Melanoma Research Review™

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Issue 15 - 2017

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Abbreviations used in this issue:

AEs = adverse events; **AJCC** = American Joint Committee on Cancer; **DMFS** = distant metastasis-free survival; **DSS** = disease specific survival; **EIS** = electrical impedance spectroscopy; **GEP** = gene expression profile; **HRQoL** = health-related quality of life; **irAE** = immune-related adverse events; **IFN** = interferon; **IPCA** = intrapatient comparative analysis; **IV** = intravenous; **LFA** = lesion-focused analysis; **MSN** = morphologically suspicious nevi; **OS** = overall survival; **PD-1** = programmed cell death protein 1; **PVM** = primary vulvar melanomas; **SC** = subcutaneous; **SDDI** = sequential digital dermoscopy imaging; **TKIs** = tyrosine kinase inhibitors; **UDN** = ugly duckling nevi.

Welcome to the 15th issue of Melanoma Research Review.

We lead this issue with two retrospective studies of PD-1 inhibitor therapy in patients with advanced melanoma and preexisting autoimmunity or ipilimumab-triggered autoimmunity. Response rates were above 30% and unrelated to immune-related adverse events. The researchers also found anti-PD-1 induced relatively frequent immune toxicities, but these were often mild and did not require discontinuation of therapy. A pooled analysis assessing the safety profile of nivolumab monotherapy for advanced melanoma concluded treatment-related adverse events (most commonly fatigue, pruritus, diarrhea, and rash) were primarily low grade, and most resolved. Another study reports the results of the secondary endpoint, health-related quality of life, of a phase 3 trial with adjuvant ipilimumab vs placebo after complete resection of high-risk stage III melanoma. No clinically relevant differences in global health status scores between groups were observed during or after induction.

We also include a number of articles with a focus on melanoma detection. A 31-gene expression profile provides valuable prognostic information and improves identification of high-risk melanomas when used together with the AJCC online prediction tool. A prospective Australian study evaluated the effect of adding an electrical impedance spectroscopy measurement at baseline to suspicious melanocytic lesions undergoing routine short-term sequential digital dermoscopy imaging. Another study shows the importance of performing an intra-patient comparative analysis using the ugly duckling sign, as it may reduce up to 7 times the number of benign nevi excised when compared to a lesion-focused analysis only.

We hope you find the selection for this month's issue useful in your practice, and we look forward to receiving your comments or feedback.

Kind Regards,

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Programmed cell death protein-1 (PD-1) inhibitor therapy in patients with advanced melanoma and preexisting autoimmunity or ipilimumab-triggered autoimmunity

Authors: Gutzmer R, et al

Summary: This retrospective study included a cohort of metastatic melanoma patients with preexisting autoimmune disorders (n=19) or previous ipilimumab-triggered immune-related adverse events (irAE) (n=22) undergoing treatment with PD-1 inhibitor therapy. The team concluded patients with preexisting autoimmunity commonly showed a flare during PD-1 innhibitor therapy, while a flare of ipilimumab-triggered irAE was rare. They reported response rates were above 30% and unrelated to irAE.

Reference: Eur J Cancer 2017 Apr;75:24-32

Abstract

Anti-PD-1 therapy in patients with advanced melanoma and preexisting autoimmune disorders or major toxicity with ipilimumab

Authors: Menzies AM, et al

Summary: This was another retrospective study assessing the safety and efficacy of anti-PD-1. Participants (n=119) with advanced melanoma and preexisting autoimmune disorders and/or major irAEs with ipilimumab were treated with anti-PD-1. Response rate was 33% in patients with preexisting autoimmune disorders (n=52); and 40% in patients with prior ipilimumab irAEs requiring immunosuppression (n=67). They found anti-PD-1 induced relatively frequent immune toxicities, but these were often mild and did not necessitate discontinuation of therapy.

Reference: Ann Oncol 2017 Feb 1;28(2):368-376

Abstract

Comment: Anti PD-1 medications for metastatic melanoma are known to cause irAEs. Patients with pre-existing autoimmune disorders or previous ipilimumab-triggered irAE were retrospectively reviewed in these two studies, and their irAE (flare or new) and tumour responses were assessed. Both studies divided their patients into two groups: Group A with pre-existing autoimmunity and group B with ipilimumab-related irAE.

Group A

The German multicentre study included 41 patients in total, in which nearly half (40%) of group A patients had a flare within 3-20 weeks while on anti PD-1 treatment. This was comparable to the study published by Menzies et al, who reported that 38% of patients in group A had a flare after a median time of 5 weeks, (from a series of 119 patients from 13 Australian, US and European sites). Flares in rheumatological disorders were the most common for both studies (55% and 52% respectively). New irAE occurred in 16% of patients from the German study and 29% from the Australian/US/European group. 35% of patients in the German and 38% in the Australian/US/European studies had immunosuppressive treatment at initiation of anti PD-1, indicating that most of patients had active autoimmunity. Tumour response rates were similar in both studies (32-45% and 33% respectively) and comparable to other studies in patients without previous autoimmunity (21-32% in pre-treated and 33-43% in naïve patients). Interestingly, the German study showed that tumour response was not related to presence of immunosuppressive treatment, exacerbation of the pre-existing autoimmune disorder or irAE. Menzies et al. reported similar tumour response rates in those who had a flare of autoimmunity compared to

those who did not flare (35% vs 31%), but lower tumour response in patients with immunosuppressive treatment at the start of anti PD-1 compared to patients without immunosuppression (15% vs 44%). This contrasts with the pooled analysis of four studies of patients receiving nivolumab (Weber, et al. J Clin Oncol. 2017 Mar;35(7):785-792), which found no significant difference in objective response rates between patients who did or did not receive systemic immunosuppressants for irAE (30 vs 32%). However, results may not be comparable since immunosuppression was given by Weber et al. to manage irAE that appeared during anti PD-1 treatment, in contrast to immunosuppression given at the beginning of treatment by Menzies et al.

Group B

Flares were rare in both studies (4.5% and 3%) but the rate of new irAE, in particular pancreatitis, colitis, hepatitis and pneumonitis, was higher in Australian/US/European cohort (34% vs. 23%), leading to treatment discontinuation in 12% of cases. This may be related to the fact that nearly all patients in the Australian/US/European study had grade 3 (76%) or 4 (10%) toxicities during ipilimumab treatment. Conversely, in the German study grade 3 (50%) and 4 (4.5%) toxicities were lower. Interestingly, tumour response rates in group B were rather high (47% in German study and 40% in Australian/US/European) compared to the previously reported rates for pre-treated patients (21-32%), suggesting that patients with autoimmunity may benefit more from subsequent anti PD-1 treatment. Weber et al. found similar results showing that patients developing any irAE had better objective response rates compared to those who did not (48% vs 17%), but altogether, no benefit in progression-free survival was noted.

In conclusion, both the German and the Australian/US/European cohort studies found that most flares of pre-existing autoimmunity and new irAE did not require anti PD-1 cessation and were well managed with immunosuppressive and/or symptomatic treatment. They agreed that the presence of autoimmunity does not contraindicate the use of anti PD-1 treatment, but risk/benefit balance needs to be carefully considered and patients closely monitored. The relationship between irAE due to ipilimumab as predictor for better tumour response to anti PD-1 is still unclear. Further studies including larger numbers of patients are needed to clarify this issue.

Safety profile of nivolumab monotherapy: A pooled analysis of patients with advanced melanoma

Authors: Weber JS, et al

Summary: Safety data were pooled from four studies, including 576 advanced melanoma patients treated with nivolumab. The authors reported 71% experienced any-grade treatment-related adverse events (AEs); most commonly fatigue (25%), pruritus (17%), diarrhea (13%), and rash (13%). They also noted 10% experienced grade 3 to 4 treatment-related AEs. Select AEs (those with potential immunologic aetiology) occurred in 49% of patients and were most frequently cutaneous, gastrointestinal, endocrine, and hepatic; with 4% of patients experiencing grade 3 to 4 select AEs. Approximately 24% of patients received systemic immune-modulating agents to manage select AEs, which in most cases resolved. Treatment with immune-modulating agents did not affect objective response rate, although treatment-related select AEs of any grade were associated with higher objective response rate.

Comment: It has been reported in the literature that approximately 40% (18-50%) of patients develop some kind of skin toxicity, most commonly papulo-pustular or maculo-papular eruptions (18-55% of patients), followed by pruritus (12-47%) and vitiligo (9-28%). (Robert C, et al Lancet 2014;384:1109–17; Topalian SL, et al J Clin Oncol. 2014;32:1020-1030; Hwang SJE, et al J Am Acad Dermatol 2016;74:455-61)

The main limitation in the published literature is the retrospective collection of data and the fact that patients are not seen by dermatologists, where the term “rash” or “pruritus” is used vaguely. Some studies subdivide the term “rash” into lichenoid reactions and eczema, like the one by Hwang et al, which reviewed 82 patients treated with anti-PD1, where 49% developed cutaneous AEs, including lichenoid reactions (17%), eczema (17%) and vitiligo (12%). Interestingly, vitiligo appears only in patients treated for melanoma, but not in those receiving treatment for other cancers. The appearance of skin reactions increases steadily from the start of treatment. It has been reported that the occurrence of skin AEs are associated with a better prognosis, however this should be interpreted with caution, as responders may receive more treatment cycles, which makes them more likely to develop skin AEs induced by the drug. In the present study, patients who experienced select AEs received a greater number of doses of nivolumab (13 vs 7) and had longer median treatment durations. Higher objective response rates seen in this group could also be related to this.

Reference: J Clin Oncol 2017 Mar;35(7):785-792
Abstract

Phase III randomized study of 4 weeks of high-dose interferon-α-2b in stage T2bN0, T3a-bN0, T4a-bN0, and T1-4N1a-2a (microscopic) melanoma: A trial of the Eastern Cooperative Oncology Group–American College of Radiology Imaging Network Cancer Research Group (E1697)

Authors: Agarwala SS, et al

Summary: This intergroup international trial aimed to test the efficacy of 4 weeks of intravenous (IV) induction with high-dose interferon (IFN) in surgically resected intermediate-risk melanoma patients. Patients (n=1,150) were randomly assigned to receive IFN α-2b at 20 MU/m2/d IV for 5 days every week for 4 weeks or observation. The researchers reported the 5-year relapse-free survival rate was 0.70 (95% CI, 0.66 to 0.74) for the observation group and 0.70, (95% CI, 0.66 to 0.74) for the treatment group (P = .964). The 5-year overall survival (OS) rate was 0.83 (95% CI, 0.79 to 0.86) for the observation group and 0.83 (95% CI, 0.80 to 0.86) for the treatment group (P = .558). They also reported treatment-related grade 3 and higher toxicity was 4.6% versus 57.9% for observation and IFN, respectively (P < .001).

Comment: Interferon was approved for adjuvant therapy for stage IIB and III melanoma patients on the basis of the E1684 trial. They tested 4 weeks of high-dose IV IFN induction followed by a subcutaneous (SC) maintenance treatment of 11 months, finding modest benefits in relapse-free and OS rates. It was hypothesised that the major benefit was derived from the initial induction phase. Therefore, the present study aimed to test the impact of treating patients only with a high-dose induction phase, avoiding the toxicity associated with the long maintenance treatment.

No differences were found in 5-year relapse-free survival rate and OS rate between high-dose adjuvant IFN and observation, however toxicity was much higher in the treated group (58% vs 4.6%). According to this study, 4 weeks of IV high-dose IFN is not better than observation in resected intermediate-risk melanomas. In light of the promising results of the recent clinical trials using immunotherapy (in particular ipilimumab) as adjuvant treatment for stage III melanoma, one may question if IFN still has a role as an adjuvant therapy for melanoma. New clinical trials comparing IFN vs ipilimumab vs anti PD-1 (nivolumab and pembrolizumab) will soon show some results regarding relapse-free survival and OS rates. The adjuvant treatment schedules to optimise risk/benefit and cost are far from being established but INF will most likely not be in the landscape.

Reference: J Clin Oncol 2017 Mar 10;35(8):885-892
Abstract

Health-related quality of life with adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): Secondary outcomes of a multinational, randomised, double-blind, phase 3 trial

Authors: Coens C, et al

Summary: This study reports on the health-related quality of life (HRQoL) of the EORTC 18071 trial; a multinational, double-blind, randomised, phase 3 trial in patients with stage III cutaneous melanoma (excluding lymph node metastasis ≤1 mm or in-transit metastasis). Participants were randomly assigned to receive either ipilimumab 10 mg/kg (n=475) or placebo (n=476) every 3 weeks for four doses, then every 3 months for up to 3 years. EORTC QLQ-C30 quality-of-life instrument was administered at baseline, weeks 4, 7, 10, and 24, and every 12 weeks thereafter up to 2 years, irrespective of disease progression. Compliance with completing the questionnaire was 94% at baseline, 75% at week 24, and 51% at week 108. Although patient mean global health scores during (77·32 [SD 17·36] vs 72·96 [17·82]; p=0·00011) and after induction (76·48 [17·52] vs 72·32 [18·60]; p=0·00067) were significantly different between groups, they were not clinically relevant.

Comment: This is a follow up publication following the initial study looking at primary outcomes. The FDA approved adjuvant treatment with ipilimumab for completely resected stage III melanoma in 2014, since recurrence-free survival was longer in the ipilimumab group (3-year recurrence-free survival 46.5% vs 34.8%). The median recurrence-free survival was 26 months in the ipilimumab group vs 17 months in the placebo group. Grade 3-4 AE were more frequent in the ipilimumab group (54%) compared with placebo (25%). Most common AEs were gastrointestinal (16%), hepatic (11%) and endocrine (8%). In the ipilimumab group 49% discontinued treatment because of a drug related AE and in approximately 40% of patients this occurred within the initial dosing period (12 weeks of treatment start). On note, five (1%) patients died because of drug-related AE. Nevertheless, HRQoL was similar between groups, as no clinically relevant differences in global health scores were observed after induction.

The authors hypothesise that a possible explanation lies in patients’ positive attitude to AEs as it was viewed as a confirmation of treatment efficacy. A factor that may have contributed to not finding clinically relevant differences, was the use of a 10-point threshold. A work published after the design of this study was completed, advocated for a 4-point cut off for treatment group comparisons in randomised clinical trials. The use of this lower threshold would result in finding more differences. Another factor is that the EORTC QLQ-C30 questionnaire is not specifically validated for immunotherapy, and several symptoms of immune-related AE are missing. Moreover, additional assessment based on overall survival is required to know the role of ipilimumab as adjuvant treatment. The anti-PD1 adjuvant trial results are due soon and most likely will have better risk/benefit data.

Reference: Lancet Oncol 2017 Mar;18(3):393-403
Abstract

References: 1. Tafinlar (dabrafenib) Product Information. **2.** Mekinist (trametinib) Product Information. **3.** Long G et al. *Lancet* 2015; 386(9992): 444–51. **4.** Robert C et al. *N Engl J Med* 2015; 372: 30–9. **5.** Flaherty K et al. *N Engl J Med* 2012; 367–1694–1703 **6.** Long G et al. *J Clin Oncol* 2016; 34(8): 871–8. **7.** Flaherty KT et al. Oral presentation at ASCO 2016: June 3–7, Chicago, Illinois.

The natural history and patterns of metastases from mucosal melanoma: An analysis of 706 prospectively-followed patients

Authors: Lian B, et al

Summary: This group examined the clinical course and patterns of metastases of mucosal melanomas across anatomical sites. The analysis included clinical and pathological data from 706 patients with mucosal melanomas; lower gastrointestinal tract (26.5%), nasal cavity and paranasal sinuses (23%), gynaecological sites (22.5%), oral cavity (15%), urological sites (5%), upper gastrointestinal tract (5%), and other sites (3.0%). Predominant metastatic sites were regional lymph nodes (21.5%), lung (21%), liver (18.5%), and distant nodes (9%). Oral cavity mucosal melanoma had a higher incidence of regional nodal metastases (31.7% vs 19.8%), and a higher incidence of lung metastases (32.5% vs 18.5%) compared to other primary mucosal melanomas. There was a 10% incidence of CKIT mutation and 12% BRAF mutation. Mucosal melanomas from nasal pharyngeal and oral, gastrointestinal, gynaecological, and urological had a similar survival.

Comment: Mucosal melanoma is frequently diagnosed at an advanced stage (21.5% stage III and 23% stage IV) and has a bad prognosis. The 5-year survival rate is around 20-30%. It is rare in the Caucasian population, but is the second most common subtype in the Asian population. Given the large Asian population in Australia, clinicians should be aware and suspect the diagnosis of melanoma when a pigmented lesion is seen in mucosal membranes.

The different locations of mucosal melanoma had similar metastatic behaviour in terms of incidence of nodal and distant metastases, site of distant metastases (lung 21%, liver 18.5%, distant lymph node 9%) and overall survival; with the exception of oral cavity mucosal melanoma, which had a higher incidence of regional nodal and lung metastases. These findings suggest that the mutational events that result in mucosal melanomas are independent of the anatomical site. Thus, systemic treatments could be used regardless of the melanoma location, but this hypothesis needs to be proven with further studies. According to this study, only 12% of mucosal melanomas had BRAF mutations, which limits the use of BRAF inhibitors in this setting. However, 10% have CKIT mutations with a wider range from 5.5 to 17% for nasopharyngeal and urological melanomas, respectively. They could be treated with imatinib or other tyrosine kinase inhibitors (TKIs) such as sorafenib, sunitinib and dasatinib. Although clinical trials show some response to TKIs, tumours still progress over few months and prognosis remains poor. Immunotherapy (anti CTLA-4 and anti PD-1) can also be considered in these patients but response rate is also poorer than cutaneous melanoma.

This very large series shows that mucosal melanomas, whatever their origins, behave similarly. Thus new trial protocols could pool cases together allowing easier recruitment of these rare subtypes.

Reference: Ann Oncol 2017 Apr 1;28(4):868-873
Abstract

Tumor thickness and mitotic rate robustly predict melanoma-specific survival in patients with primary vulvar melanoma: A retrospective review of 100 cases

Authors: Nagarajan P, et al

Summary: The objective of this retrospective review was to determine the parameters predictive of survival in primary vulvar melanoma (PVM). The investigators concluded tumour thickness, dermal mitotic rate, lymphovascular invasion, microscopic satellitosis, and absence of precursor nevus independently predicted shorter OS. Whereas tumour thickness and increased dermal mitotic rate (≥2/mm2) independently predicted shorter disease specific survival (DSS).

Comment: Staging of mucosal melanomas follows the American Joint Committee on Cancer (AJCC) guidelines for primary cutaneous melanomas. However, it remains controversial whether these parameters apply to PVM. This study assessed clinical and histopathologic parameters in 100 PVM, and found that factors predictive of survival were similar but additional parameters that affected survival were identified. Decreased OS was also related to older age (> 56 years) and absence of precursor nevus. Moreover, age, midline, and/or multifocal involvement, and lack of regression were associated with decreased DSS. Tumour thickness and increased dermal mitotic rate (≥ 2/mm^2) were the strongest factors independently associated with reduced OS and DSS. Of note, they found no significant difference with 1 dermal mitosis/mm^2. The authors found that the AJCC T-category was a good prognosis tool for thick melanomas (Breslow > 2mm; pT3 and pT4) but was less accurate for ≤ 2mm Breslow melanomas (pT1a/b and pT2a/b). Therefore, they proposed a refined T-category which better predicted OS and DSS in their study: (pT1*) tumour thickness ≤ 2.00 mm and dermal mitotic rate <2/mm^2 versus (pT2*) tumour thickness > 2.00 mm and/or dermal mitotic rate ≥2/mm^2.

Interestingly, the findings contradict the latest edition of the 8th edition AJCC staging guidelines, which do not include the mitotic rate as a staging criterion for T1 tumours. These results need to be considered when developing new staging systems to predict prognosis for PVM and are especially important to correctly stratify patients in trials.

Reference: Clin Cancer Res 2017 Apr 15;23(8):2093-2104
Abstract

Identification of high-risk cutaneous melanoma tumors is improved when combining the online American Joint Committee on Cancer Individualized Melanoma Patient Outcome Prediction Tool with a 31-gene expression profile-based classification

Authors: Ferris LK, et al

Summary: This study compared the accuracy of a 31-gene expression profile (GEP) in combination with risk determined using the web-based AJCC Individualised Melanoma Patient Outcome Prediction Tool. Analysis of 205 stage I/II cutaneous melanomas revealed significant risk classification of distant metastasis-free survival (DMFS) and OS (hazard ratio range 3.2-9.4, P < .001) for both tools. The authors noted 21% of cases had discordant GEP and AJCC classification.

Comment: There is a need to identify which early stage melanomas (stage I-II) will recur and cause death since they comprise the vast majority of melanoma diagnosis and so account for two thirds of the deaths due to melanoma. The 31-GEP test evaluates 31 genetic targets to provide a binary classification of low (class 1; 5-y DMFS of 91%) or high (class 2; 5-y DMFS of 75%) risk of metastasis. It has been validated in 2 multicentre studies and shown to be an accurate independent prognosis tool. The authors tested the GEP in combination with the AJCC in stage I-II melanomas with 5-year survival data; hypothesising that when used together it could aid the detection of high-risk patients in the "low risk" group according to the AJCC classification.

The GEP test had higher sensitivity but lower specificity compared to the AJCC. When used in combination sensitivity increased (the combined GEP + AJCC 79% tools accurately identified risk of recurrences, distant metastasis, and melanoma-specific deaths at 90%, 88%, and 82%, respectively, with specificities of 71%, 63%, and 62%, respectively). Interestingly, 85% of deaths in the study group were predicted as high risk by the GEP. These patients could have benefited from more intensive surveillance to detect recurrence and begin an early treatment or even adjuvant treatment to prevent recurrence. Conversely, patients classified as low risk could avoid intensive follow up schedules. The small sample size (205 patients) is a limitation of this study. These promising results should be confirmed with a larger study. The molecular testing is seen as the future of melanoma diagnosis but the cost of these types of panel have not been evaluated. Nevertheless, we hope that the possibility of stratifying patients more accurately will ultimately help managing follow up and treatments.

Reference: J Am Acad Dermatol 2017 May;76(5):818-825.e3
Abstract

Ugly duckling sign as a major factor of efficiency in melanoma detection

Authors: Gaudy-Marqueste C, et al

Summary: The objective of this study was to assess the agreement of dermatologists on identification of the ugly duckling nevi (UDN) and estimate the contribution of intra-patient comparative analysis (IPCA) to the diagnosis of melanoma. The same 2089 digital images of the nevi of a sample of 80 patients, as well as 766 dermoscopic images from a subset of 30 patients were randomly presented to the same 9 dermatologists for blinded assessment. Of the 2089 clinical images of nevi, all melanomas were labelled UDN and as morphologically suspicious nevi by the 9 dermatologists. The authors concluded the specificity of IPCA was 0.96 for clinical images and 0.95 for dermoscopic images vs 0.88 and 0.85, respectively, for lesion-focused analysis.

Comment: In the IPCA set of 2089 images, 7 were melanoma. Of the subsample of 766 dermoscopic images, 6 were melanoma. The mean number of nevi labelled UDN by the dermatologists was 80 in the clinical images (3.8%) and 42 in the dermoscopic images (5.5%). When performing the lesion-focused analysis (LFA), the mean number of nevi labelled as morphologically suspicious nevi (MSN) was 292 clinically (38%) and 132 dermoscopically (17%).

This study shows the importance of performing an IPCA using the ugly duckling sign, as it may reduce up to 7 times the number of benign nevi excised when compared to a LFA only. These findings are relevant as teledermatology is becoming more widely used. When performing teledermatology, usually only one or only a few lesions are sent for assessment, which does not allow an IPCA. In our opinion, teledermatology may be very useful when there is a lesion of concern in patients with few lesions, but in patients with multiple lesions or dysplastic nevus syndrome, the IPCA would be more efficient as it decreases the number of excisions. Dermatologists who cannot evaluate the patient's entire skin are not as effective as they could be, thus assessing only a few images transmitted electronically will not achieve the greatest accuracy. This needs to be taken into account when using and interpreting teledermatology.

Reference: JAMA Dermatol 2017 Apr 1;153(4):279-284
Abstract

Analysis of an electrical impedance spectroscopy system in short-term digital dermoscopy imaging of melanocytic lesions

Authors: Rocha L, et al

Summary: This Australian prospective study evaluated the effect of adding an electrical impedance spectroscopy (EIS) measurement at baseline to suspicious melanocytic lesions undergoing routine short-term sequential digital dermoscopy imaging. These investigators adopted a protocol with a higher EIS score positive cut-off than the normal cut off score of ≥4. Lesions were excised immediately when the EIS score was ≥7, and lesions with a score <7 were monitored with standard sequential digital dermoscopy imaging (SDDI) over a 3 month period. From a total of 160 lesions analysed, 128 of 154 benign lesions received an EIS score of 0-6; with sensitivity for melanoma diagnosis of 83.1%. Five of the six melanomas identified had an EIS score ≥7; with sensitivity for melanoma diagnosis of 83.3%. When EIS 0-6 lesions were subsequently followed up with standard SDDI one additional melanoma was detected (EIS=6) giving the sensitivity for the diagnosis of melanoma overall of 100% and the specificity 69.5%.

Comment: Australian Guidelines have included the impedance system in their new review (2016). This automated instrument gives a scale of likelihood of melanoma with a completely different approach to any other methods that have always been based on morphology and images. The automated instruments have been a disappointment historically for a lot of non-specialists because when non-melanocytic lesions are assessed by the machine, most of them are diagnosed as melanoma, but when tested in specialist hands (who better triage non-melanocytic lesions) then the sensitivity is high but specificity low and may lead to more excisions. This article is an original way of resolving this problem when only the most suspicious lesions are monitored (digital dermoscopy) and undergo the impedance measurement. The limitation is that it is one centre and a small study. It would be interesting also to know if the sparing of a second visit covers the cost of the machine and electrodes.

Reference: Br J Dermatol 2017 Apr 19
Abstract

Melanoma Research Review™

Independent Commentary by Associate Professor Pascale Guitera and Dr Helena Collgros.

Associate Professor Guitera is currently Director of the Sydney Melanoma Diagnostic Centre (SMDC) and academic dermatologist at the Melanoma Institute Australia (MIA), with a position of Associate Professor at the University of Sydney. She undertook her dermatology fellowship in Saint Louis hospital in Paris. She was awarded the highest distinction for her PhD at the Curie Institute and SMDC on the application of instrumental techniques for the diagnosis of skin tumours. She has lived in Sydney since 2005, where she has achieved global recognition as one of the top 10 researchers of *in vivo* confocal microscopy. Dr Guitera was awarded the 2013 Wildfire Premier's award by the Cancer Institute NSW for outstanding research. She organises courses in imagery for the diagnosis of skin cancer on a yearly basis

Dr Helena Collgros (MD) completed her Dermatology and Venereology specialisation in Barcelona in 2014. Afterwards she worked as a dermatologist in the public university hospital *Germans Trias i Pujol* in Barcelona (2014-2016). Her fields of expertise and research interests include pigmented lesions, melanoma, skin cancer and imaging techniques. She is currently working in the Sydney Melanoma Diagnostic Centre at the Royal Prince Alfred Hospital in Sydney, covering an Area of Need Position attending patients at high risk for developing melanoma and skin cancer.

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