize the decision of referring or not to the specialist with little risk to the patient.

## **MELANOMA CUTANEOUS METASTASES TREATED WITH CRYOTHERAPY AFTER TUMOR RESECTION: STIMULUS FOR THE ABCOPAL EFFECT?**

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### **BACKGROUND**

Melanoma with cutaneous satellite metastases occurs in 5-10% of patients with melanoma. The presence of locoregional metastasis is a risk factor for distant metastasis, and it significantly affects the prognosis of the disease and the patients' quality of life. Currently there are some therapeutic options such as tumor resection, isolated limb infusion, imiquimod, difenciprona, intralesional IL-2, electrochemotherapy and radiotherapy, chosen to accord to the size and tumor location and the patient status, but most of them are expensive and have low efficacy evidence. We present a case where the treatment option was cryotherapy after tumor resection.

### **OBSERVATION**

A 76-year-old woman with a history of pigmented tumor resection in the left leg in 2013. The diagnosis was an extensive ulcerated superficial melanoma with 3 mm tumor thickness. In August 2015 appeared 3 violaceous lesions adjacent to the surgical scar that were resected and the anatomopathological diagnosis was melanoma cutaneous metastases. Three months later, the patient returns with new lesions. Again, the lesions were resected, and with the aim of increasing the destructive effect around them, cryotherapy with liquid nitrogen (2 cycles with 1 minute thawing time) was performed. The patient is currently being followed up, free of locoregional recurrence and without evidence of distant metastases. The anatomopathological control resulted in a cicatricial process without residual neoplasia.

### **KEY MESSAGE**

The abscopal effect is a phenomenon observed in the treatment of metastatic cancer, in which the localized treatment of a tumor acts not only on itself but also on distant lesions. This is due to an increase in the immune response against the tumor. In this context, the massive antigenic release resulting from the cryostruction of solid tumors would be a key element in the process of stimulating the immune response of the host, already reporting the association of cryotherapy with tucic immunotherapy. Despite the limitations in proving the cause and effect relationship in the presented report, cryotherapy appears as an important way of increasing the immune response in the treatment of advanced melanoma in the immunotherapy era.

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## **THE INFLUENCE OF THE NUMBER OF DISSECTED SENTINEL LYMPH NODES ON THE TREATMENT OF PATIENTS WITH MELANOMA**

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### **BACKGROUND**

Melanoma is the least-incident but more deadly skin cancer due to its early dissemination capacity, representing a public health problem. Sentinel lymph node (SLN) biopsy anticipates the detection of lymph node metastasis and supports the staging of the disease. It also assorts patients more likely to undergo a more aggressive treatment, such as a radical lymphadenectomy, being an essential prognostic factor in melanoma. In the last decade, efficacy and indications for sentinel lymph node biopsy had been brought up for the discussion. According to the current literature, the SLN biopsy is most indicated for lesions with Breslow depth greater than 0,8mm or ulceration, regardless of thickness. There is no statement regarding SLNB therapeutic impact regardless of the number o SLN removed.

### **METHODS**

Data from 217 medical records of patients with melanoma submitted to a sentinel lymph node biopsy by the same oncological surgery team from 2005 to 2014 in Belo Horizonte, Brazil were included and analyzed in a non-interventional retrospective study.

### **RESULTS**

Extensive superficial melanoma (62.6%) was the most common subtype, and the Breslow average found was 2.3mm. Sentinel lymph node positivity for metastasis was detected in 22.7% of the cases and was directly associated with Breslow thickness ( $p=0.027$ ). No correlation was found between the number of resected lymph nodes and the positivity or negativity for melanoma metastasis, being either up to two, three or more lymph nodes ( $p=0.490$ ). Melanoma recurrence was significantly associated with sentinel lymph node positivity ( $p=0.002$ ), but there was no correlation between the number of SLN removed or percentage of metastatic SLN.

### **CONCLUSION**

The invaluable role of the sentinel lymph node biopsy in staging and guiding the treatment of melanoma has been proved. According to our protocol, almost all patients with metastatic SLN undergo radical lymph node chains dissection. We believe that this radical surgery underpowers the possible impact of the number o SLNB removed. Maybe following actual guidelines of not proceeding radical lymph node dissection after metastatic SLN would open the possibility to establish a correlation between the number o SLN positive removed and clinical outcome.

## **PRIMARY CARE GENERAL PRACTITIONER KNOWLEDGE ABOUT MELANOMA COMPARED TO DERMATOLOGISTS IN BELO HORIZONTE, BRAZIL**

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### **BACKGROUND**

Melanoma is a very aggressive tumor. In the public health system, the general practitioner (GP) is the front-line doctor for population and could be able to manage suspected lesions. The delay of diagnosing, often related to a lack of knowledge about the disease, can be one of the greats responsible for its high mortality rates. This study aimed to evaluate GP's practice in cutaneous melanoma screening compared to dermatologists (specialists). Also, to define which needs are relevant to improving the service provided efficacy to manage cutaneous melanoma patients.

### **METHODS**

It was a prospective, and descriptive research carried out in the period from March to October 2017. A multiple-choice questionnaire to assess knowledge and daily practice of lesions suspicious of melanoma were offered to GP's and dermatologists that agree to participate in this research. The questionnaire was composed of sociodemographic questions, and 13 items focused on melanoma.

### **RESULTS**

The sample was composed of 73 dermatologic specialists and 147 general practitioners. The percentage of physicians who examine the entire skin of the patient at high risk for melanoma was 91.8% among the specialists and 25.3% among GP's ( $p < 0.001$ ). Over 90% of specialists have examined the skin of a patient with a previous history of melanoma, while among generalists this proportion was only 52.6% ( $p < 0.001$ ). When asked about the "ABCDE" rule, 96.2% of the specialists compared to only 35% of GPs were familiar with it ( $p < 0.001$ ). More than 90% of physicians in both groups said they lacked policies of permanent education focused on the knowledge of the melanoma and other skin cancers.

### **CONCLUSION**

The doctors who work in the primary health care have less appropriate knowledge about melanoma compared to the dermatologists. We inferred that unfamiliarity with this pathology could be a factor that implies delaying in the diagnosis of melanoma and all its implications. Continuing pigmented lesions education should improve GPs practices and help melanoma early diagnosis.

## **A BRIEF REPORT ON THE IMPORTANCE OF HAIRDRESSERS AND TATTOOISTS IN THE DETECTION OF CUTANEOUS MELANOMA**

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### **BACKGROUND**

Mostly patients and general public are responsible for early detection of melanoma. It is known that a better knowledge about the disease relates to early diagnosis of primary lesions and therefore better prognosis. Beauty professionals could play a role at melanoma diagnosis. A pilot study to estimate melanoma's knowledge level among hairdressers and tattooists was conducted in Belo Horizonte, Brazil.

### **METHODS**

We randomly selected 30 beauty salons and tattoo shops in all areas of the city. Initially they were contacted by telephone and then a visit was scheduled. Participants answered a questionnaire that evaluated their knowledge about melanoma. It was graduated in: None (don't know the term); Intermediate (know it's a cancer related to pigmented lesion); Great (know that is a serious skin cancer related to moles). Among the participants who reported a prior identification of any suspicious lesion on their clients, we asked what was their reaction to the communication to the client and if there was any feedback after medical consultation. At the end of the interview, in order to provide an instructive character to the project, all participants received instructional booklets of the Brazilian Melanoma Group (GBM). Furthermore, we showed melanomas images, teaching strong signs of the lesions related to ABCDE rule.

### **RESULTS**

Out of 30 participants enrolled in this survey, 13 (43.3%) agreed to participate in the interview: 4 tattoo shops and 9 hair salons. In 82% of these companies, the owner himself was the one who received the researchers and in 18% were managers or employees. Of 65 professionals interviewed, 57 were hairdressers and 8 were tattoo artists. When asked about their knowledge about melanoma, 3 (4.6%) indicated it was great, 9 (13.9%) intermediate and 53 (81.5%) none. Two hairdressers with intermediate knowledge reported that they had identified some suspicious lesion and communicated it to their clients who were receptive, giving return after consulting a doctor. In addition, they communicated to other employees of the salon advising on the real importance of observing suspicious lesions on their clients. It was a common sense the interest in learning more about skin cancers.

### **CONCLUSION**

This findings and comments support the need to study in detail the participation of hairdressers and tattooists as important players in melanoma detection and orientation of individuals with suspicious lesions to search for medical care.

## **1A,25-DIHYDROXYVITAMIN D3 DECREASE CD73 EXPRESSION AND ACTIVITY IN HUMAN CUTANEOUS MELANOMA CELLS**

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### **BACKGROUND**

We hypothesize that vitamin D decreases rates of adenosine formation in human cutaneous melanoma cells through the inhibition of extracellular ATP breakdown, thereby affecting tumor cell viability. Thus, the objective of this study was to verify the mechanisms of action of 1,25(OH)<sub>2</sub>D<sub>3</sub> on the activity and expression of ectonucleotidases in cutaneous melanoma cells.

### **METHODS**

Human melanoma cell line, SK-Mel-28, were cultured and treated with 1-50 nM concentrations of the active vitamin D metabolite (1,25(OH)<sub>2</sub>D<sub>3</sub>) during 24h followed by determination of NTPDase/CD39 and ecto-5'-nucleotidase/CD73 activity and as well as of expression rates of the purinergic system-related NTPASE1, NT5E and adenosine deaminase and vitamin D receptor. MTT was utilized to evaluate the cellular viability.

### **RESULTS**

The results show that 1,25(OH)<sub>2</sub>D<sub>3</sub> was able to decrease AMP hydrolysis by ecto-5'-nucleotidase/CD73 and expression of CD73, while do not change NTPDase/CD39 activity but increases the CD39 expression. It was also observed an increase of the cell viability in the concentration 1nM, but this viability decreased as the concentrations of vitamin D active metabolite was increased to 50nM. No differences were observed in genes expression.

### **CONCLUSION**

We show for the first time a mechanism of control in adenosine production through the modulation of the purinergic system in cutaneous melanoma cells treated with the active metabolite of vitamin D. This study provides original information on mechanisms, by which vitamin D plays a key role in preventing tumor progression in human melanoma cells.

## **CUTANEOUS COLLISION TUMORS: MELANOMA, BASAL CELL CARCINOMA AND SQUAMOUS CELL CARCINOMA - REPORT OF A CASE**

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### **BACKGROUND**

Cutaneous collision tumors are characterized by the coexistence of two cancers in the same anatomical site and its pathogenesis remains controversial. Although uncommon, the association of basal cell carcinoma and melanocytic nevus is the most common among combinations of skin tumors. The association of two malignant tumors is even rarer. We report a case of tumor collision representing melanoma and basal cell carcinoma and a squamous cell carcinoma in distance, at the same time, on the face.

### **METHODS**

Female patient, 79 years old, phototype II. She came to medical care presenting a 2 years history of a blackened lesion on the nose region, with slow and progressive growth. Adjacent the hiperchromic macula, she noticed the appearance of a pearly papule, in the last 8 months, with progressive growth. The lesion was asymptomatic. She also presented an eritematous nodule with spontaneous bleeding and fast growth on the left upper lip.

### **RESULTS**

Dermatological examination showed a 3 cm in diameter brownish-eritematous macula, presenting colors variation and irregular edges, associated to eritematous nodule, with pearl-like rim surrounding a central crater on the nose. Also eritematous nodule, with hematic central crust and infiltrated borders on the left upper lip. The first lesion's dermoscopy found blue-gray pepperings at perifollicular openings, making annular-granular structures and rhomboidals structures at the brownish part. Arborizing vessels with shiny white streaks at the lesion's nodular portion. The second lesion's dermoscopy found shiny white streaks , white halo surrounding the blood vessels, atypical vascular pattern, rosettes, central keratin plug and ulceration, all these structures disposed above a red pseudonetwork.

### **CONCLUSION**

The nose's histopathological examination showed a collision tumors: atypical lentiginous junctional melanocytic proliferation, melanoma in situ, and basaloid cells tumor with peripheral palisading, basal cell carcinoma, in the adjacent dermis. The lesion on the upper lip showed a squamous cell carcinoma. Histopatologically, in most reports, there is no mixing of cells of each tumor and the boundaries of each are well-defined. The meeting of invasive melanomas associated with BCC is unusual; usually a melanoma in situ is highlighted.

## **NEUROLOGICAL SYMPTOMS IN THE DYING PROCESS OF TERMINAL MELANOMA PATIENTS WITHOUT MORE THERAPEUTIC OPTIONS**

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### **BACKGROUND**

Melanoma is the less prevalent in all skin cancers and is responsible for the bulk of skin cancer-related deaths. The Brazilian data does not reflect the dimension of the problem of the mechanism of death in this patients. Symptoms are diverse, which makes harder to provide a treatment protocol for melanoma terminally ill patients. Metastases to the brain far outnumber primary brain tumors. Melanoma central nervous system metastases are increasing, and the challenges presented by this patient population remain complex, mainly when there are no more therapeutic options to offer. This study aimed to establish the prevalence of neurological symptoms in patients dying because of melanoma. We attempted to show how important is to identify these symptoms, seeking a better quality of death.

### **METHODS**

This project was based on secondary data of patients (interview with relatives and consultation of medical records) attending a referral service in the treatment of melanoma in Belo Horizonte, Brazil. A convenience sample of 32 participants was selected according to the primary inclusion criteria: patients deceased for a condition related to the diagnosis of Malignant Melanoma; a family member who signed the Informed Consent Form and followed the patient firmly in the last 30 days of life.

### **RESULTS**

At the time of death, the central nervous system was the second most affected by metastases (25.0%), followed by lungs (15.6%). Two or more sites of metastases (37.5%) were the most frequent site of metastases. Neurological symptoms were found in just 3,1% of the patients. More prevalent symptoms were (81,26%), skin wounds (37.5%), weight loss (81.2%), pain (65.6%), hemorrhage (34.4%), depression (59.4%), inappetence (71.9%). Thirty days before death 9,5% of patients report a headache, seizures were present in 15,63% of the patients, and in 3,1% one week before. Depression was found in 53,1% of the patients, one week before death. From the week before death, 6,25% of the patients experienced depression.

### **CONCLUSION**

Knowing the main symptoms of patients whose death was related to metastatic melanoma is the first step to provide correct management of quality of life and death of these patients. It is also required a multi-professional approach, that can ensure better treatment for these patients. Although cerebral metastasis has a high prevalence in advanced melanoma patients, surprisingly, neurologic symptoms were not a significant concern at melanoma end of life process.

## **AXILLARY LYMPH NODE SENTINEL SCREEN AFTER PAST OF DISSECTED AXILLARY CHAIN: A CASE REPORT**

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### **BACKGROUND**

The number of lymph nodes involved is the most important prognostic factor for patients with lymph node metastases and is assessed after complete chain dissection or sentinel lymph node biopsy. If the pathology study of the sentinel lymph node is positive for micrometastases, complete dissection of the lymph node used to is performed. Although, there are patients that had a complete chain dissection previously because melanoma or other cancer and later have a new melanoma that could demand a Sentinel Lymph node Biopsy(SLNB) which Sentinel Lymph Node(LS) can be detectable even after. The study aims to discuss cases of the presence of lymph node detectable in the lymph node chain previously and wholly dissected in patients with cutaneous melanoma.

### **CASE REPORT**

A 65-year old woman was referred to the service by a dermatologist due to the diagnosis by excisional biopsy of superficial spreading melanoma level III of Clark and 0.85 mm of Breslow in the upper right limb. The patient presented a previous history of right mastectomy and axillary lymphadenectomy in 2003. Margins enlargement of melanoma lesion and sentinel lymph node screening was required. Although technically the lymph node chain was previously resected, it was identified, and the axillary sentinel lymph node was negative for metastatic disease by anatomopathological and immunohistochemistry exams.

### **CONCLUSION**

Based on this case report it was possible to note the necessity to develop further studies about the best conduct of patients with cutaneous melanoma and detectable lymph nodes after complete dissection of draining lymph node chain. These studies will be relevant to determine causes, to evaluate current surgical techniques and to investigate patients undergoing these procedures (complete lymph node dissection and lymphoscintigraphy on relapse) also in other underlying neoplasms, such as breast cancer.

## THE INCIDENCE OF LOCALLY ADVANCED MELANOMA IN A BRAZILIAN PUBLIC HEALTH UNIT

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### BACKGROUND

Locally advanced melanomas (LAM), defined as lesions with tumoral stages I and III, are commonly present when the diagnosis is delayed. Their finding is ill-fated, as these patients are generally considered just for palliative care and have a poor prognosis. Additionally, the prevalence of LAM at diagnosis might be used as an indirect indicator of healthcare quality, as it reflects how the late diagnosis is being made, which negatively impacts the outcomes of the disease. In Brazil, it is estimated that 6.290 new cases of melanoma would occur in 2018, but we do not have precise data of in which stage.

### METHODS

A retrospective study analyzed medical charts of patients with diagnosed melanoma, confirmed with a surgical biopsy, admitted to a Brazilian public tertiary hospital between January 2017 and June 2018

### RESULTS

Among the 50 patients in the study, 10 (20%) presented with high staged locally advanced melanoma at diagnosis, 3 of which were aged between 18 and 35. All ten patients had tumor thickness measured in centimeters, whereas this measure is usually given in millimeters. If compared to early-stage melanomas, the prognosis of LAM is significantly more miserable, with a mean 5-year survival rate of 77%, and depending on staging and other prognostic factors, may be as low as 32%, in contrast to 98% in stage I.

The diagnosis of LAM is unfortunate, as treatment options are very limited, especially in higher stages, and most interventions are made to improve quality of life and prevent advance and spreading disease. This elicits the necessity to diagnose melanomas in an early stage, in which the lesion is confined to the epidermis, usually curable after surgery.

Moreover, advanced disease at diagnosis is more prevalent in minorities and less wealthy groups, indicating that socioeconomic factors influence the outcome. As in most cases, the initial suspicion of melanomas is made by close persons or the patients themselves and requires precise knowledge of malignancy signs in skin lesions. This is a factor that should be taken into consideration in a Brazilian population.

### CONCLUSION

The high prevalence of LAM found in this study and in other parts of Brazil reveal a negative aspect in melanoma care in the Brazilian public health system, despite a recent decrease in melanoma mortality. Therefore, public healthcare measures should be taken to decrease late diagnosis of melanomas, mainly as it is commonly found in young age.

## LATE RECURRENCE OF MALIGNANT MELANOMA IN BRAZILIAN PATIENTS

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### BACKGROUND

Cutaneous melanoma is the most lethal of the skin cancer subtypes. Although the prevalence of melanoma in Brazilian population is low, its lethality is high when compared to global average, probably due to under notified cases and late diagnosis due to public health's difficult access. After a biopsy contemplating the full tumoral thickness is necessary to determinate melanoma subtype and Breslow thickness, directly linked to prognosis prediction and survival rate. Most patients at early diagnosis became cured but when not, it usually spreads fast with multiple metastases after early recurrences. However, some patients have an intermediate, late recurrence that is defined as the arising of metastases after five years, late recurrence after ten years, and ultra-late recurrence after 15 years of primary diagnosis. It is very rare and usually with a high tendency of late diagnosis because most patients are not at follow-up anymore and the majority are not concerned about melanoma.

### METHODS

A total of 618 medical charts of patients with melanoma were reviewed in a private melanoma reference unit in Belo Horizonte, Brazil.

### RESULTS

From them, 10(1,6%) patients were identified with late recurrence within 20% presenting local recurrence, while the other eight presented at regional lymph nodes, soft tissue (77,7%) followed by internal organs (22.3%). No predominance between gender or any other factor was seen that could predict tumor dormancy and late recurrence.

### CONCLUSION

Melanoma occurs due to a build-up of genetic and epigenetic mutations that progressively cause uncontrolled proliferation of tumoral cells. Most of the patients have a continuous and progressive process with predictable metastases and early recurrence following initial stage. Although we know many genes and epidemiologic data, it is not possible to predict or define among the prognostic factors, to identify a group at high risk for late recurrence. An interval of five years without the disease does not mean cure. It is crucial a follow up for ten years, for the screening of recurrence and dermatoscopy for identification of a second primary lesion.

## **SENTINEL LYMPH NODE BIOPSY IN ANORECTAL MUCOSAL MELANOMA: A SERIES OF CASES**

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### **INTRODUCTION**

Anorectal melanoma is a rare and aggressive disease that may present asymptotically or through nonspecific signs and symptoms, such as anal discomfort, rectal bleeding, and melanotic or amelanotic lesion. Thus, this type of melanoma is usually diagnosed late, leading to a worse prognosis. This study aims to analyze the use of Sentinel Lymph Node Biopsy (SLNB) as a tool for the diagnosis and for the regional staging of anorectal melanoma, allowing to complete propaedeutic stagement and proper treatment, including inguinal radical lymphadenectomy and adjuvant treatment.

### **MATERIAL AND METHODS**

This retrospective series case study included five patients, aged 40 to 70 years old, with primary anorectal melanoma. Patients were submitted to serial lymphoscintigraphy for sentinel lymph node (SLN) localization using technetium and blue patent dye injection on the scar of the previous resection. Afterward, margin expansion (ME) and SLN resection were performed at day hospital under local anesthesia and venous sedation.

### **RESULTS**

Four patients have submitted to local treatment with ME and a regional treatment guided by SLNB. Inguinal metastases were identified by SLNB and treated with radical lymphadenectomy. One patient did not present migration of the marker in lymphoscintigraphy and, therefore, was not submitted to SLNB but only ME. In none of the cases local or regional recurrence happened. Lymphography and surgical techniques will be presented at posters.

### **CONCLUSION**

The use of SLNB allows regional staging of the disease, once anorectal drainage is directed to the superficial lymphatic system. This allows a more accurate indication for inguinal lymphadenectomy, sparing patients without metastasis of radical surgery morbidities. SLNB is a feasible, accurate procedure and should be included in the staging of patients with anorectal melanoma. It is important to emphasize the relevance of maintaining the follow-up of these patients to identify recurrences and/or new primary tumors.

**DIFFICULT IN DIAGNOSING MELANOMA IN THE PUBLIC HEALTH SYSTEM IN BRAZIL**

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**BACKGROUND**

The incidence of cutaneous melanoma is rising faster than any other cancer in the world. The rise in the incidence of melanoma reflects more skin biopsies. This study aimed to perform a qualitative and quantitative survey of melanoma patients process biopsy to histopathology reports at a Public High Complexity Unit. Over 160 millions of Brazilians(80%) depends on the public health care system in Brazil where access to a dermatologist is extremely scared and also suspicious

**METHODS**

This was a prospective and descriptive study conducted at a Public High Complexity Unit in Belo Horizonte, Brazil, in the period from May 2016 to June 2018, interviewing patients with a histopathology confirmation of melanoma. A questionnaire was used and included questions like: "Was the biopsy performed in the public or private setting?", "Was the first medical appointment at public or private setting? Also a relationship between when the patient identified a suspected lesion and the first time a patient has a doctor appointment.

**RESULTS**

The final sample was composed by 124 patients and consisted of 41 (33%) men and 83 (67%) women. The first medical appointment was not in the public health system in 33 cases (26%). Almost 33% of patients had to pay by their pocket for a private biopsy performed in a private institution because they decide not to wait for a late schedule biopsy in the public setting. These patient were not able to continue their treatment in the private service because they were uninsured and had to move to a public one. As an extreme example, there was a case in this group; a patient spent six years from the suspicious lesion until the diagnosis at the public health system.

**CONCLUSION**

The relevant number of biopsies outside Public System at the private context in an impoverished population that could not pay for it shows a weak link at Brazilian public health system, just at the more strategic step of melanoma management that could promote early diagnosis, less expensive melanoma management and more critical, the cure. This high demand for private biopsy to treatment in the Brazilian public health system point out that inclusion policies regarding diagnostic services are of critical importance to ensure melanoma comprehensive care.

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## **THE LACK OF KNOWLEDGE OF MELANOMA PATIENTS ABOUT THE DISEASE IN A BRAZILIAN PUBLIC HEALTH SYSTEM UNIT**

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### **BACKGROUND**

In the last decades, melanomas have shown an increasing incidence in several countries. Early, thin melanoma lesions can usually be seen by patients, and surgical excision of these lesions almost always leads to cure without further treatment. Hence, in theory, increasing public awareness and promoting early detection and treatment should help many people to have melanoma discovered and removed at an earlier stage and thereby reduce mortality from melanoma. Therefore, the purpose of this study was to better understand the population awareness before having the diagnosis of this skin cancer.

### **METHODS**

A cross-sectional descriptive study was conducted at a public High Complexity Health Unit in Belo Horizonte, Brazil, in the period from May 2016 to June 2018, whose sample consisted of patients with a histopathology confirmation of melanoma. The patients were invited to answer a survey that included questions about melanoma awareness and knowledge like familiarity with the term melanoma, early signs of melanoma, self-examination practices (including reasons for not examining the skin and examination frequency) before having the diagnoses. Also, socioeconomic data were collected.

### **RESULTS**

The sample consisted of 124 patients: 41 (33%) men and 83 (67%) women. Almost 74% were Hispanic whites. Most of them (78%) had less than 12 years of education and low household income. Survey questions on melanoma awareness and knowledge, when asked: "Did you know what melanoma is?" nearly 80% (99) of respondents did not know the term, 10% heard about it but did not know what it was, and 12 patients knew it to be a type of skin cancer. Also, more than 90% (114) of participants have never strictly examined their skin.

### **CONCLUSION**

Socioeconomic status and educational level were found to be important correlated with melanoma knowledge. Thus, our findings support that public education campaigns should be improved with a focus on early detection of melanoma.

**PREVALENCE OF ACRAL LENTIGINOUS MELANOMA IN A POPULATION-BASED PUBLIC HOSPITAL**

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**BACKGROUND**

Acral lentiginous melanoma (ALM) is the fourth variant of cutaneous melanoma and was described by Reed in 1976, adding the other three forms initially reported: extensive superficial melanoma, nodular melanoma, and lentigo malignant melanoma. ALM is notorious by its predilection for distal areas of the body, particularly the plantar region, and is a rare subtype of melanoma, accounting for about 2-7% of cutaneous melanomas in the general population, although its proportion among all melanomas is highest in non-white.

**METHODS**

A retrospective study of patients diagnosed with cutaneous melanoma was performed at a reference public health system hospital in Belo Horizonte, Brazil. Medical charts were analyzed through a questionnaire. Demographic data such as sex, age, self-declaration of skin color and variables related to the pathology, such as topography, thickness, stage of the primary lesion, time elapsed between the perception of the tumor and search for medical assistance until the definitive diagnosis was collected during the last two years period, and the prevalence of ALM was analyzed.

**RESULTS**

Eighteen (14.5%) of the sample had ALM subtype. The ALM series showed the more significant involvement of females (72.2%) than males (27.8%) and a higher prevalence in advanced ages, between 53 and 92 years, with a mean age of 65 years. About 50% of the cases diagnosed as ALM occurred in patients who declared themselves to be black, brown and yellow. As to the topography, 15 (83.3%) cases affected the feet and 7 (38.88%) in the plantar region and the podactyls. Regarding the thickness at the time of diagnosis, 10 (55.5%) patients had Breslow greater than 2.0mm, 4 (22%) less than 1.0mm and only 4 had a diagnosis of ALM in situ. Finally, it was observed that 6 (33.3%) patients took more than one year to seek medical attention after seeing the lesion and, after the first consultation, only 5 (27.8%) patients received the definitive diagnosis in less than one month.

**CONCLUSION**

The data from this study support the findings described in the literature. However, it demonstrates a high prevalence of ALM in this population. The predominant occurrence in non-exposed sites, the lack of patient's orientation to the risk of skin cancer (non-white) and elderly, reinforce the lack of knowledge of the disease. These justify the delay in the search for medical assistance, impairing early diagnosis necessary to improve patient's survival.

## **ANALYSIS OF THE QUALITY OF THE ANATOMOPATHOLOGICAL REPORT ON THE DIAGNOSIS OF MELANOMA: IMPLICATIONS FOR DIAGNOSIS AND CONDUCT**

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### **BACKGROUND**

Melanoma is a malignant neoplasm originating from melanocytes which feature high dissemination capacity and high rates of morbidity and mortality. For 2018 the Brazilian National Cancer Institute estimates 6270 new cases. In the United States, melanoma is the sixth most prevalent cancer in men, as well as in women. This study aimed to evaluate the impact of the slide and the anatomopathological report revision on the staging, conduct, and prognosis of patients with melanoma.

### **METHODS**

A retrospective observational study of series of cases, cross-sectional, compared original anatomopathological report and slide review report from a reference laboratory from the cutaneous melanoma's patients treated in a reference melanoma service in Belo Horizonte, Brazil. The presence of histological characteristics of primary melanoma validated by the American Joint Committee on Cancer (AJCC) was also assessed at the reports.

### **RESULTS**

Partial results from 107 medical charts were analyzed, and 24 were considered eligible for the research. Regarding the medical conduct, there was a change after the review in a reference laboratory in nine cases, which corresponds to 37.5% of the sample. This change was more related to sentinel lymph node biopsy's indication. The histological characteristics of primary melanoma, such as tumor thickness, mitotic rate, and ulceration, are essential features for prognosis, staging and therapeutic decision but only 42.9% of original reports had complete valid information. These variables should be as accurate and informative as possible to drive better treatment and patient outcome. The subjective interpretation of the lesion may be the primary problem. An undervaluation of primary melanoma can compromise a patient's life, while overvaluation leads to radical conduct, often mutilating, all of it with high stress and cost to patients and family.

### **CONCLUSION**

The anatomopathological review of the slides modified the medical conduct in a relevant percentage of cases. The laboratory and pathologist experience may also be prognostic factors for this neoplasm. We recommend a pathological review of all cases of primary melanoma diagnosis.

## POPULATIONAL KNOWLEDGE ABOUT MELANOMA IN A BRAZILIAN POPULATION – A PILOT STUDY

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### BACKGROUND

Skin cancer is the most common of all cancers, and 90% of these tumors are curable since they are early detected. Among skin cancers, melanoma is the most serious and often deadly. It is known that its diagnosis is fundamentally visual, and the patient himself or people close to him are responsible for the initial suspicion. In this way, its recognition by the population becomes an essential ally in the success of the early diagnosis and curable treatment. This study aimed to evaluate the level of melanoma's knowledge in this population.

### METHODS

We developed a specific questionnaire composed of three sections as sociodemographic features, melanoma knowledge, and self-examination. After filling out the questionnaire, volunteers received a melanoma information brochure.

### RESULTS

A pilot study with 30 volunteers to validate the questionnaire indicated that all questions were easily understood and answered. The mean age was  $37.7 \pm 15.9$  years old, 50% of males. 46.7% of the individuals had white skin color, and 33.3% had finished high school. Regarding the profession, only one was a health professional, and 43.3% had monthly family income less than 1090 USD. About melanoma knowledge, 43.3% said they did not know what melanoma was, and 33.3% said it was skin cancer. Among those who knew what melanoma was, 47.1% received this information from the media. The most common answer about melanoma features were black lesions and lesions that grew or evolved (41.2% for both). The most common risk factor pointed was chronic sun exposure (88.2%), and the most commonly reported prevention pointed was the use of sunscreen (88.2%) Only four individuals reported had done a self-examination of the skin. Among those who did not perform the self-examination, most never thought about it (65.4%). For those who performed, 75% looked for nodules/lumps and/or new spots, and only one individual seek help from another person in case of any finding.

### CONCLUSION

These partial results indicated that the questionnaire was feasible to be used in a big populational group, stratified by net income, professional occupation, and educational level. The results from this small sample indicated that almost 50% of it did not know anything about melanoma. This group was very grateful to receive information about the disease, risk factors, and prevention. We believe that the final data could guide future public health campaigns, investing in the most common doubts of the population.

**DERMOSCOPIC FEATURES OF MELANOMA METASTASES: A THREE-YEAR FOLLOW-UP**

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**KEY WORDS**

dermoscopy, melanoma, neoplasm metastases

**BACKGROUND**

Skin metastases of melanoma may present distinct clinical features and can be the first clinical presentation in 2-8% of patients with cutaneous melanoma (1). Differential diagnoses include melanocytic nevi, hemangioma, blue nevus, and primary melanoma.

**FOCUS OF INTEREST**

The case here reported illustrates the clinical and dermoscopic variability in a patient with cutaneous metastases of malignant melanoma (CMMM).

**CASE REPORT**

A 62-year-old male patient had a recurrent melanoma on his thorax (Breslow 3,2 mm) removed in 2013. The sentinel lymph node biopsy was positive and a left axillary lymphadenectomy was performed. A previous lesion at the same location had been removed 3 years before, but no biopsy was carried out. Adjuvant interferon alpha-2b was started in December 2014. In April 2015, multiple cutaneous metastases appeared in the thorax, most of them with a vascular pattern on dermoscopy. Since then, the patient has been treated with dacarbazine, ipilimumab, vemurafenib, pembrolizumab, vemurafenib/cobimetinib. We describe the clinical behavior and the dermoscopic aspect of the numerous cutaneous metastases during the use of the above mentioned drugs.

**DISCUSSION**

Locoregional metastases occur in about 50% of the patients with metastatic melanoma (2). The clinical presentation might be heterogeneous, though it presents more frequently as multiple and small papules or nodules with symmetrical distribution (1-3).

The following dermoscopic patterns are described in CMMM: homogeneous, sacular, amelanotic, polymorphous (3), perilesional erythema (4), vascular, different colors (pink-red, brown-grey, dark, blue), pigmentary halo and peripheral grey spots. Polymorphous vascular pattern is the most common presentation, showing punctate, thick hairpin, dotted, and corkscrew vessels (1,2,5,6). Considering the new systemic treatment options for advanced melanoma, which are responsible for a longer survival of the patients, the knowledge of the distinct dermoscopic patterns of CMMMs is critical.

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**CUTANEOUS MELANOMA IN YOUNG ADULT PREGNANT PATIENTS: TWO CASE REPORTS**

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**BACKGROUND**

Melanoma is the most aggressive skin cancer and is currently the sixth most common cancer in women in the United States. Melanoma is not uncommon in pregnancy, with an estimated occurrence rate of 1:1,000. Melanoma is the cancer with the highest incidence of metastases to placenta and fetus, although it is not the most common in pregnancy.

**METHODS**

The present cases were diagnosed and treated in 2 centers of reference in oncology in Goiânia, Goiás, Brazil (Hospital Araújo Jorge and Cebron) and the relevance is based on the controversies regarding the treatment and prognosis of melanoma in pregnancy.

**RESULTS**

CASE 1: 29 years, 12 weeks of gestation, G2P1A0, phototype IV with a history of pigmented lesion in the dorsal region 10 years ago, with pruritus, enlargement and alteration of the relief, with 2.5x1.8cm. Excisional biopsy with diagnosis of extensive superficial melanoma, Breslow 0.7 mm, IM=0/mm<sup>2</sup>, absent ulceration.

CASE 2: 29 years, 32 weeks of gestation, G1P0A0, phototype III, with right plantar pigmented lesion for 6 years, with increase and alteration of the relief, with 1.8X1.0cm. Excisional biopsy with diagnosis of acrolentiginous melanoma, Breslow 2.1 mm, IM=0/mm<sup>2</sup>, absent ulceration.

**CONCLUSIONS**

CASE 1: submitted to enlargement of the margins at the 20th week of gestation. Histopathology showed no residual disease. The histopathological findings of the placenta and its attachments were unchanged. In follow-up.

CASE 2: submitted to enlargement of the margins and biopsy of the inguinal sentinel lymph node after delivery. Histology without evidence of residual disease and negative lymph node. Placenta examination was not performed. In follow-up.

About 30 to 35% of women with melanoma are of childbearing age at the time of diagnosis. For years, it has been widely accepted that the prognosis of melanoma was worse in pregnancy and that subsequent pregnancies increase the risk of recurrence. However, current scientific literature argues that melanoma prognosis, recurrence and incidence appear to be unaffected by pregnancy.

Treatment of the initial stage of melanoma is the same regardless of gestation. Preoperative lymphoscintigraphy and sentinel lymph node biopsy maybe performed safely in pregnant women. Finally, we emphasize that the conduct in the pregnant patient with melanoma does not differ from the other patients, although the melanoma treatment can be postponed if the patient is close to the parturition, as in case 2.

## **EVALUATION OF THE SURGICAL MARGIN IN VIVO AND EX VIVO AT SURGICAL MANAGEMENT OF MELANOMA**

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### **BACKGROUND**

Melanoma is 5% of primary cutaneous neoplasms and has the worst prognosis. Surgical treatment is a heading factor and should have free surgical margins. However, studies have shown that retraction of the surgical specimen may imply divergences between in vivo and ex vivo measurements and in vitro, which may lead to imprecise pathological analysis, unnecessary re-ampliation and legal issues. Thus, this study aims to evaluate and quantify the retraction of the surgical specimen at all step surgical sample process, as well as to analyze possible factors related to shrinkages, such as formalin fixation, age, gender, and location.

### **MATERIAL AND METHODS**

150 patients diagnosed with melanoma and proposed surgical margin enlargement were prospectively evaluated. Primary resection surgical scar had their definitive margins enlargement marked and were measured with a sterile ruler. After resection, a measurement of the resulting surgical defect before reconstruction at patient and a new measurement of the surgical specimen (ex-vivo retraction) were performed approximately 10 minutes after excision in ambient air. New measurements were obtained by the pathologist when analyzing the specimen already fixed in formalin. A multivariate analysis was performed for comparison of in vivo and ex vivo results.

### **RESULTS**

Most of the 150 lesions analyzed were located in the trunk and dorsum, and the sites that presented significant shrinkage of cutaneous surgical specimens were neck and upper limbs. We are finishing our cohort to reach sample size of 200 lesions to final statistical analysis, but it indicates that the highest rate of retraction of the surgical specimen, close to 30% occurs essentially when compared to the measurements in vivo and ex vivo, corroborating some of the studies. We expected that this study could stratify it according to sex, age, body topography and other consistent factor specific of shrinkage of melanoma margin enlargement specimens.

### **CONCLUSION**

Differences between measurements of ex vivo and in vitro margins of the workpiece can lead to unnecessary reoperations leading to mutilations and functional disabilities, as well as delaying the onset of adjuvant therapies and burdening the health system. For this reason, helping in establish relevance of surgical margin among pathological margin and qualify and quantify surgical specimen's shrinkage is necessary to allow better surgical results, recurrence and also prognostic.

**HOW TO PROCEED WHEN A PATIENT HAD A RESECTION OF 5 LESIONS PLACED IN THE SAME VIAL AND ONE TURN OUT TO BE A T2A MELANOMA WITHOUT SITE IDENTIFICATION?**

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**BACKGROUND**

Although cutaneous melanoma represents only 4% of skin cancers, it accounts for the majority of deaths due to its high metastatic ability. Therefore, early and precise diagnosis is indispensable to a better chance of treatment and histopathology remains the gold standard for accurate melanoma diagnosis.

**CASE REPORT**

Patient with an atypical situation which five pigmented suspicious lesions (right temporal, nasal, left inguinal, right and left axillary) were removed and submitted to pathological review at the same vial without identification of the primary site of each. First, the pathological report established that one of them was a T2a melanoma without microscopic free margin. Standard procedure for it was margin enlargement and Sentinel Lymph Node Biopsy (SLNB), but we were unable to proceed without knowing which of the five scars that macroscopically had no residual pigment lesion, was the site of T2a melanoma. The pathologist was asked to review all five specimens and considering features like histological layers, skin glands appearance, solar damage, hair follicles aspects, corneous keratin layers, cell types and other histological features; the pathologist predicted that melanoma was originated probably from the inguinal lesion. In this scenario to avoid morbidity with five margin enlargement plus SLNB, it was performed margin enlargement starting from pathologist less suspicious melanoma origin. After the first four resections, none present residual melanoma suggesting that the last one, the inguinal one suspected by the pathologist, was the melanoma lesion. Margin enlargement was performed showing residual melanoma staged as T2. SLNB that was negative for metastatic disease. The patient is free of recurrence after five years of follow up. One of the most important prognostic factors of melanoma is the time of diagnostic. The sooner suspected lesions are discovered, submitted to histological analysis and adequate treatment, better for the patient.

**CONCLUSION**

Melanoma is a severe disease and implicates high mortality especially if the diagnosis is made in advanced stages. So it is essential to accomplish the right placement and identification of surgical specimens from a biopsy, mainly for patients with multiple suspected lesions. Even though in cases as reported here, particular pathological analysis qualifying specific skin features from different topography could help on it.

**MELANOMA IN BRAZIL: INCIDENCE AND MORTALITY IN THE LAST 15 YEARS**

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**BACKGROUND**

According to the Brazilian National Cancer Institute – INCA – the projection for 2018 is to have 6,260 cases of melanoma, accounting for 3.6% of all skin cancers, with 1,547 related deaths. Brazil is a large country with deep regional contrasts and a population formed by an admixture from three different ancestral roots - Amerindians, Europeans and Africans - resulting in a great variability of skin pigmentation. Melanoma incidence and mortality in this heterogeneous population is poorly described in the literature.

**METHODS**

The main objectives of this research were to evaluate temporal trends in incidence and mortality. The data came from Brazilian Population Based Cancer Registries, and the National Mortality Information System from 2000 to 2014. To describe trends in change in incidence and mortality rates, the Average Annual Percentage Change (AAPC) was calculated.

**RESULTS**

Between 2000 and 2013, in men, the median incidence rate adjusted for the world population rose from 2.52 to 4.84 per 100,000, with an AAPC of +21.5% (95% CI +15.4 to +28.0); while among women, in the same period, the increase was from 1.93 to 3.22 per 100,000, with an AAPC of +13.9% (95% CI +8.1 to +20.0). Regarding mortality, between 2000 and 2014, the rates went from 0.85 to 0.90 per 100,000 for men (AAPC = +0.8, 95% CI +0.4 to +1.1), and from 0.56 for 0.53 per 100,000 for women (AAPC = -0.1, 95% CI -0.2 to 0.0), respectively.

**CONCLUSION**

In Brazil, after 2000, both incidences in men and women started to climb and an additional doubling of incidence rates happened moving from 2.52 to 4.84 in men and from 1.93 to 3.22 per 100,000 inhabitants in women. Whereas incidence rates have continued to increase in recent birth cohorts, mortality rates have stabilized. Understanding the incidence and mortality trends attributed to melanoma is important for behavioral counseling interventions that focus on promoting skin cancer prevention.

**COMPLETE RESPONSE OF MULTI-TREATED MELANOMA PATIENT CARRING LEUKEMIA**

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**BACKGROUND**

The current treatment options for melanoma are surgery, immunotherapy, targeted therapy, chemotherapy, biochemotherapy and radiation therapy. In patients with a BRAF mutation, treatment with targeted therapy drugs might be helpful and may present improvement in overall survival and progression-free survival.

**METHODS**

This case report was based on medical chart analysis of a patient assisted in a reference melanoma center in Belo Horizonte, MG, Brazil.

**RESULTS**

A 63-year-old man presented a metastatic cutaneous melanoma for skin, and lymph nodes with BRAF mutated and chronic lymphocytic leukemia (CLL). The diagnosis of melanoma was in 2014. He was treated by surgery for stage IIIC disease with left axillary lymph node dissection as the sentinel lymph node biopsy was positive. He started *Dacarbazine* and had partial response followed by progression when initiated *Ipilimumab*. Followed clinical response he had bulk tumor necrosis complicated with infection and life treating erysipelas. Infected necrosis lesions in the left hemithorax had to be surgically resected. At the fourth *Ipilimumab* dose, the patient presented new lesions. Therapy was changed to *Pembrolizumab* with an alternation between partial response and stable disease. Some new lesions were controlled by local surgery and electron beam therapy. In 2016 after progressive melanoma he started *Vemurafenib* with complete response, but shortly he had aggressive progression of CLL symptoms and stop melanoma treatment to star Chlorambucil. In May 2017, leukemia was relatively under control, but the patient had bulk melanoma progression with many necrotic lesions and pigmented cutaneous nodules on chest and shoulder. Another LLC progression required to interrupt melanoma treatment. Dealing with two aggressive tumors, from September 2017 to the present date, the patient has been receiving *Vemurafenib* associated with *Cobimetinib*. The patient presents a complete response with PS of 100%. Some melanoma lesions including a new lesion in the leg developed a vitiligoid halo.

**CONCLUSION**

Management of melanoma requires a committed multi-professional team, and personalized treatment can lead to a complete response. When necessary surgery can be useful to reduce tumor load always in joint management with the clinical oncologist and radiotherapist. Sincronic tumor-like LCC can be treated among melanoma with close control of LCC worsening induced by BRAF inhibitor.

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## MELANOMA INCOGNITO IN A RENAL TRANSPLANT RECIPIENT

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### BACKGROUND

Renal transplantation is associated with an increased risk of cancers at multiple sites. Patients who received renal transplantation have an incidence ratio 2.48 for melanoma. Risk factors for developing melanoma include older age, male sex recipient, white race, living donors and cyclosporine therapy. Besides, melanoma may present as a clinically equivocal lesion and be difficult to diagnose. This report demonstrates a case of melanoma with extensive regression features in a renal transplant recipient with multiple risk factors.

### METHODS

The patient was a 69 years old man, who was a renal transplant recipient since 2012. In addition, he had type 2 diabetes mellitus, dyslipidemia, systemic arterial hypertension and obesity, and was taking immunosuppressive drug therapy including cyclosporine and mycophenolate mofetil. He was referred to our department for the first skin evaluation since the transplant. After inspection, we found a pigmented lesion in the right lateral lumbar region that was unknown to him. Clinically it presented as brownish macule and in dermoscopic examination showed a pinkish to tan background, structureless areas, peripheral dots and linear irregular vessels. The dermoscopic pattern was unspecific and suggestive of a lesion with extensive regression. An excisional biopsy was performed and the histopathological examination revealed a superficial spreading melanoma with total dermal regression associated with a melanocytic nevus. Immunohistochemistry was positive for melan-A and tyrosinase in the scarce remnants of tumor cells. He was referred to wide excision and follow-up.

### CONCLUSION

Total body skin examination is mandatory in high risks patients like renal transplant recipients. The majority of these patients use immunosuppressive therapy, and this alone has been shown to be a prominent risk factor for melanoma because it impairs immune surveillance and has direct oncogenic activity. Therefore, adequate primary and secondary prevention of melanoma among this population is crucial. Objectively, it is recommended that multidisciplinary follow-up with a dermatologist should be started from the moment of the transplant, and that the patient be educated regarding measures of photoprotection and frequent cutaneous revision. Furthermore, it is of fundamental importance to biopsy clinically equivocal lesions with unspecific pigmented pattern and with extensive regressive features at dermoscopy, not to miss a melanoma incognito.

## IS SLN BIOPSY NECESSARY IN THE CONJUNCTIVAL MELANOMA?

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### BACKGROUND

Conjunctival melanoma (CM) is a lesion of the ocular surface characterized by an atypical pigmented tumor in any region of the conjunctiva. It is rare, accounting approximately 2%-5% of all ocular tumors and 5%-7% of all ocular melanomas, but it is a potentially fatal form of melanoma with a high mortality rate of up to 20% in 10 years. This type of melanoma may present invasion, spreading through regional lymph nodes first via a sentinel lymph node (SLN), but also invading the orbit, eyelids, paranasal sinus and the brain. There is no evidence about the best management of this tumor, but the current pattern of treatment is wide local incision, double freeze-thaw cryotherapy to the margins and alcohol application when it is possible.

The SLN biopsy may detect micrometastasis which is not detected by conventional methods, but it is useful, and indications are not established for conjunctival melanoma. The purpose of this report is to analyze if SLN biopsy is feasible and describe morbidity for management of conjunctival melanoma.

### METHODS

Early on the day of surgery patients received an ocular injection of radiotracer using technetium around conjunctival melanoma. Lymphography was done to identify local and number of sentinel lymph node. Early afternoon patients were admitted. All cases were done under local anesthesia plus sedation on day hospital regimen.

### RESULTS

Five patients diagnosed with CM were submitted to SLN biopsy, three male, and two female. Four patients had all SLNs histologically, and immunohistochemically (S-100, Melan-A, HMB-45) negative for metastatic involvement whereas one SLN was inconclusive because of insufficient material. All SLN migrated to intra parotid gland lymph nodes. There was no case of definite facial nerve palsy or any other definitive morbidity including satisfactory functional and esthetic results of treatment.

### CONCLUSION

Lymph node biopsy has a lower cost and less morbidity than prophylactic or therapeutic lymphadenectomy. Although it is technically sophisticated, it is a secure procedure committed by a multidisciplinary team.

**SEBORRHEIC KERATOSIS-LIKE MELANOMA: AN OCCASIONAL FIND AFTER SKIN EVALUATION**

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**BACKGROUND**

Seborrheic keratosis is among the most common benign skin neoplasms and it is universally distributed. Prior studies found that a little percentage of the lesions sent to pathologists as seborrheic keratosis were actually melanomas.

After the introduction of dermoscopy, the diagnostic accuracy for skin tumors and seborrheic keratosis has significantly improved, reaching a sensitivity above 90%. However, there are melanomas that present dermoscopic features that mimic seborrheic keratosis, just like scaly surface, hyperkeratosis, epidermal hyperplasia, milia-like cysts and comedo-like openings.

Therefore, we present a case of a patient with a lesion that resembles clinically a seborrheic keratosis, but was suspected as melanoma after dermoscopic evaluation and confirmed by histopathologic examination.

**METHODS**

The patient, a man born in 1946, with diagnosis of hypertension and dyslipidemia and without familial history of melanoma, was referred to our department due to an exophytic lesion on the right ear that appeared two years ago. A previous incisional biopsy showed a non-ulcerative basal cell carcinoma. After inspection of the skin, we found other two suspected lesions. The first one was located nearby the basal cell carcinoma, at the jawbone ramus and presented as a brownish macule with irregular follicular openings, annular-granular pattern and early rhomboidal structures. The lesion was classified as a superficial spreading melanoma with Breslow thickness of 0,25mm.

The second occasional finding was described as a brownish lightly elevated scaly plaque with well shaped borders on the left arm which resembled clinically seborrheic keratosis. At dermoscopy there was multicomponent pattern with reddish background, blue-white areas, millia-like cysts, yellowish-surface, irregular globules and dots, shiny white streaks. The histopathological features were compatible with superficial spreading melanoma *in situ*, presenting follicular plugs.

The patient was referred to wide excision and follow up. Nowadays, he is in medical attendance with no abnormal signs or symptoms.

**CONCLUSION**

The recognition of seborrheic keratosis-like melanoma can be challenging. Therefore total body skin examination is mandatory to high risk patients and can improve detection of seborrheic keratosis-like melanoma.

We know that some features suggests seborrheic keratosis-like melanoma, just like: pigment network, globules and dots, streaks, blue-black color, blue-white veil and regressive phenomenon. Besides, melanoma can also present dermoscopic features such as follicular plugs that are frequently found in seborrheic keratosis and may be a reason for misdiagnosis.

Thus the dermoscopic assessment of the lesions that resembles seborrheic keratosis, especially in individuals over fifty years and with previous skin malignancies, is primordial to avoid the late diagnostic of seborrheic keratosis-like melanoma.

## CUTANEOUS MELANOMA IN A REGION OF SOUTHERN BRAZIL

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### BACKGROUND

Cutaneous melanoma (CM) is a neoplasia with an increasing incidence worldwide. In Brazil, skin cancer corresponds to 30% of all malignant tumors and CM represents 3% of them. The incidence rate of CM is particularly high in western Santa Catarina State due to phenotypic characteristics of population.

### Methods

Descriptive, cross-sectional study which included patients with diagnosed CM between 2002 and 2016, at the Reference Center for Diagnosis and Treatment of Cancer in western Santa Catarina.

### RESULTS

In this period, 1146 patients were treated. An average of 76.4 cases per year were observed. Most patients had skin phototype I and II (91.2%) and had or still have a profession with high sun exposure (71.6%). The average age was 52.67 years (SD = 15 years), most of them were women (58.8%). The most common CM types were superficial spreading (66.5%), nodular (16.4%), lentigo maligna (4.9%) and acral (2.7%). The average depth of lesion was 1.15 mm and most cases were classified as Clark IV (33.8%). It was observed that 29.7% of the patients had ulcerated CM and 18.1% presented regression of the primary cutaneous lesion; 54.6% of the lesions presented intratumoral infiltrate, while 66.1% were peritumoral. Sentinel lymph node screening occurred in 49.1% of the patients, and in 18.7% there was a metastatic lesion. The majority of patients (63.5%) were in the initial stages (I and II) and the overall survival in seven years was 87%.

### CONCLUSION

The western region of Santa Catarina presents a high prevalence of CM, similar to that presented by papers that studied populations with similar phenotypic characteristics in European countries and Oceania. Perhaps this fact occurs due to the association between migratory and geographical characteristics of the local population.

**GENERATING HIGH QUALITY SYNTHETIC SKIN LESIONS FOR BOOSTING AUTOMATED SCREENING**

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**BACKGROUND**

Currently, Deep Learning is the state-of-the-art for automated skin cancer classification. To push the results further, we need to address the lack of annotated data. To bypass this problem, we propose generating realistic synthetic skin lesion images from real lesions. Here we investigate Generative Adversarial Networks (GANs) methods for generating high-definition, visually-appealing, and clinically-meaningful synthetic skin lesion images.

**METHODS**

GANs model the real image appearance by forcing the synthesized samples to be really similar from real images. To teach the network the malignancy markers (pigment network, negative network, streaks, mlia-like cysts, and globules) while incorporating the specificities of a lesion border, we feed such information directly to the network, using a *semantic map* and an *instance map*. Semantic maps are blobs that show the presence and the location of the 5 malignancy markers within the same lesions' segmentation masks. Instance maps take information from superpixels, which group similar pixels creating visually meaningful blobs, limiting each unit regarding their meaning. We compare 4 approaches:

- A. A traditional GAN that lacks fine-grained detail;
- B. The progressive GAN: here the model is progressively fed with images of increasing resolution along the training;
- C. A GAN for generating high-resolution images, using only semantic map;
- D. The same GAN of (C), using both semantic and instance map.

**RESULTS**

We show that the generated images have increasing quality from (A) to (D). We generated high-resolution lesions, presenting malignancy markers with coherent placement and sharpness. To the best of our knowledge, our results are the first to show visually-appealing synthetic images that comprise clinically-meaningful information. Unfortunately, we cannot provide pictures in the abstract. Also, to evaluate the relevance of synthetic images, we train a skin cancer classification network including synthetic images to the real dataset, reaching an improvement of 1 percentage point.

**CONCLUSION**

The results show that the synthetic images carry clinically-relevant information. Taking advantage of synthetic images for classification is promising since helps to boost the performance of automated skin lesion classifiers, without the onus of acquiring and annotating new real images.

**CHRYSLIS STRUCTURES IN SEBORRHEIC KERATOSIS****KEY WORDS: CHRYSLIS STRUCTURES, SEBORRHEIC KERATOSIS, DERMOSCOPY, HISTOLOGY**

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**INTRODUCTION**

In recent years, clinical relevant and notable differences between skin lesion appearance under polarized dermatoscopy (PD) and non-PD are documented. In particular, the identification of shiny, bright white, orthogonally oriented linear streaks, also metaphorically known as crystalline or chrysalis structures (CS), only visible under PD<sup>1-3</sup>.

The CS has been suggested to represent the increased amount of dermal collagen seen in benign lesions and in malignant lesions, stand for tumor-induced stromal reaction and extracellular matrix changes. CS were described in dermatofibromas (DFs), Spitz nevi, scars, basal cell carcinomas (BCC), and melanomas<sup>1,3</sup>.

The aim of this study is to report a rare case of seborrheic keratosis (SK) with CS and measure with literature.

**CASE REPORT**

A30-year-old man was referred to our Dermatology Service unit due to a recent growing pigmented lesion on abdomen. He denied local trauma, bleeding, personal or family history of skin cancer. Clinical examination showed brown-black plaque with 1 cm of diameter. Dermoscopy using a DL-3 dermatoscope (3Gen, LLC, Dana Point, CA) with non-PD revealed cerebriform pattern, with horny cysts and brown background, suggesting the diagnosis of SK (Fig.1a). After polarized contact dermatoscopic image it was possible to identify short white shiny lines, without an organized distribution corresponding to CS (Fig.1b).

As CS recognition is an unusual finding in SK, thereby a biopsy was performed for histopathologic examination. Hematoxylin-eosin staining showed epidermal proliferation formed by basaloid keratinocytes, with acanthosis, papillomatosis, and horny pseudocysts (Fig.2). The superficial dermis exhibits slight fibroplasia, and discrete mononuclear infiltrate (Fig.3). With those histopathological findings, the diagnosis of seborrheic keratosis was made.

**DISCUSSION**

The use of PD has allowed the identification of new dermatoscopic dermal structures such as CS and microvasculature. CS were already described in melanocytic and nonmelanocytic lesions, but the clinical significance of this singular structure has not been established yet.

A recent prospective study systematically demonstrated the incidence of CS among 11.225 lesions, in which were observed in melanoma (70%; 14/20), BCC (51.2%; 39/76), lichen planus like keratosis (53.3%; 8/15), AK (29.4%; 5/17), squamous cell carcinoma/Bowen/keratoacanthoma (12.5%; 5/40) and scars (100%; 2/2), but rarely in benign nevi, SK or solar lentigines<sup>4</sup>.

The study correlated the presence of CS with highly suggestive of malignance among melanocytic neoplasms, due to their observation in over two thirds of melanomas. Thus, they suggested the CS as an additional feature for distinguishing melanomas from nevi<sup>4</sup>.



They also showed that CS were 3.4 times more commonly encountered among invasive (41%) than among in situ (17%) melanomas<sup>4</sup>. Indeed, these findings are in line with other study that demonstrated a statistically significant correlation between the presence of CS and increased depth of invasion<sup>5</sup>.

### **CONCLUSION**

Based on the available preclinical data, the presence of CS in invasive melanomas may reflect de novo synthesis or remodeling of type I collagen in the papillary dermis, signifying changes in the extracellular matrix induced by tumor progression and dermal invasion<sup>6</sup>.

In benign lesions, CS has no relation with clinical behavior, which supports this notion are their common presence in biopsy of scars and DFs, whose histopathologic hallmark is dermal fibrosis<sup>4</sup>.

In conclusion, CS are a rare finding in SK with no clinical behavior influence, may be particularly important in the diagnosis of melanomas, interpreted in the context of other dermatoscopic structures and the overall pattern.

**BALLOON CELL PRIMARY NODULAR MELANOMA: DERMATOSCOPY EVIDENCES**

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**BACKGROUND**

An 84-year-old Caucasian woman was referred to our skin cancer unit because of an asymptomatic nodule on the right leg for the past 4 months, with no personal or family history of melanoma or nonmelanoma skin cancer. Physical examination showed a well-defined, reddish nodule measuring 1 cm in diameter. Dermatoscopy revealed yellowish structureless areas, white lines, irregular hairpin-shaped, and curved vessels.

**CASE REPORT**

Due to suspicious for melanoma, an excisional biopsy was performed for histopathologic examination. Hematoxylin-eosin staining showed an atypical melanocytic proliferation, with an architecturally disorganized predominantly intradermal component, composed of cells contained hyperchromatic pleomorphic nuclei and a ballooned appearance with vacuolated cytoplasm, mitotic figures, and discrete areas of intradermal pagetoid spread. No ulceration, lymphovascular and perineural invasion, satellitosis, or regression was noted. Breslow thickness was 4.1 mm with moderate mitotic activity with 4 mitotic figures seen per square millimeter.

Immunohistochemical stainings showed positivity for melanocytic markers S100, HMB45 in dermal component and MELAN-A confirming the diagnosis of BCM. Staining with Ki67 was positive in balloon cells.

**DISCUSSION**

There are only four previously published dermatoscopic images of BCM in literature, 3 of primary tumors and one of BCM satellite metastasis. In 2013, the first dermatoscopy report described an amelanotic nodule, with structureless yellow lesion, central ulceration, presence of terminal hairs, curved and dotted vessels in old man with previous history of local trauma<sup>4</sup>.

In 2014, a satellite metastasis of BCM was pointed as milky red structureless background, yellowish structureless areas, few irregular linear, hairpin-shaped, and curved vessels. As balloon cells generally lack melanin, this study proposed the association of milky red and yellowish structureless areas as a considerable clue for the diagnosis of BCM<sup>5</sup>. We also reported the presence of yellowish structureless areas.

Likewise, in 2014 an Australian case report showed a pale papule with structureless white area, structureless brown in periphery, white lines, few linear curved and dotted vessels<sup>3</sup>. The last published report was in 2016, a papule with structureless blue-gray centrally and brown peripherally, negative pigment network, linear, serpentine, and dotted vessels<sup>6</sup>.

**CONCLUSION**

The dermatopathological diagnosis of BCM is reportedly challenging both careful clinico-pathological correlation as well as correctly interpreted immunohistochemical stains. Clinically BCM could be presented as nodular, ulcerated, polypoid and papillomatous, and with common absence of pigmentation<sup>7</sup>.



Currently the data are restricted by a low number of reports, in this way a define dermatoscopy pattern of BCM is still not documented. Jaimes et al published the definition of a balloon cell nevi (BCN) combining dermatoscopic and histology features. Dermatoscopy evidences showed numerous aggregated white globular structures, which correspond to nests of pigmented melanocytes in the lower epidermis, papillary and/or lower dermis in histology<sup>8</sup>.

BCN and BCM seem to have no similarity in dermatoscopy, since no white globules structures were found in BCM in literature. In this case the presence of recent raised amelanotic nodular lesion, with white lines and polymorphous vessels in dermatoscopy suggested malignancy, although the diagnosis of BCM were histologically defined.

**EVALUATION OF SURGICAL APPROACH OF ELDERLY PATIENTS DIAGNOSED WITH MELANOMA**

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**BACKGROUND**

Melanoma is the most aggressive skin cancer, and its incidence is higher in the elderly, besides being also associated with a worse prognosis. Studies have investigated whether the worst outcome is due to a conservative treatment, based on the age of these patients. Therefore, this study aims to show the approach of patients over 65 diagnosed with melanoma.

**METHODS**

We revised 50 medical charts of patients admitted, in a Brazilian public tertiary hospital, between January 2017 and June 2018. From all the 50 patients evaluated all of the presented a confirmed diagnosis of melanoma through incisional or excisional surgical biopsy and were conducted to complete the surgical approach of lesions according to its staging. From the initially evaluated patients, 24 of them were older than 65-years old, and 20 of this latter group were submitted to ample margin excision with sentinel lymph nodal biopsy, and 3 underwent ample margin excision with radical lymphadenectomy, and one of them passed away before surgical approach.

**RESULTS**

The elderly represent a particular group of patients who deserve an individualized approach. It is known that the treatment of the primary melanoma is surgical and when procedures of lymphadenectomy are compared in elderly and young patients, the first ones are less approached, which is usually justified by the high surgical morbidity. Pre-existing diseases, anticoagulation, and functional limitation should be limiting factors to be considered, in other words, age cannot be the only factor that defines the conduct.

Thus, from the global evaluation of the elderly evaluated in this study, no effort was spared in the surgical approach of patients diagnosed with melanoma. Of the 24 patients over 65 years of age, all patients received adequate treatment for the stage of their disease. Thus, it was seen that age, in isolation, was not a limiting factor for therapeutic decisions, since the main criteria considered were those that cover the functional capacity of the patient.

**CONCLUSION**

The literature has questioned whether the conservative therapeutic approach has influenced the worse prognosis of the elderly diagnosed with melanoma. Because of the lack of knowledge about the fragility indexes used in the evaluation of the elderly population, age has been erroneously used for this purpose. It is essential, thus, that a broad geriatric assessment is performed to identify the patients most likely to benefit from melanoma treatment.