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Auckland

Saturday, June 10, 2017 (Room 5)

8:30 - 9:25 WS #99: Interactive Case Studies on Melanoma

9:35 - 10:30 WS #111: Interactive Case Studies on Melanoma (Repeated)

Melanoma case studies

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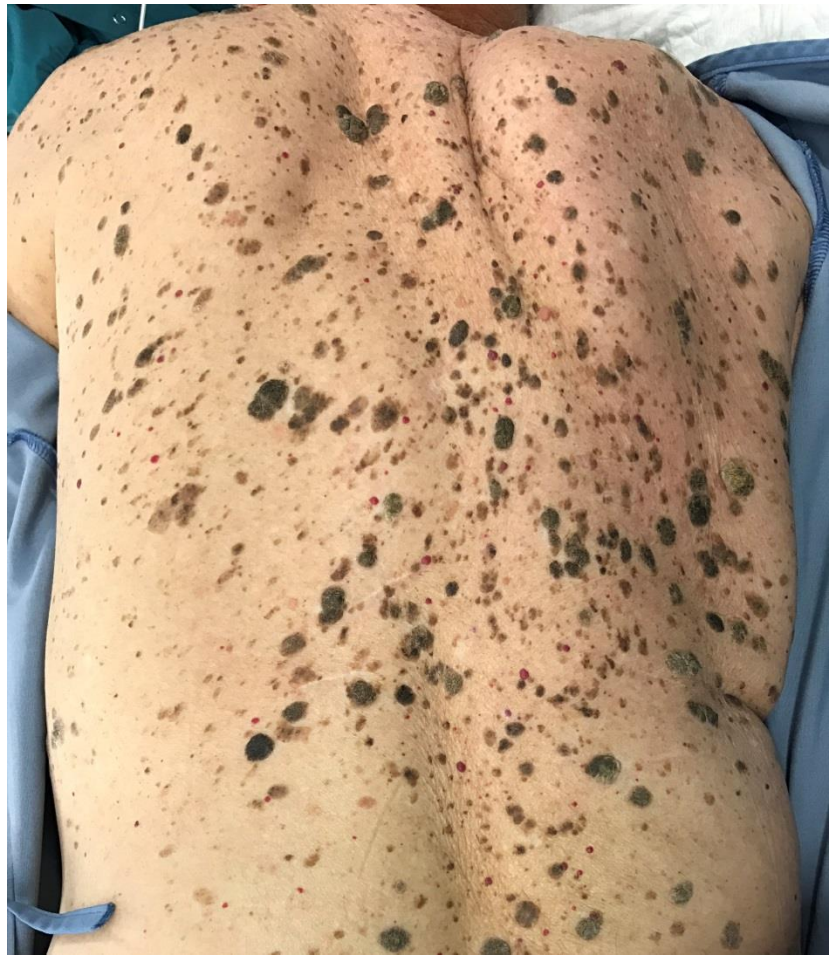
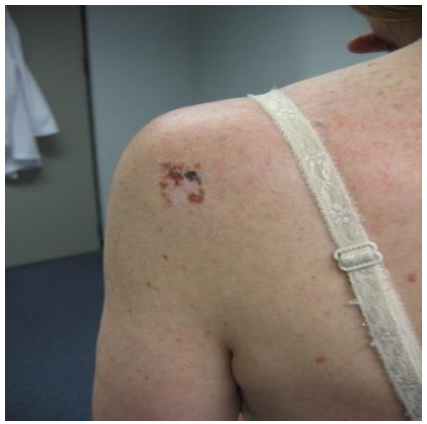
MelanomaUnit
COMPREHENSIVE INTEGRATED MULTIDISCIPLINARY CARE

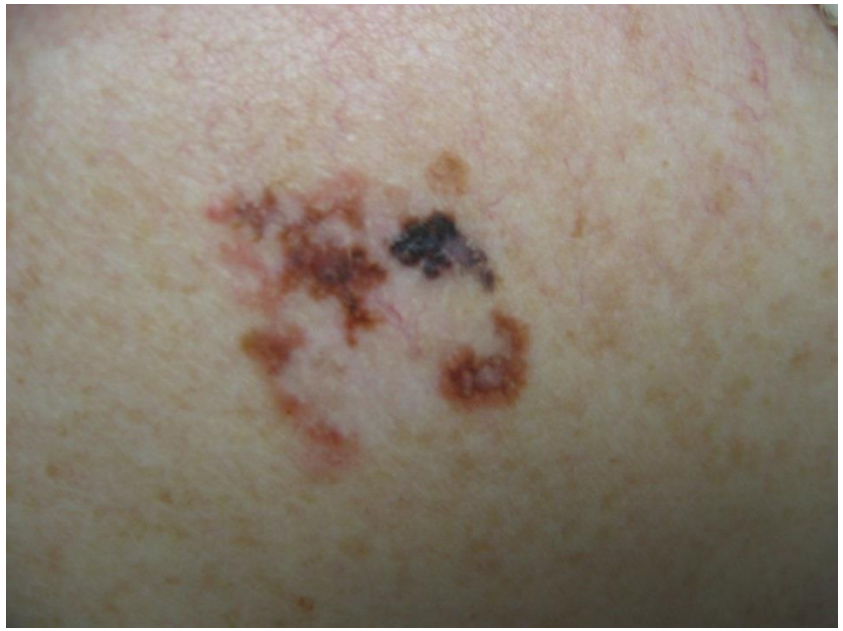
Waitemata District Health Board
Te Wai Awhina

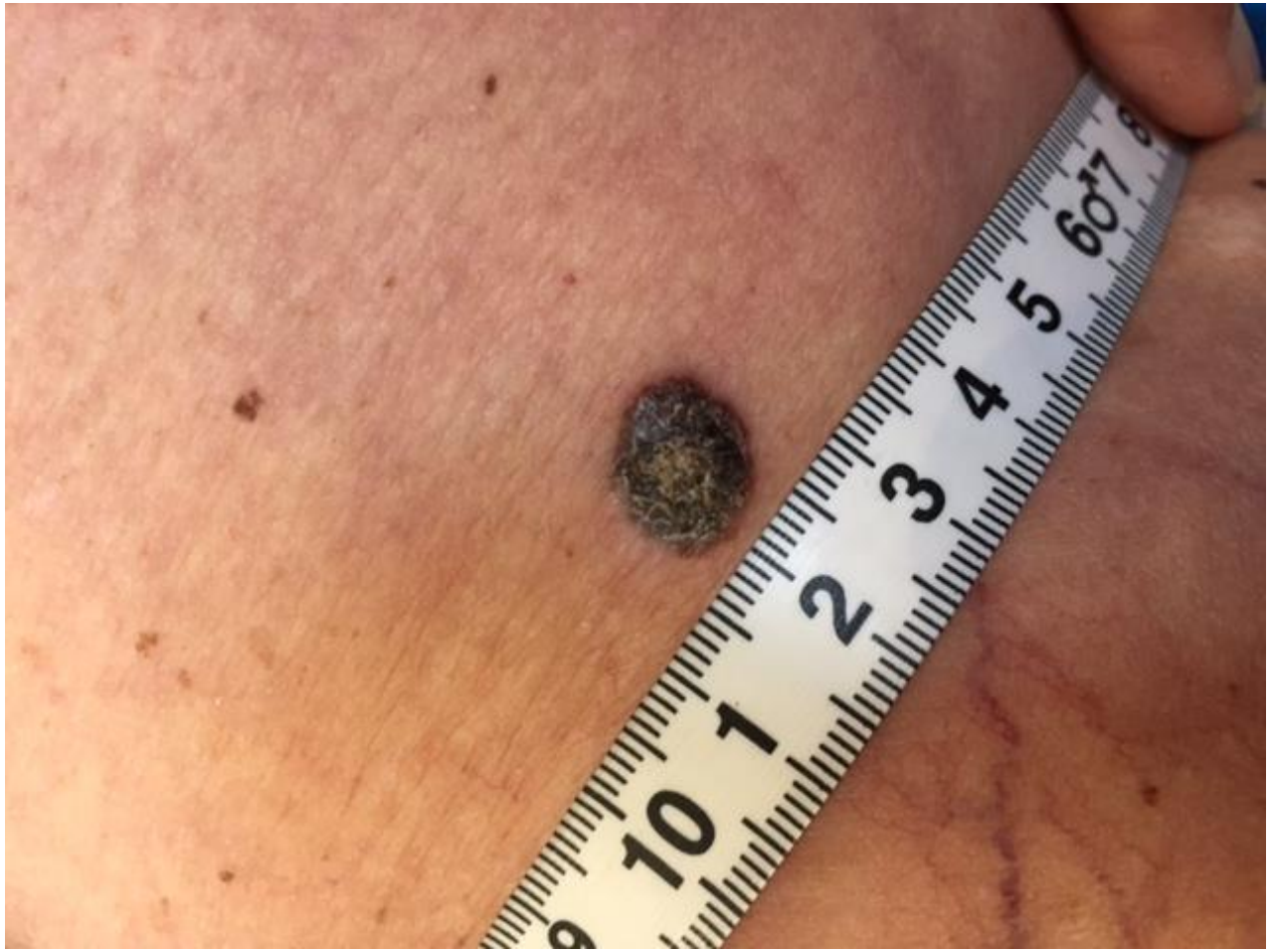
PROUDLY SUPPORTING Melanoma New Zealand

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau





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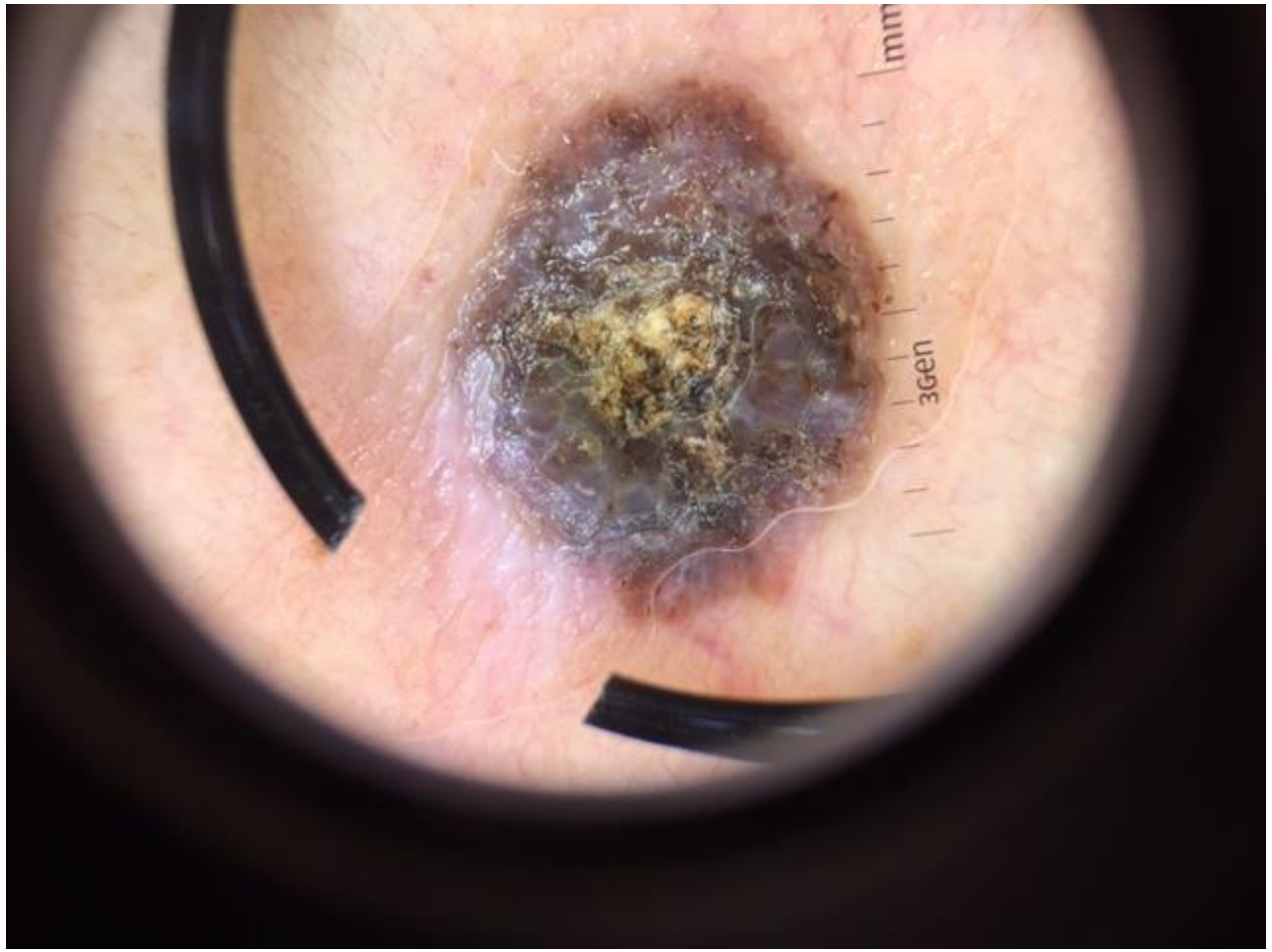
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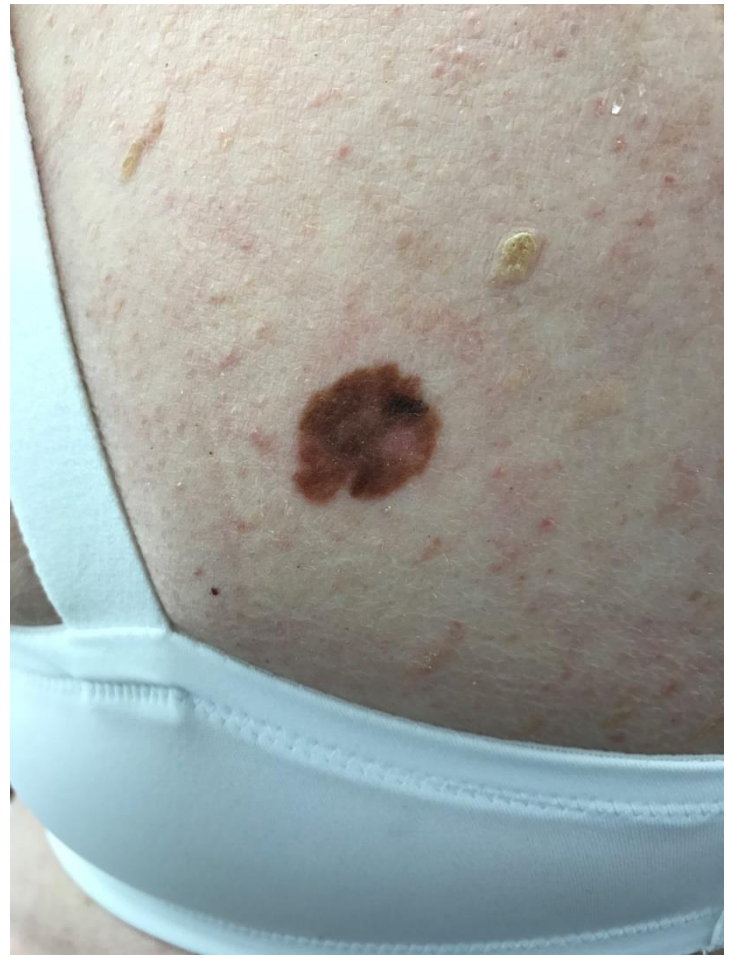

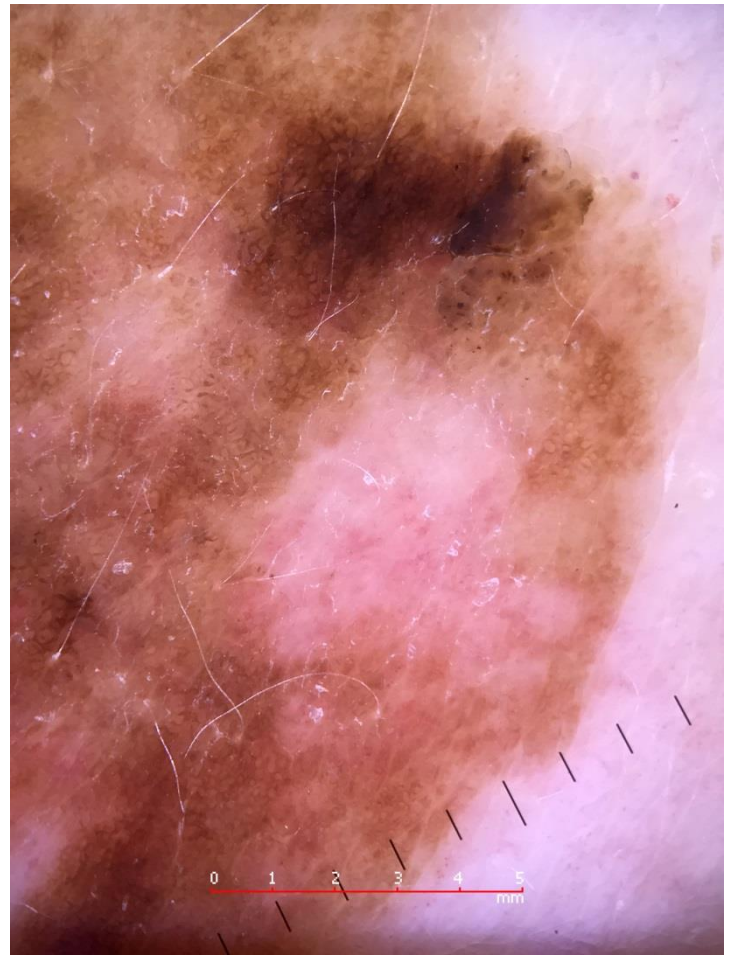
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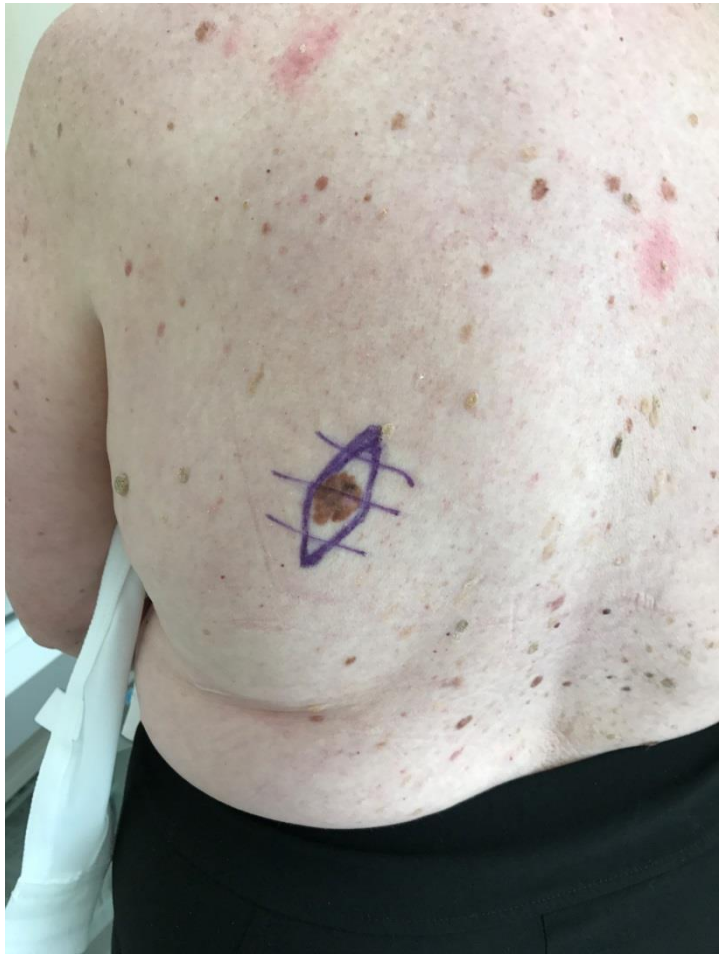
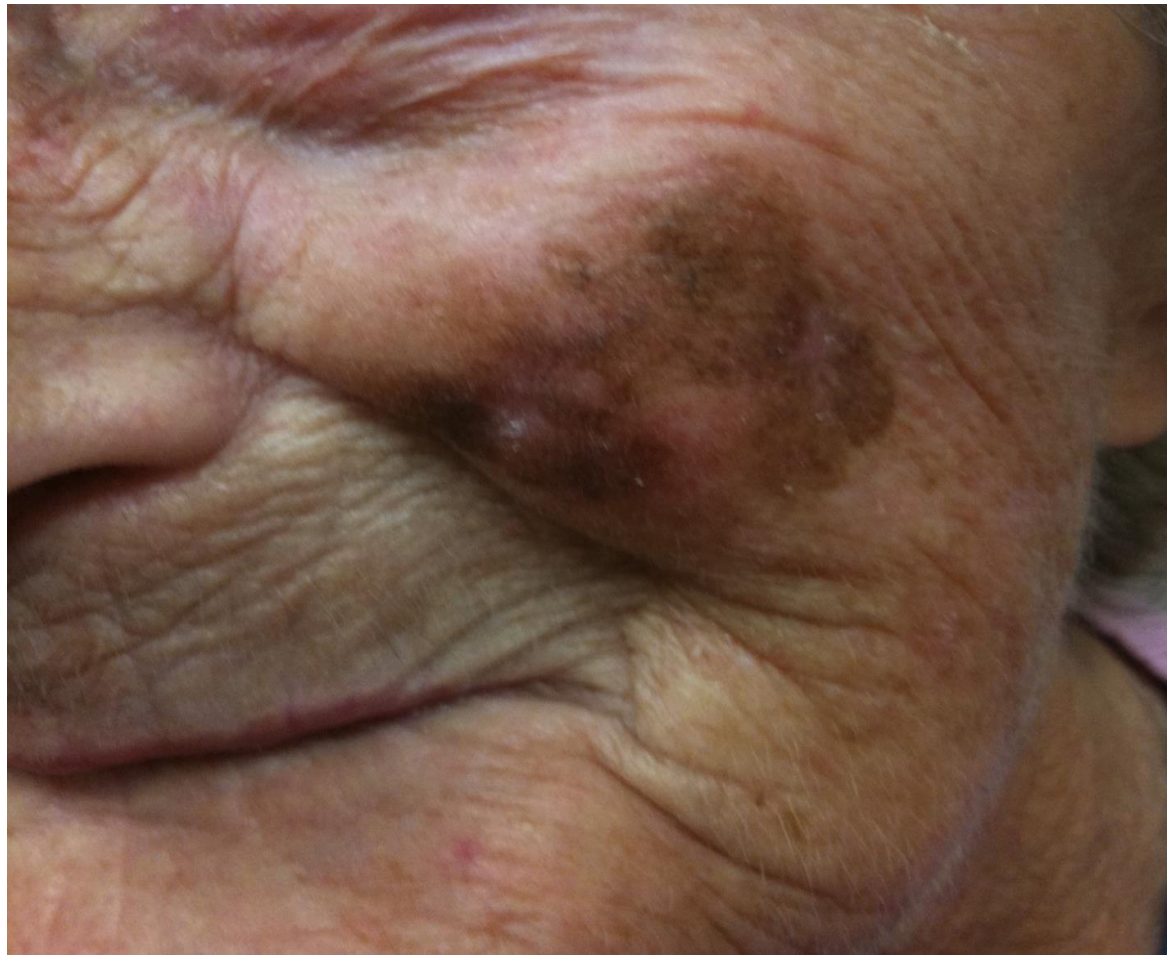
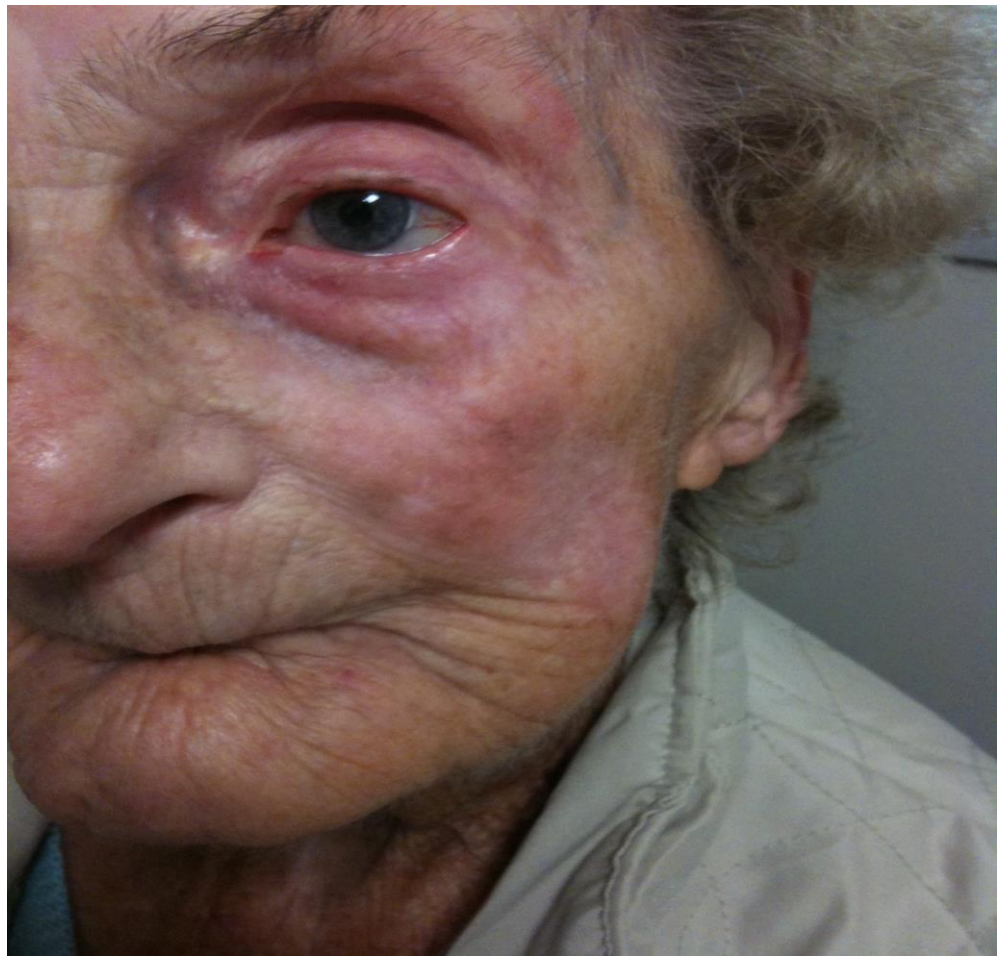
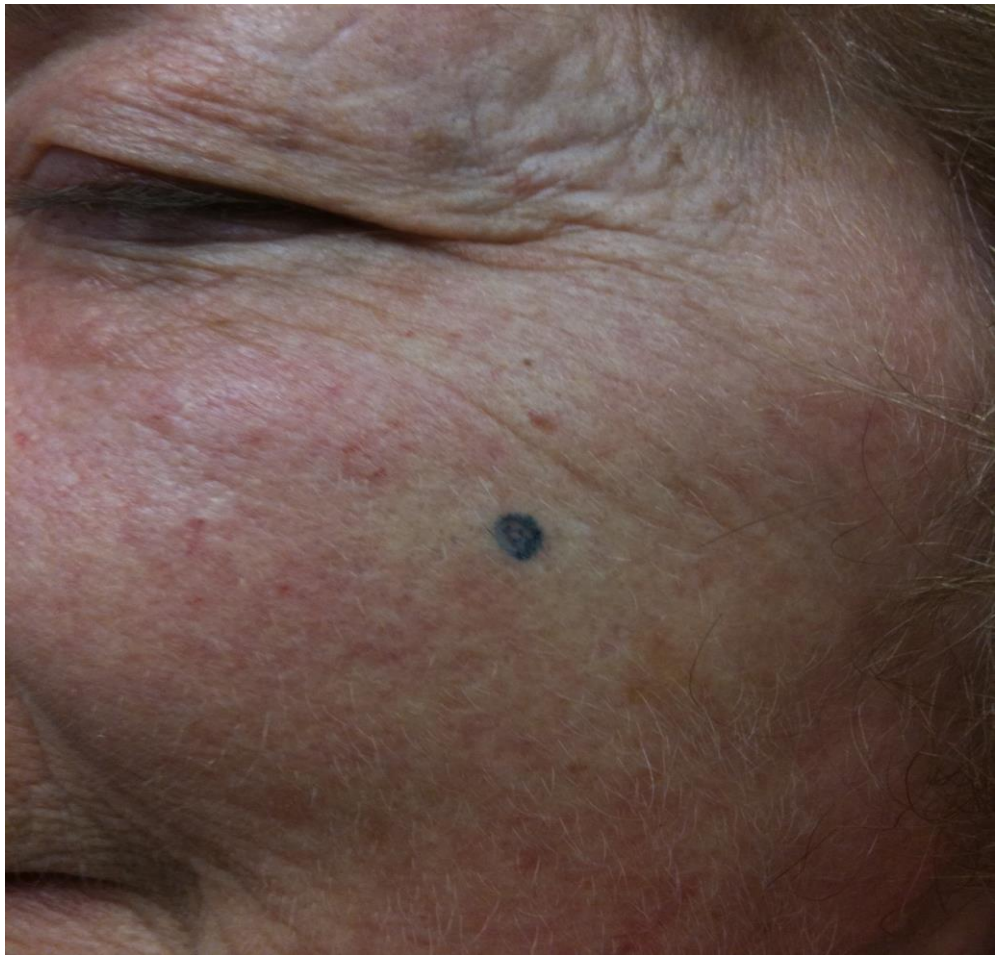
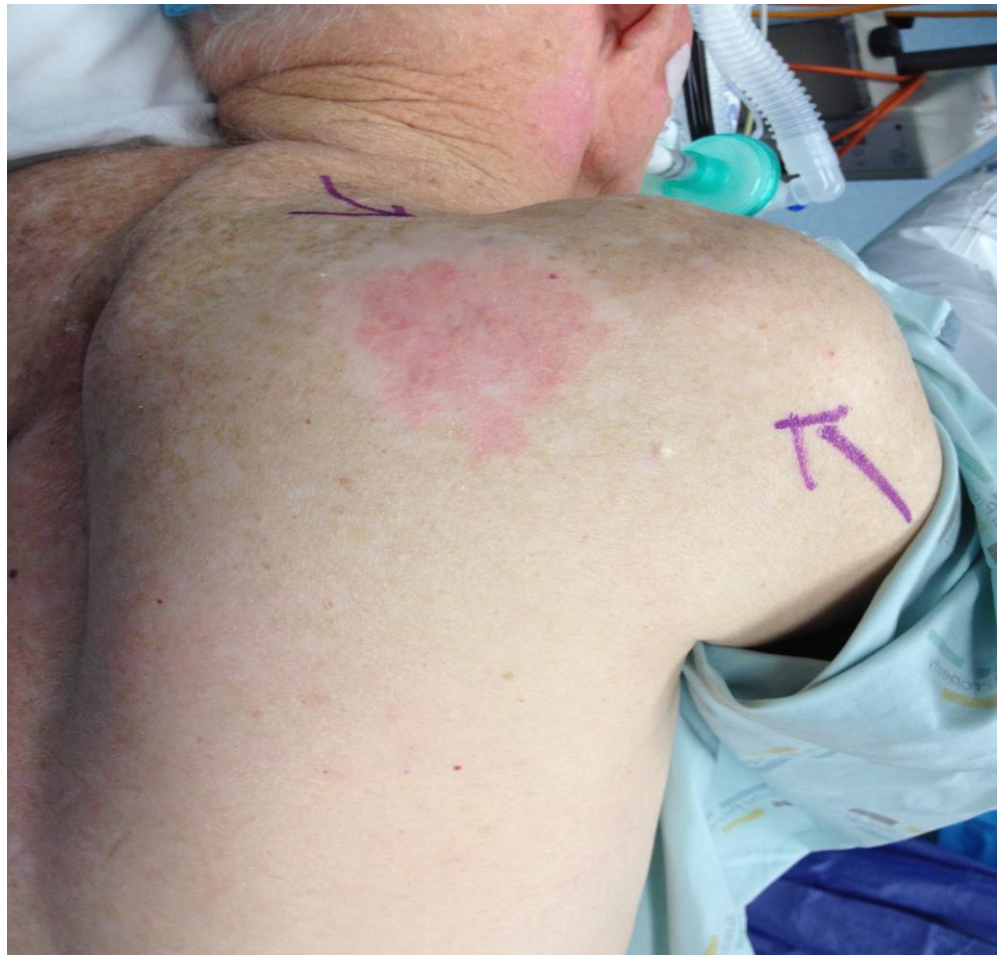
0.6mm melanoma



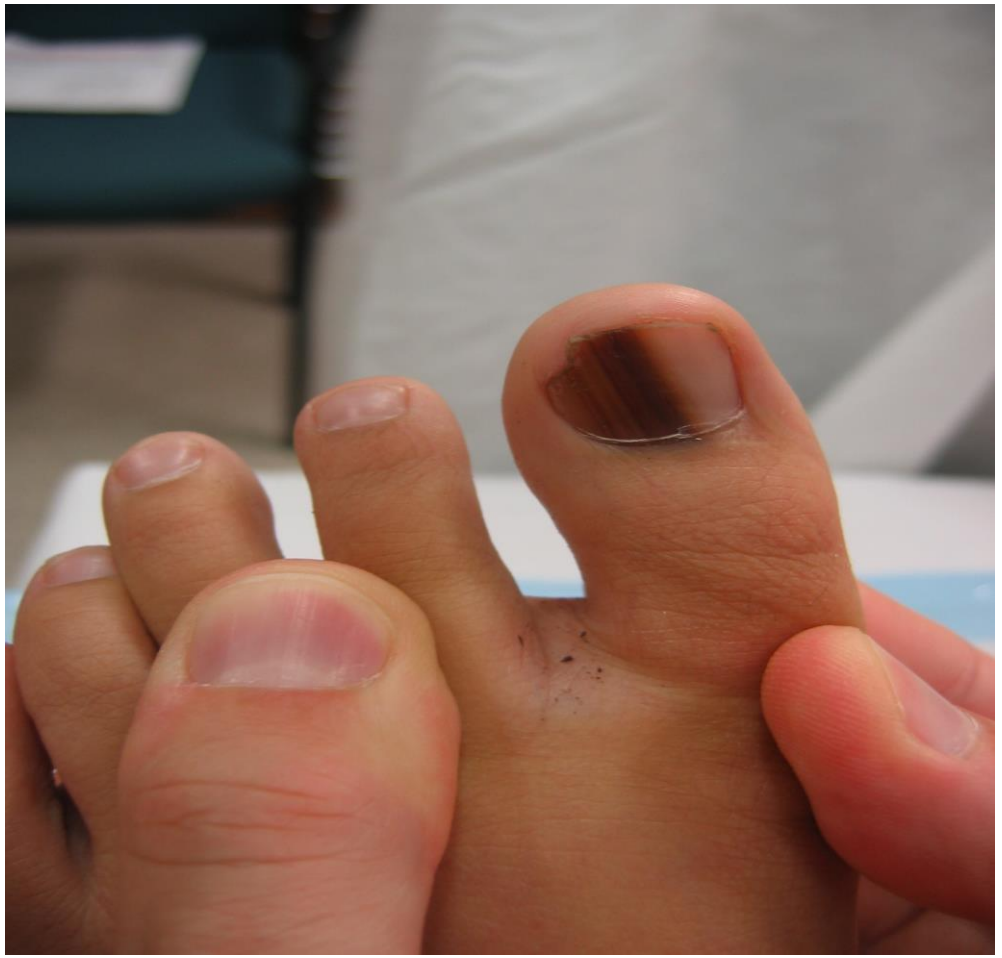


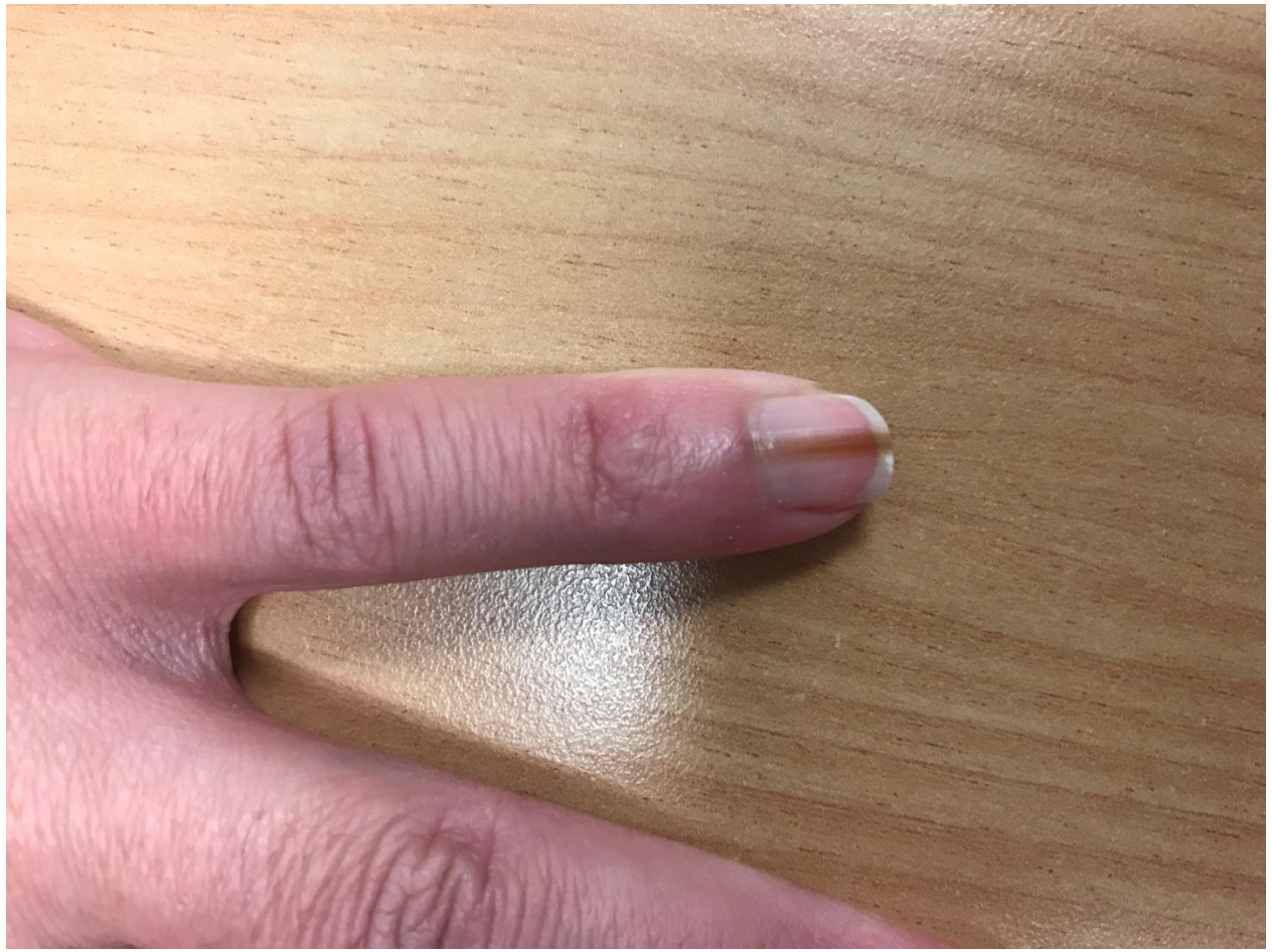


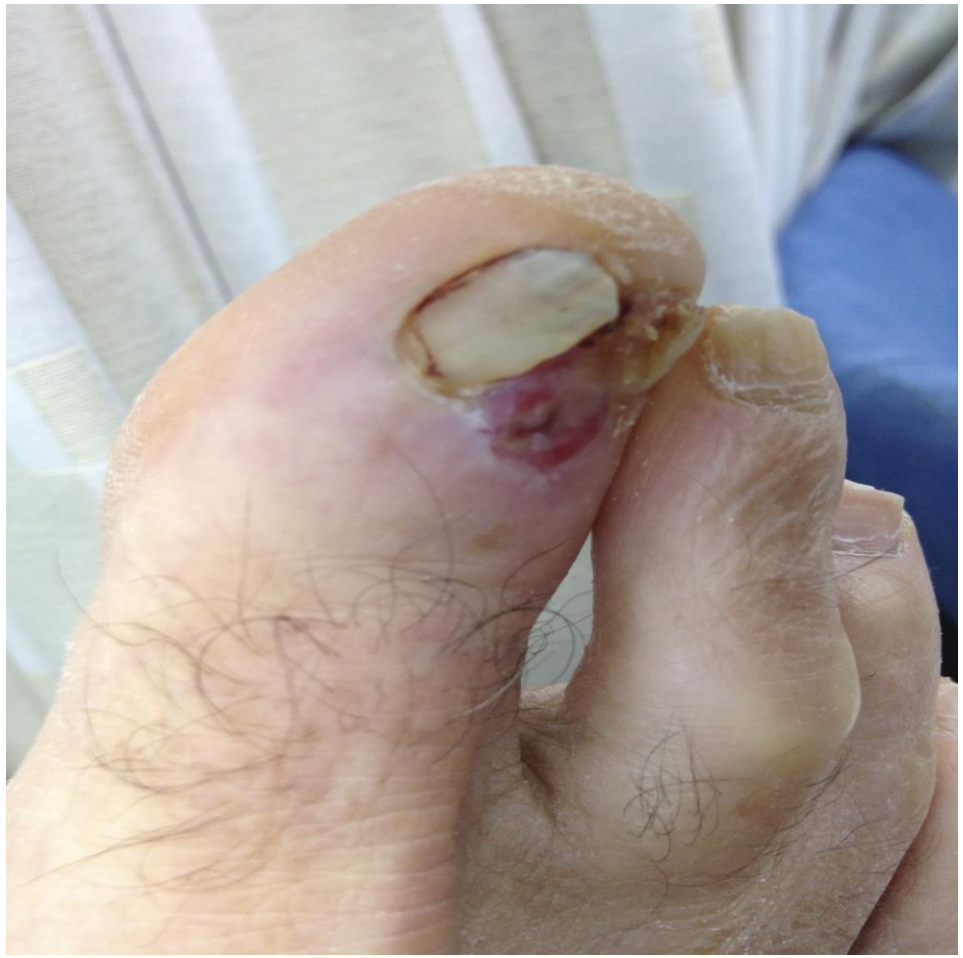


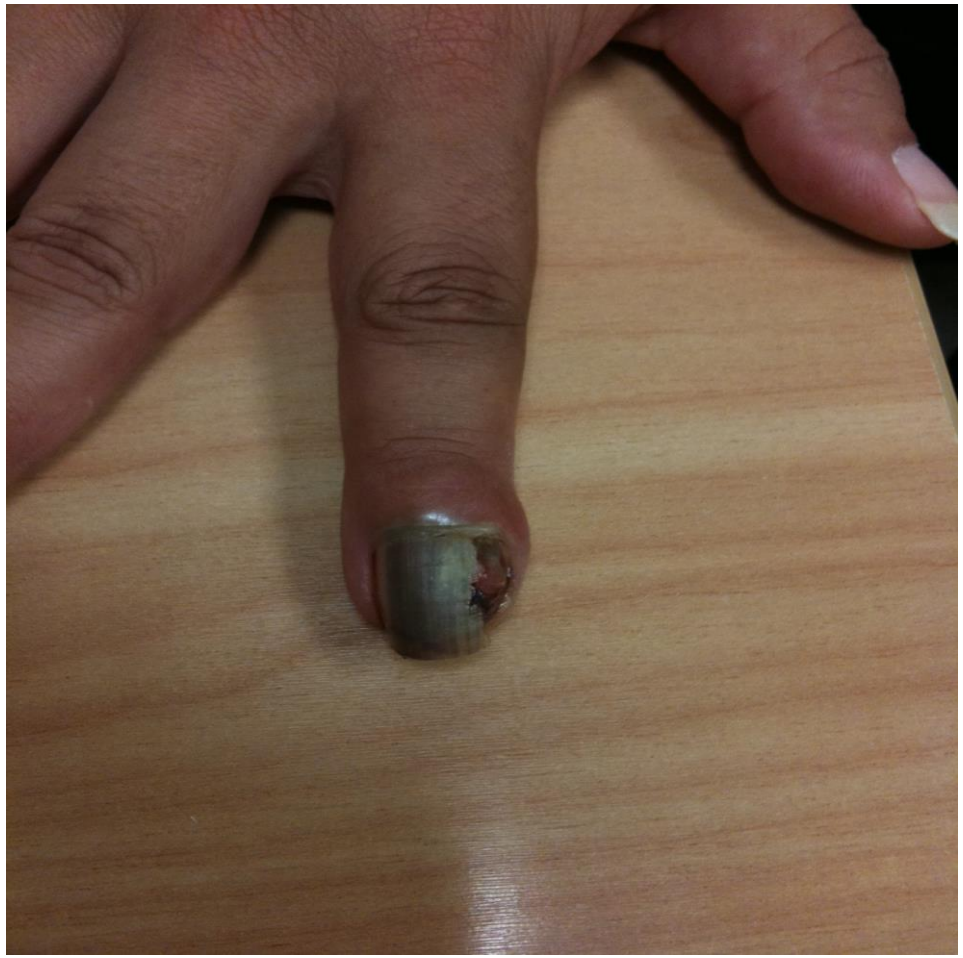


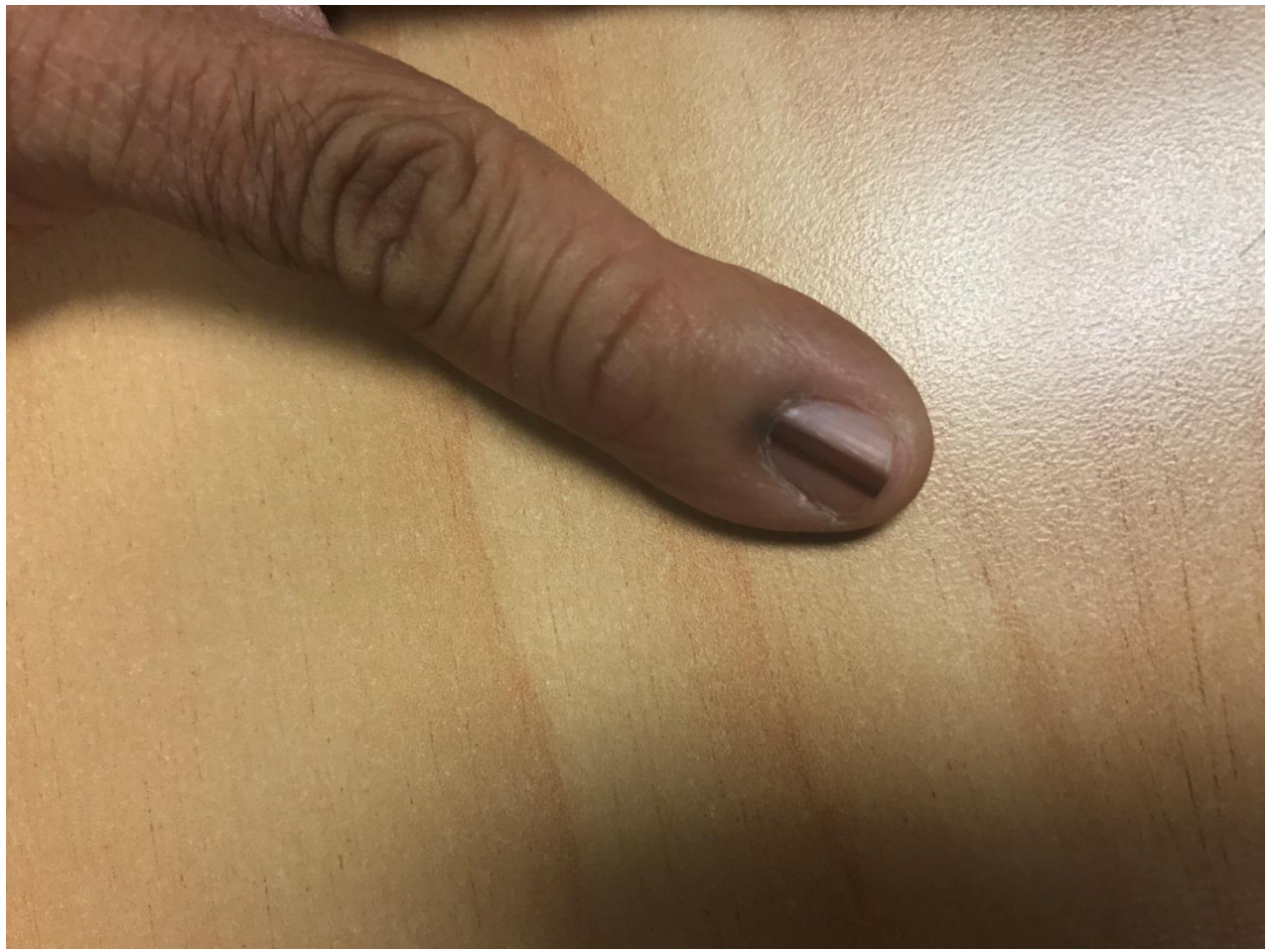
Pigmented nail lesions

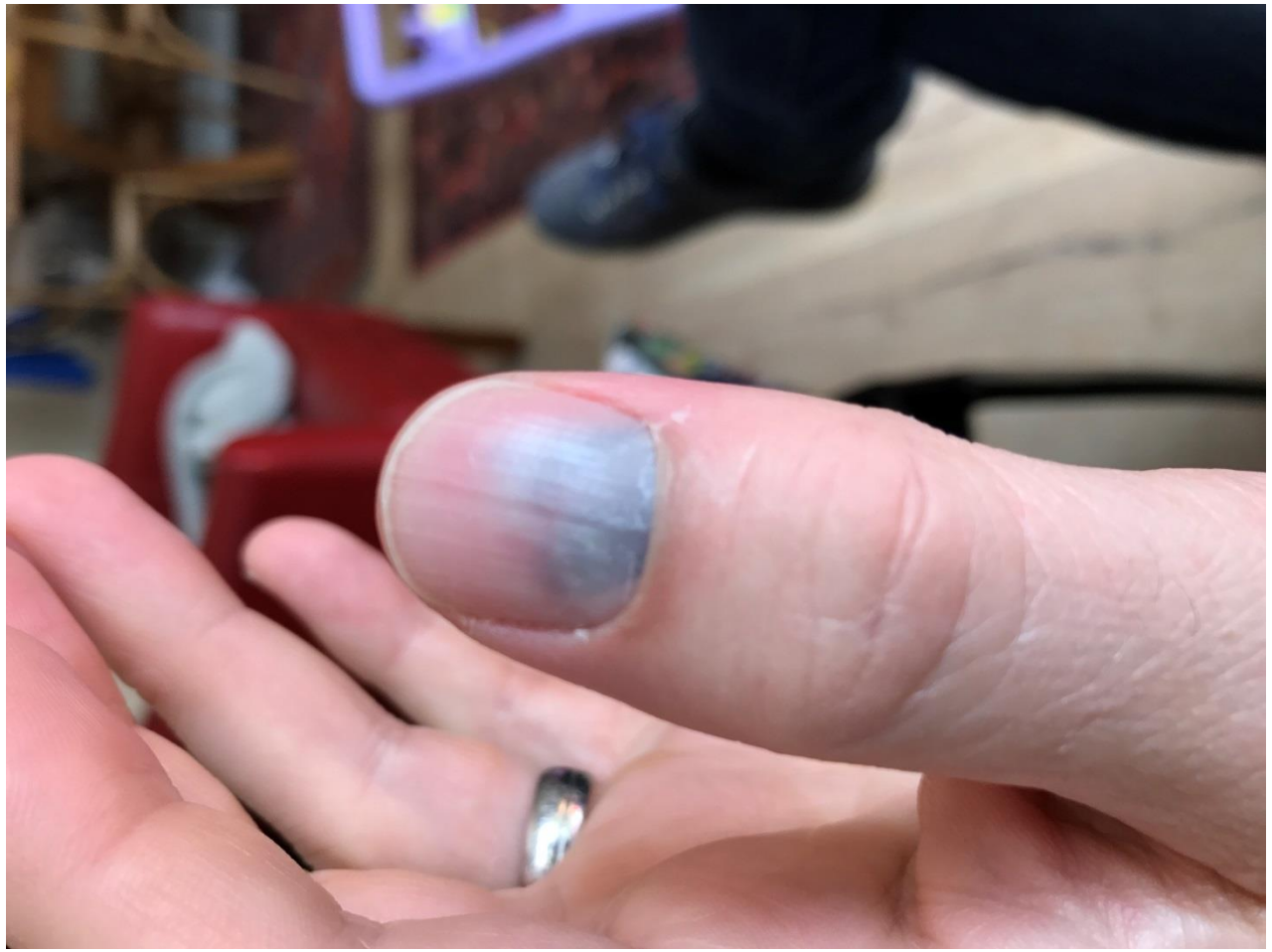


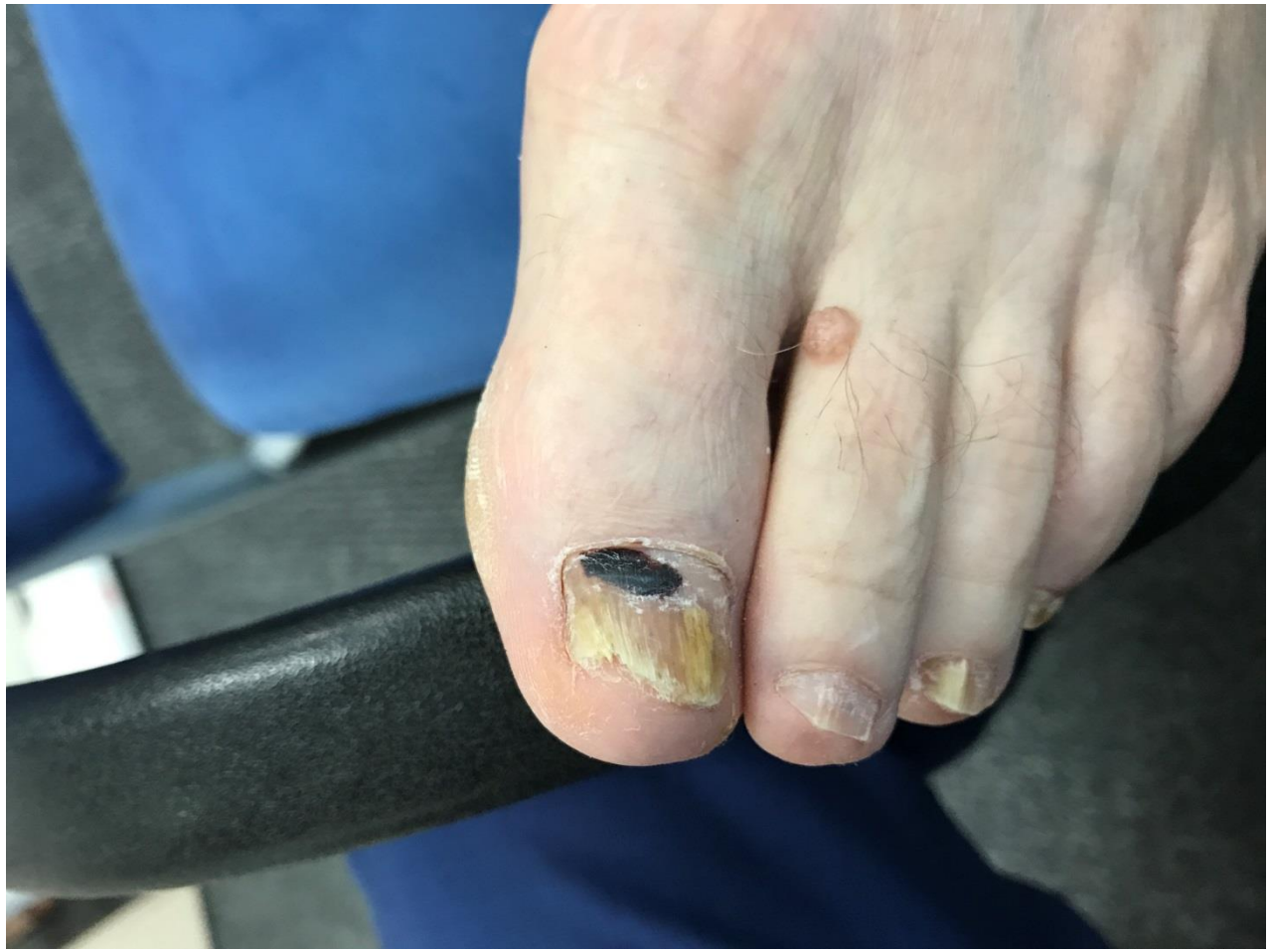


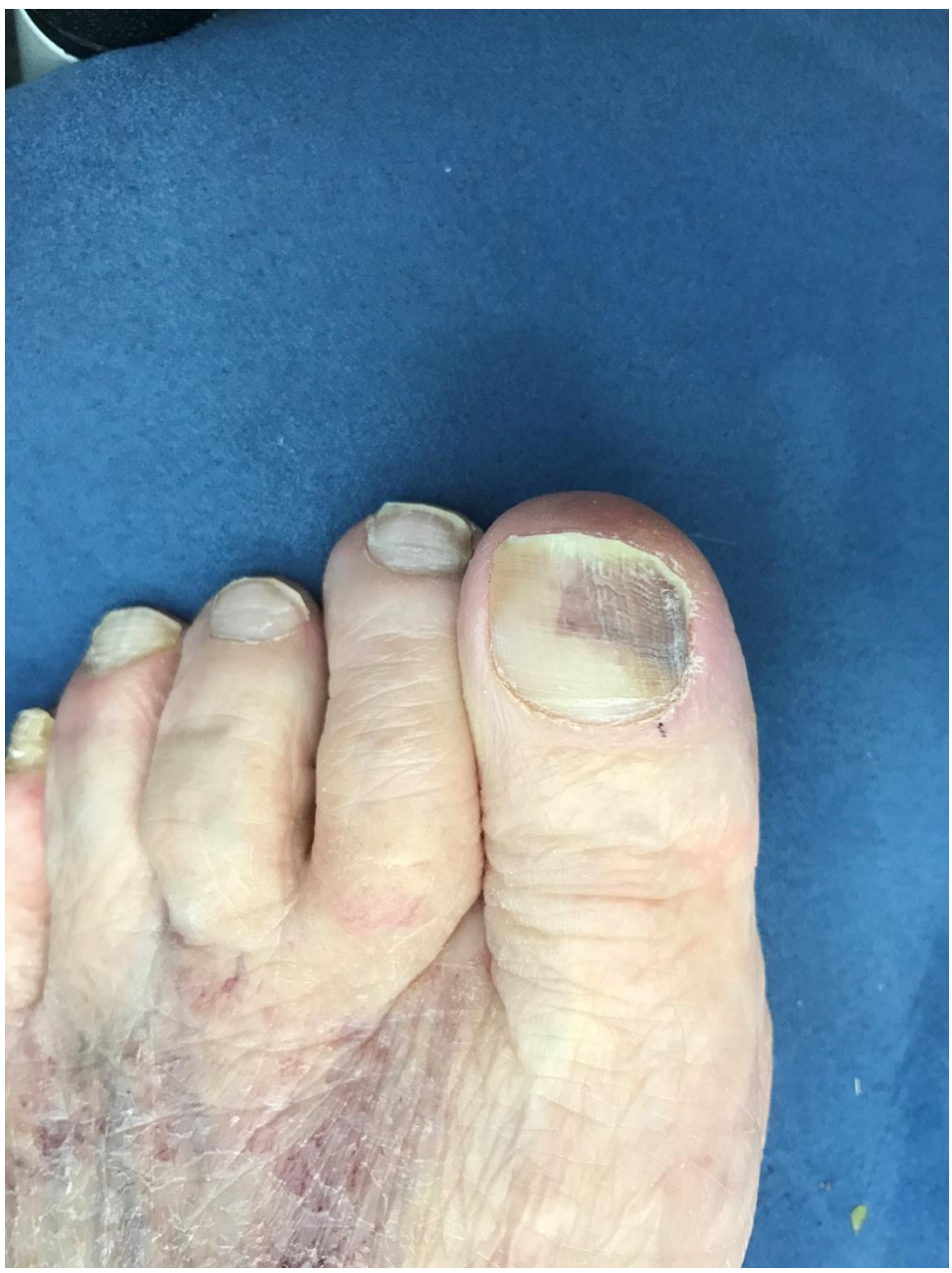


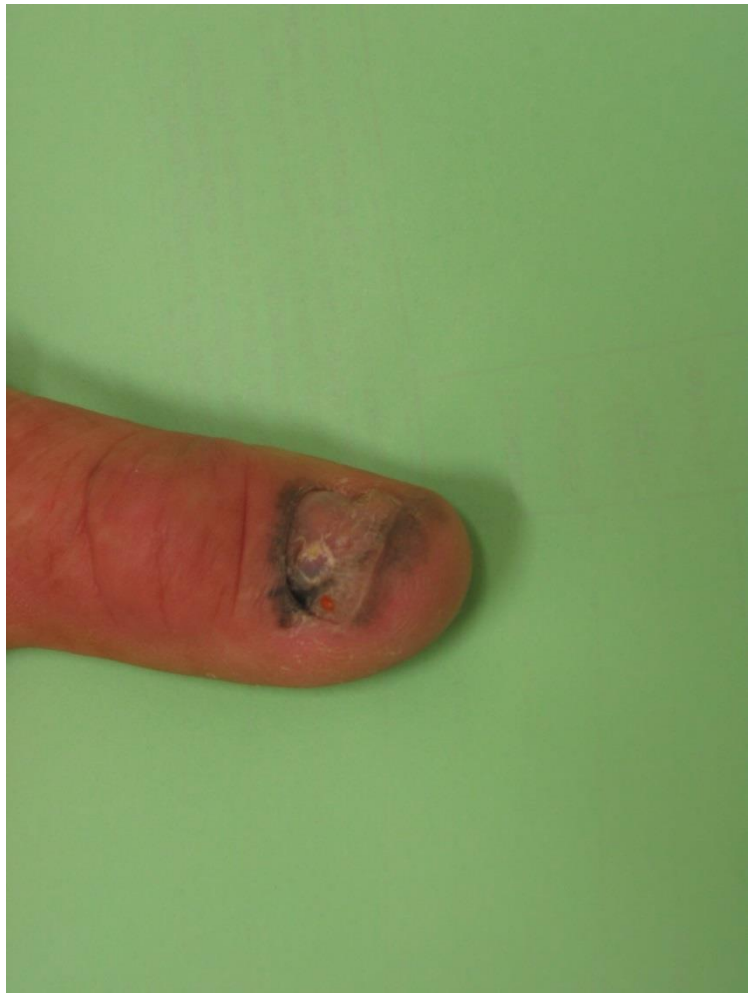










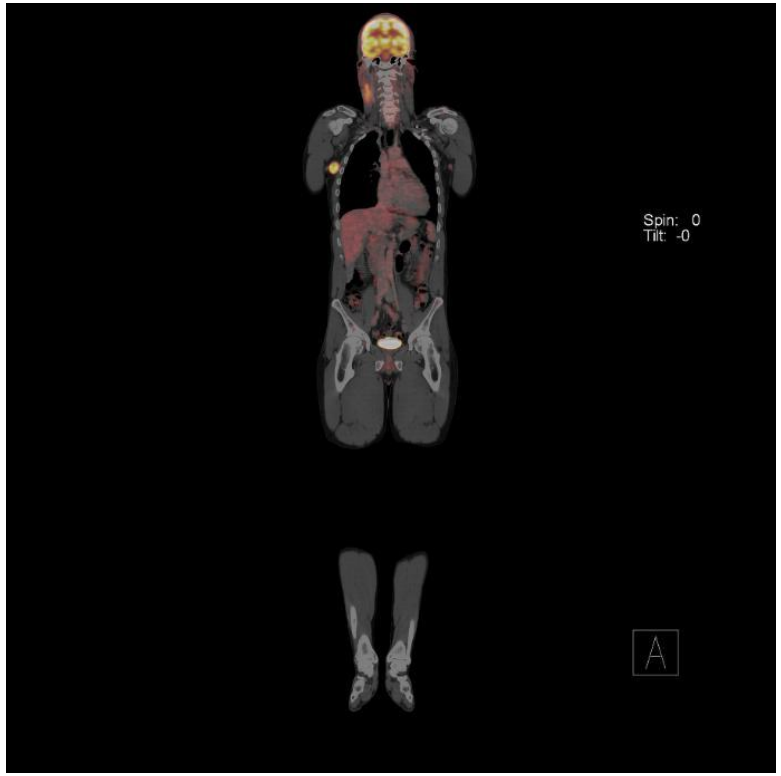


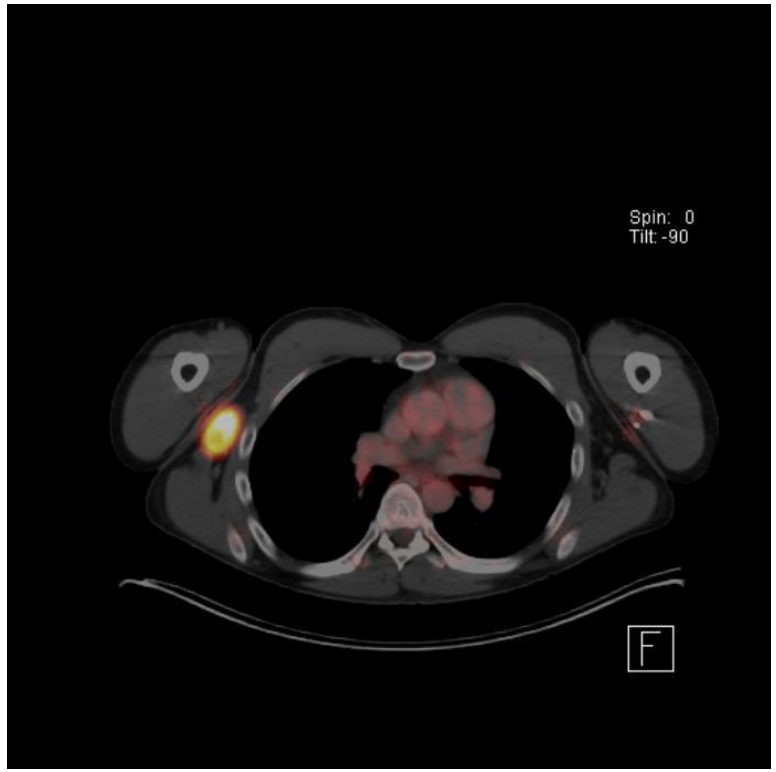
Rosendahl, Dermatology Practical and Conceptual, 2012

30yo Male, right anterior chest Melanoma

- SYNOPTIC REPORT FOR INVASIVE MALIGNANT MELANOMA
- Tumour Type: Invasive superficial spreading
- Clark Level: 4
- Breslow Thickness: 1.1 mm
- Ulceration: Absent
- Mitotic Rate: 3 per mm2
  - *Comment WE advised by Pathologist*

4 years later…





45yo Male

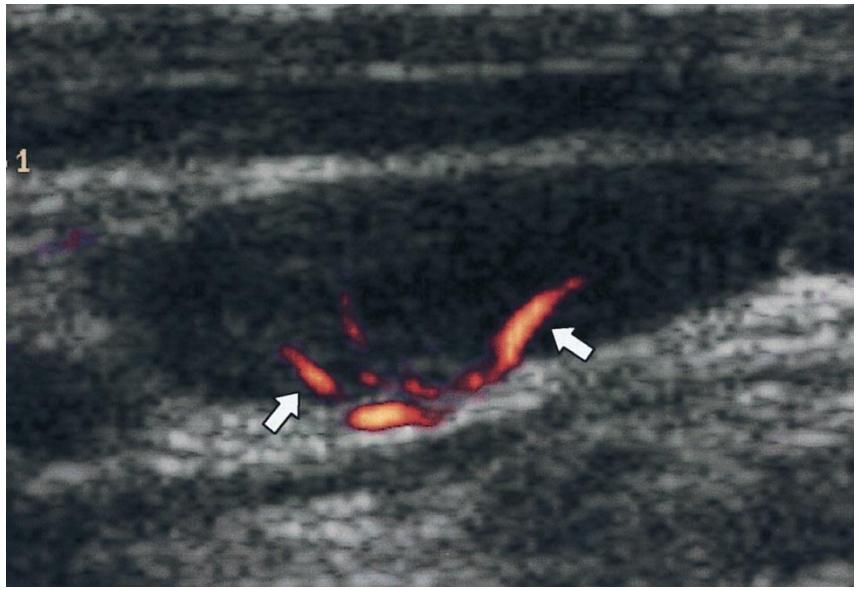
- Left ankle, October 2012
- Tumour Type: Invasive malignant melanoma arising in an area of melanoma in-situ
- Clark Level: 3 Breslow
- Thickness: 0.75mm Ulceration: Nil
- Lymphovascular Invasion: Nil
- Perineural Spread/Neurotropism: Nil
- Mitotic Rate: **2 per sq mm**
- Radial Margin of Excision: Clear. Closest side margin 4mm. Other side margin 4.5mm. Associated Naevus: Nil

SNB

- SENTINEL NODE BIOPSY RIGHT GROIN MEDIAL Gross Description. The specimen consists of one lymph node 18 x 8 x 8 mm encased in fatty tissue. Fatty tissue not processed. A3 R melaSNP Microscopy. Sections show a lymph node with a normal architecture. **There is a minute focus of Melan-A and HMB-45 positive melanocytes. This is almost impossible to measure but is estimated to consist of 5 cells and measure 0.05mm.** There is no extracapsular spread. MINUTE FOCUS OF METASTATIC MELANOMA

Follow up

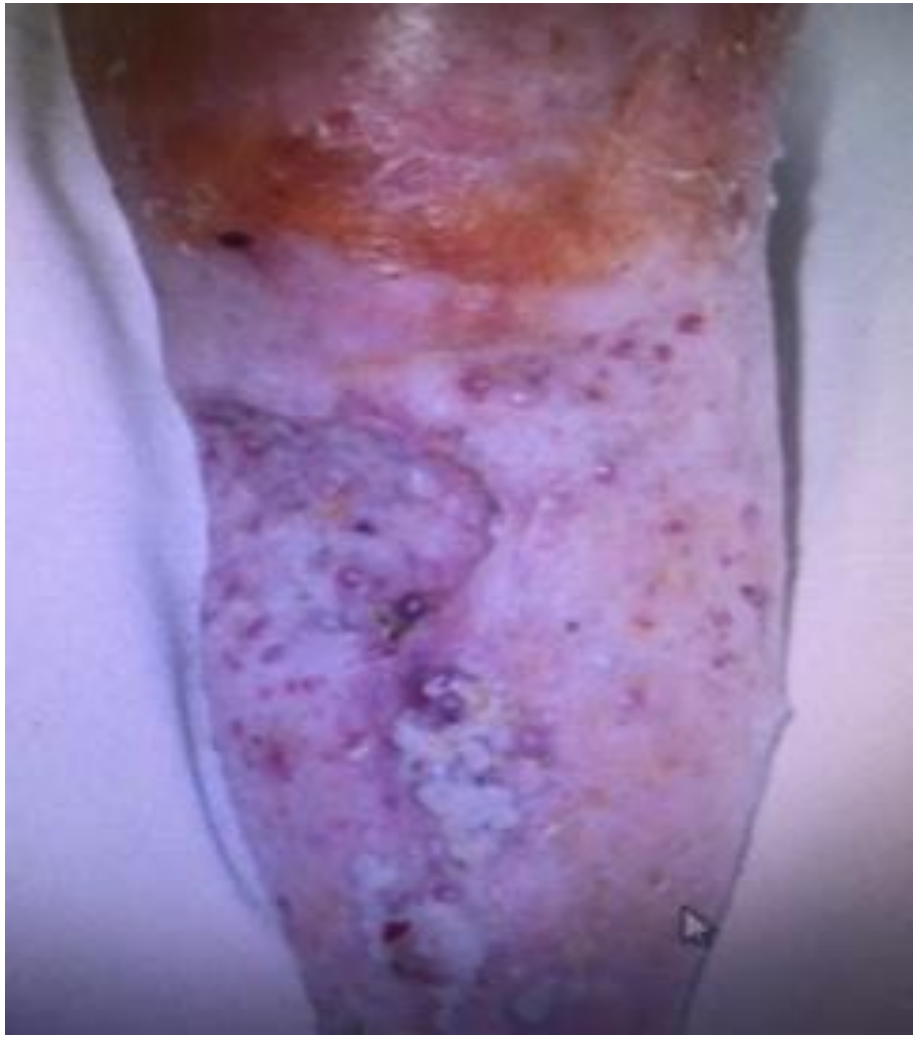
- U/S surveillance every 6 months
- Disease free 5 years later



In-transit disease: 76 year old woman

- 17/12/2014 Excision of 6mm melanoma of left anterior shin, with positive margins and LVI.
- 30/10/2015 Further wide local excision of the recurrence of melanoma in the left leg.
- 02/12/2015 Wide local excision with incomplete margins.
- July 2016 “Innumerable” lesions left leg

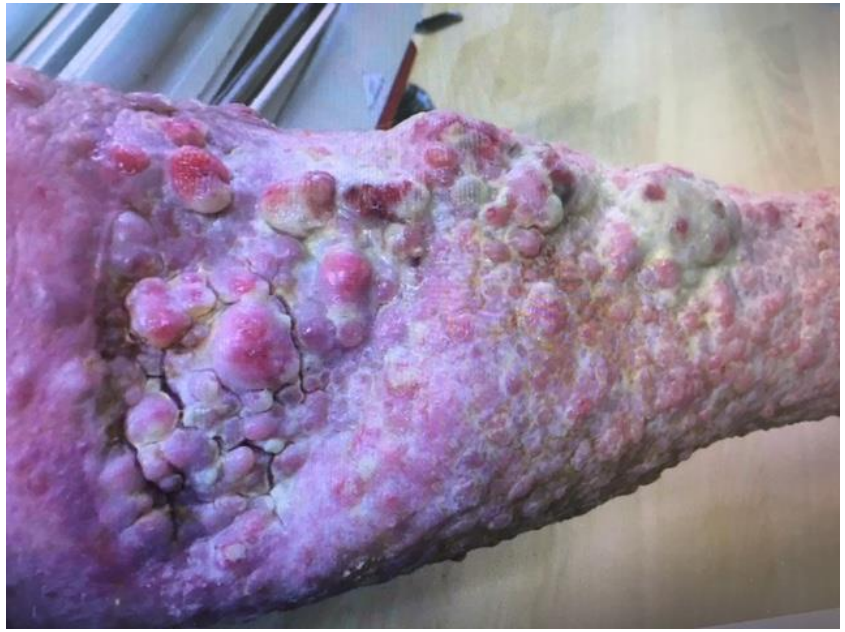
July 2016



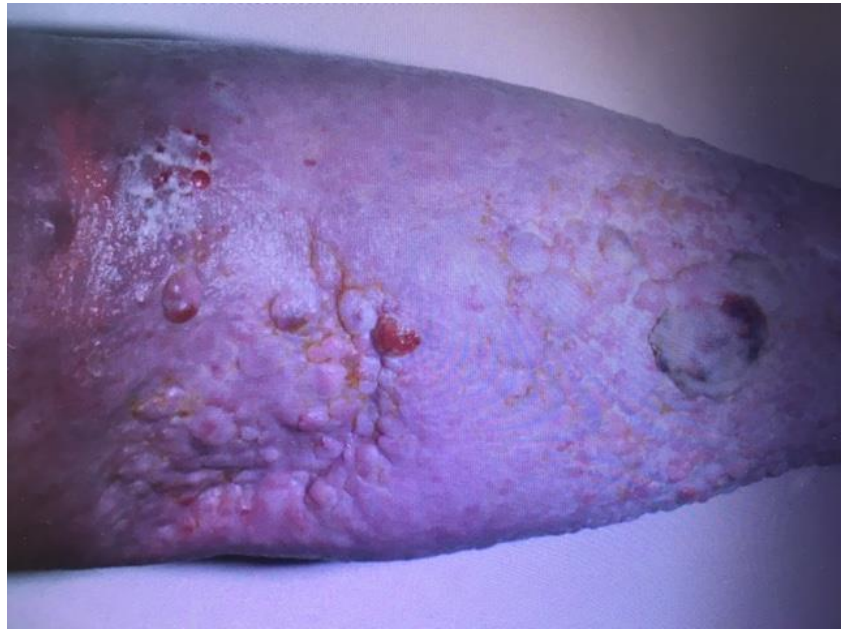
- Options
  - Isolated limb infusion?
  - PD-1 inhibitor?
- Admission to ICU with sepsis from leg Aug 2016

Commenced nivolumab Sep 2016

September 2016



February 2017



Local vs systemic control 1

- 29 year old male
- Congenital lesion on back
- 01/09/2015 Seen in Dermatology Clinic with 2-3 month history of change in the congenital lesion with bleeding and discharge.
- 30/11/2015 Excision biopsy of nodular melanoma, Breslow thickness 7.6 mm, BRAF V600E mutant.
- 23/12/2015 Cytologically positive left axillary node.
- 06/01/2016 PET CT left axillary lymph node 18 mm, multiple lung nodules, largest 7 mm.
- Patient pushing for axillary dissection
- MDM recommendation?

Case 1

- Oncologist recommendation for systemic therapy
- Entered clinical trial of BRAF/MEK inhibitor March 2016 with good partial response
- Sep 2016 Progressive disease, changed to pembrolizumab
- Dec 2016 Progressive disease and death

Local vs systemic control case 2

- 62 year old woman
- Thin melanoma excised from right ankle 20 years ago
- Presents Nov 2016 with nodule right upper thigh – excision confirms melanoma
- April 2017 Further nodule excised right upper thigh
- PET-CT Two lung nodules approx 1 cm
- Clinically has progressed in upper thigh
- MDM recommendation?

Case 2

- Proceeded to excision nodules right thigh, as they were symptomatic
- Repeat PET June 2016 – mild progression lung nodules
- After much agonising…recommendation for pembrolizumab rather than thoracic surgery

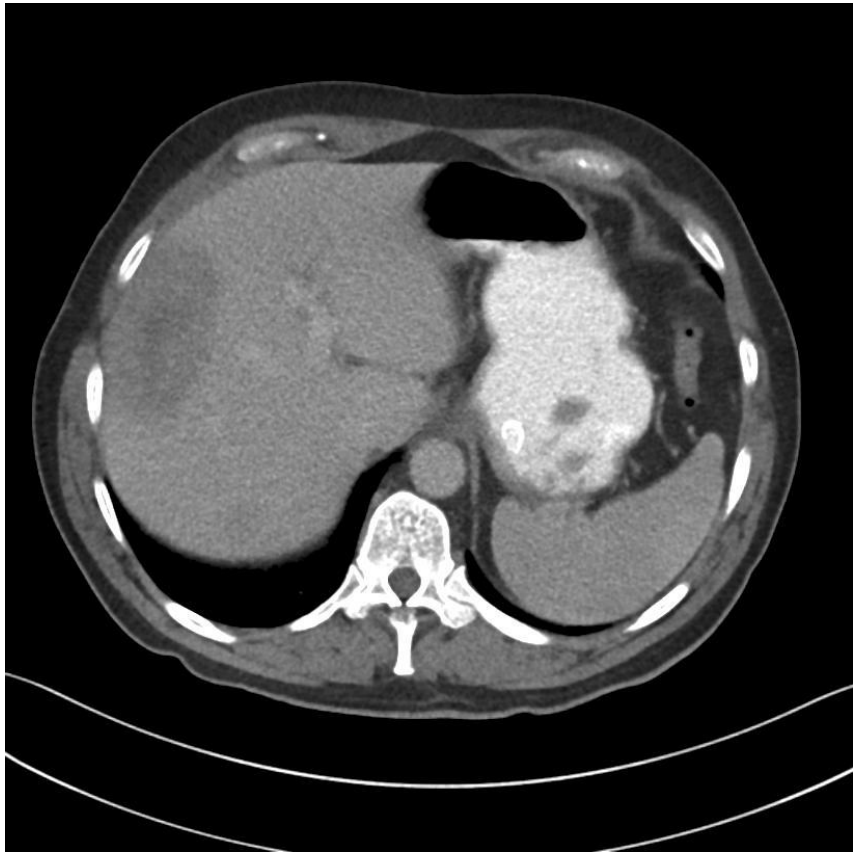
First line BRAF/MEK treatment

- 1999: malignant melanoma widely excised from back, 1.8 mm thickness
- Nov 2013: presented to MMH with one month of nausea, vomiting and headaches
  - CT brain – multiple metastases
  - Liver and lung metastases
  - Liver biopsy confirmed metastatic melanoma, BRAF V600E mutant

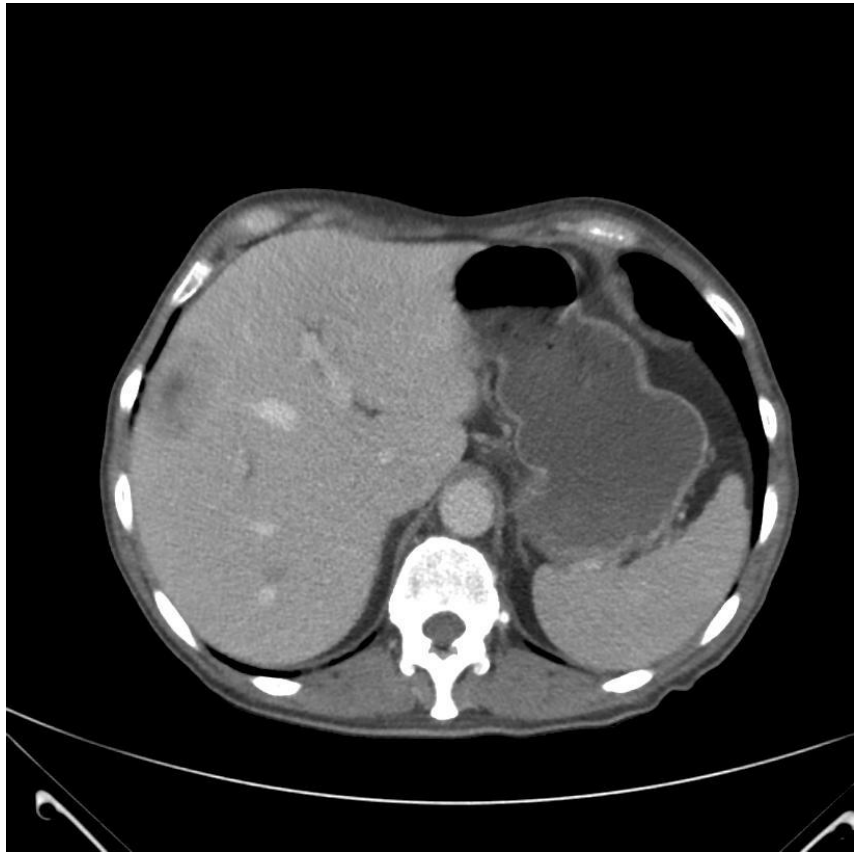
Progress

- Dec 2013: Completed whole brain radiotherapy
- Jan 2014: Frequent generalised seizures
  - CT showed progression in brain
- Jan 2014: Commenced dabrafenib and trametinib treatment
  - Frail; attended MMH ED on day treatment started with seizure

Excellent response to dabrafenib and trametinib

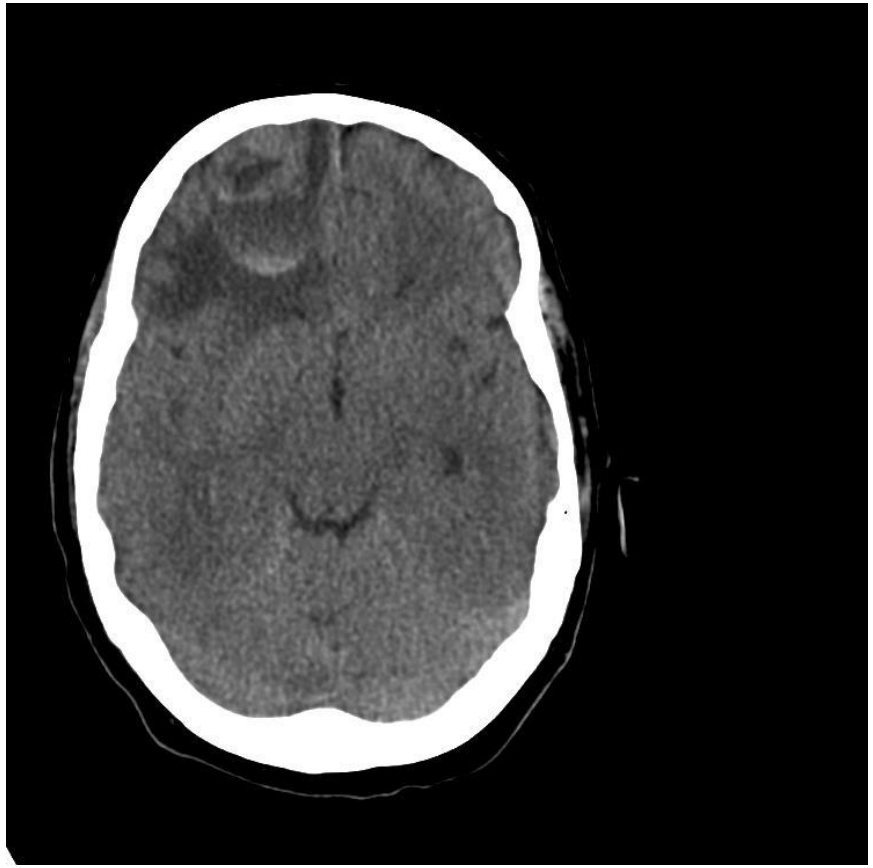


January 2014



April 2014

Seizures stopped!



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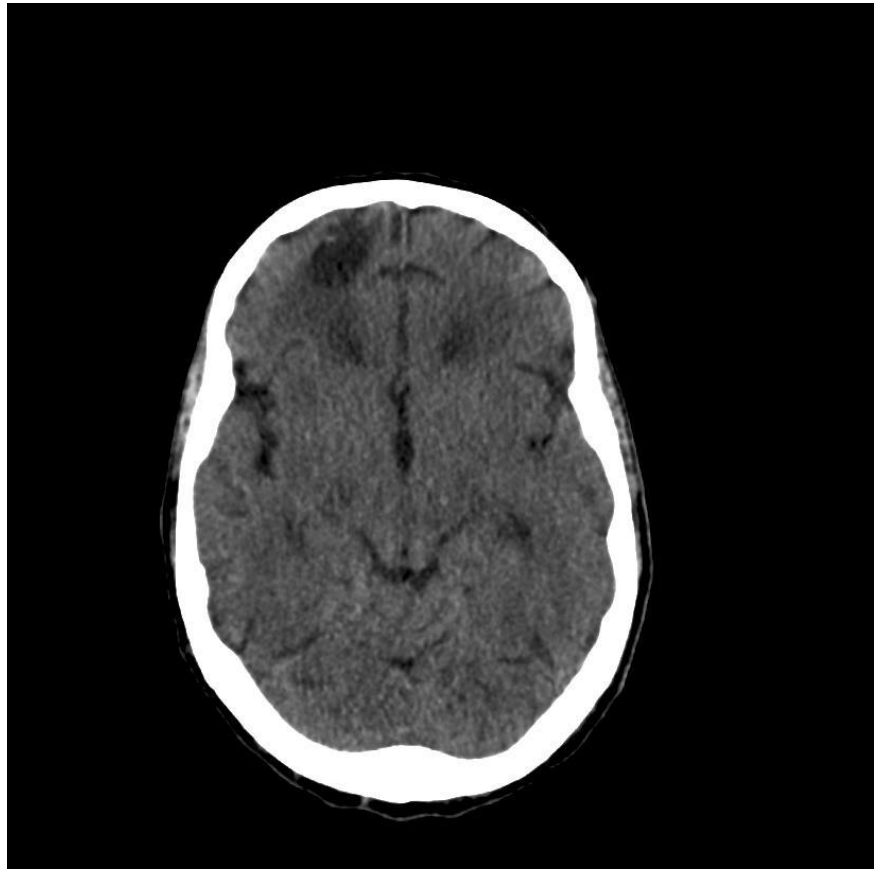


April 2014

First line Rx: BRAF/MEK vs checkpoint inhibitor

- 55 year old man
- 2009 WLE of 2mm melanoma foot, non-ulcerated. Sentinel node negative
- 2014 Right groin dissection. 3/12 nodes positive, largest 50 mm with extracapsular spread. Adjuvant radiotherapy
- Oct 2015 Chest wall lump. FNA confirmed melanoma. BRAF V600E mutation present.
- Staging PET – chest wall nodule, 3 cm kidney met
- What now?

Progress

- History of psoriatic arthritis
- Nov 2015 commenced pembrolizumab
- Partial response after 4 cycles
- Complete response after 8 cycles
- Oct 2016 Patient choice to stop pembro due to bad joints, skin, sinuses
- May 2017 Remains in complete remission

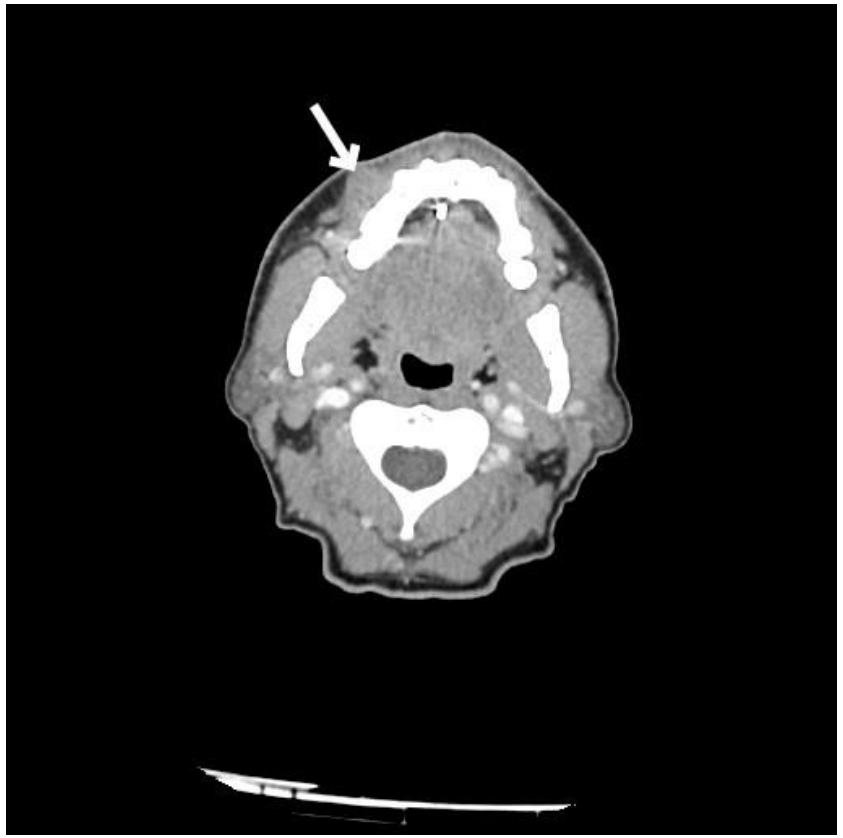
Sequential treatment

- 67 year old man
- 2010 Malignant melanoma with Breslow thickness 4.5 mm. Clark's level IV, mitotic range of 5, no LVI, no regression.
- Nov 2014 Right pleural chest pain. Staging CT showed right hilar mass with multiple liver mets with possible left adrenal and buttock mass. Metastatic melanoma confirmed on biopsy, BRAF mutation present.

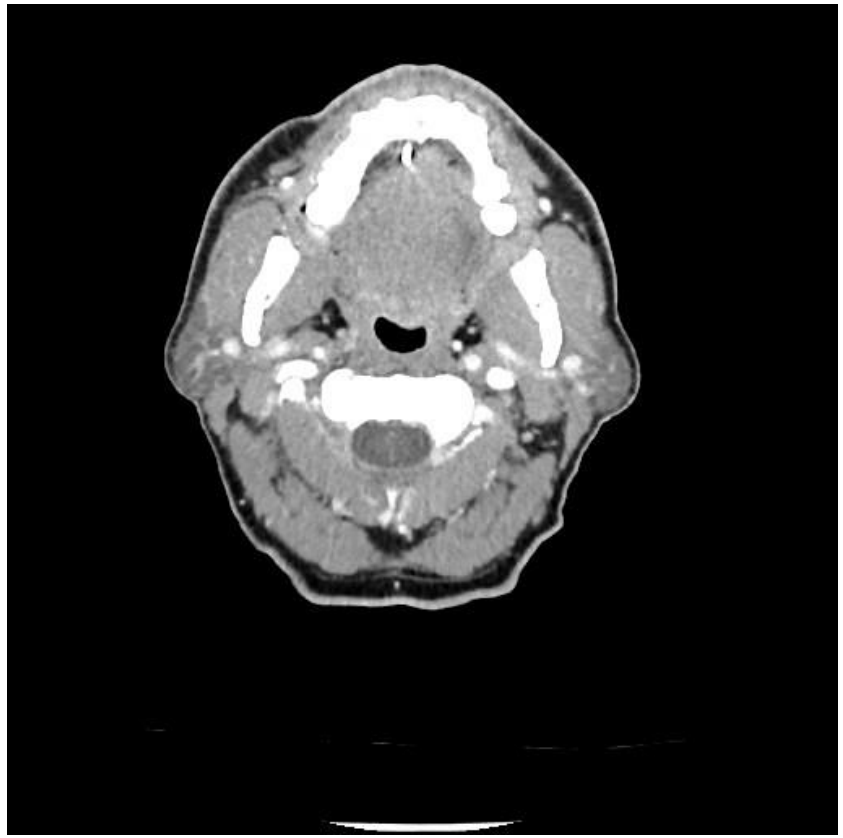
- Feb 2015 Commenced dabrafenib and trametinib to good partial response.
- July 2015 Dabrafenib + trametinib abandoned due to significant toxicities with fevers and fatigue.
- August 2015 CT scan showed excellent response to treatment with shrinkage of all metastatic deposits, only remaining evidence of malignancy is 5 mm liver met.
- Feb 2016 Progressive disease. CT restaging shows soft tissue mets entering the right maxilla, base of tongue, bone. Mets to the right parietal skull, enlarged left axillary node and conglomerate right hilar nodal mass. Enlarging left adrenal metastatic lesion. New spleen metastasis and multiple soft tissue paraspinal lesions.
- 05/02/2016 ORIF of left humerus with pathological fracture.

Maxillary mass

Feb 2016

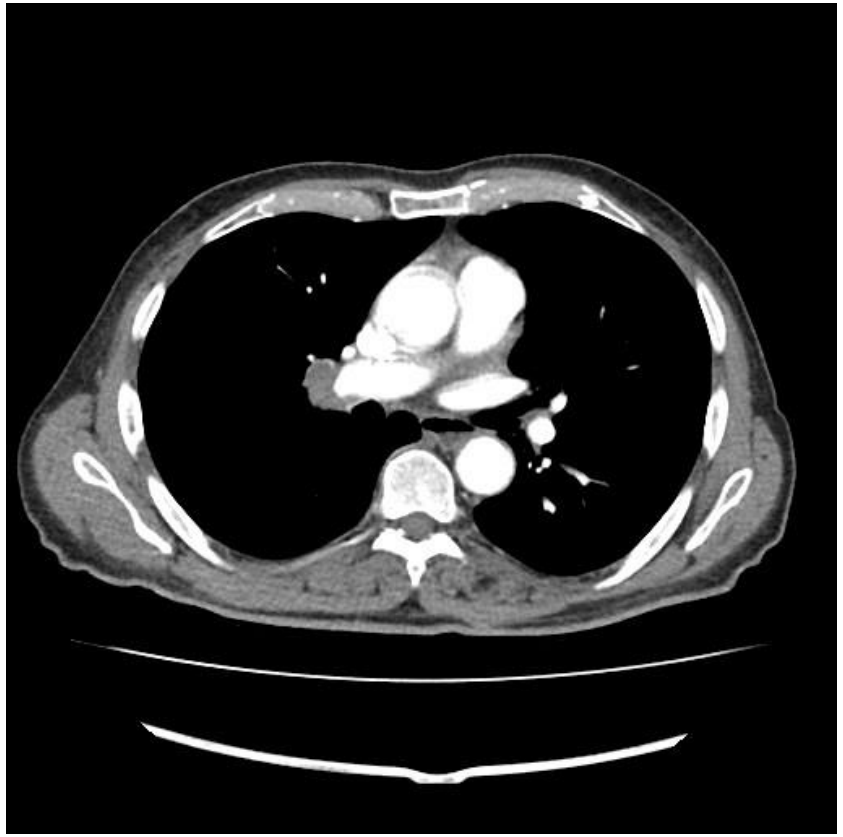


Nov 2016

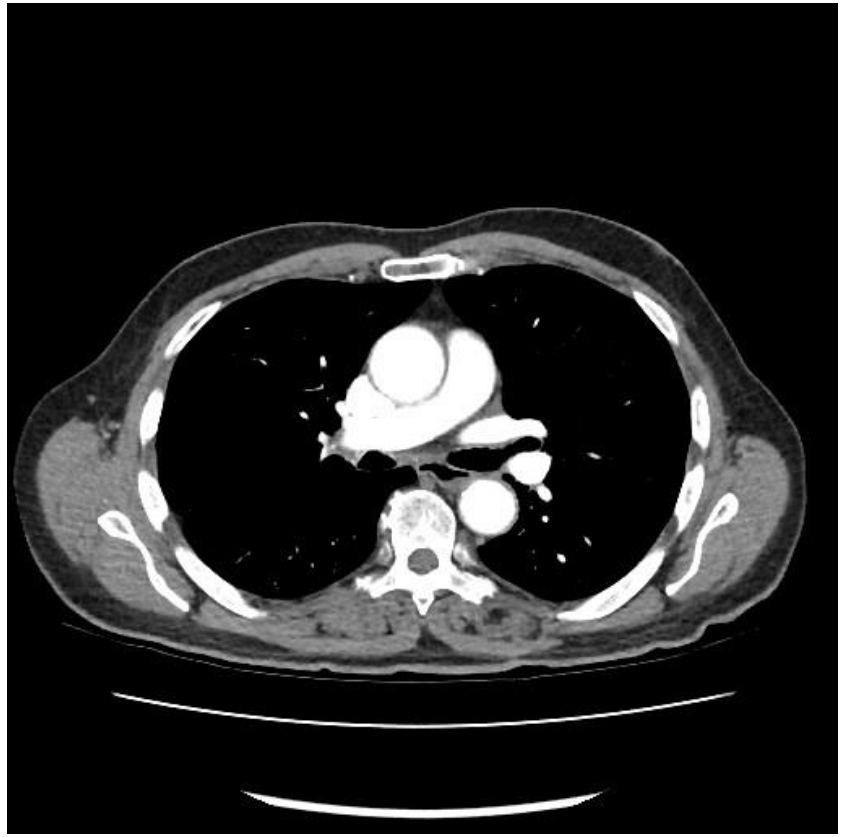


Hilar lymphadenopathy

Feb 2016



Nov 2016



June 2017: Continues to respond. Treatment complicated by colitis. How long to continue??

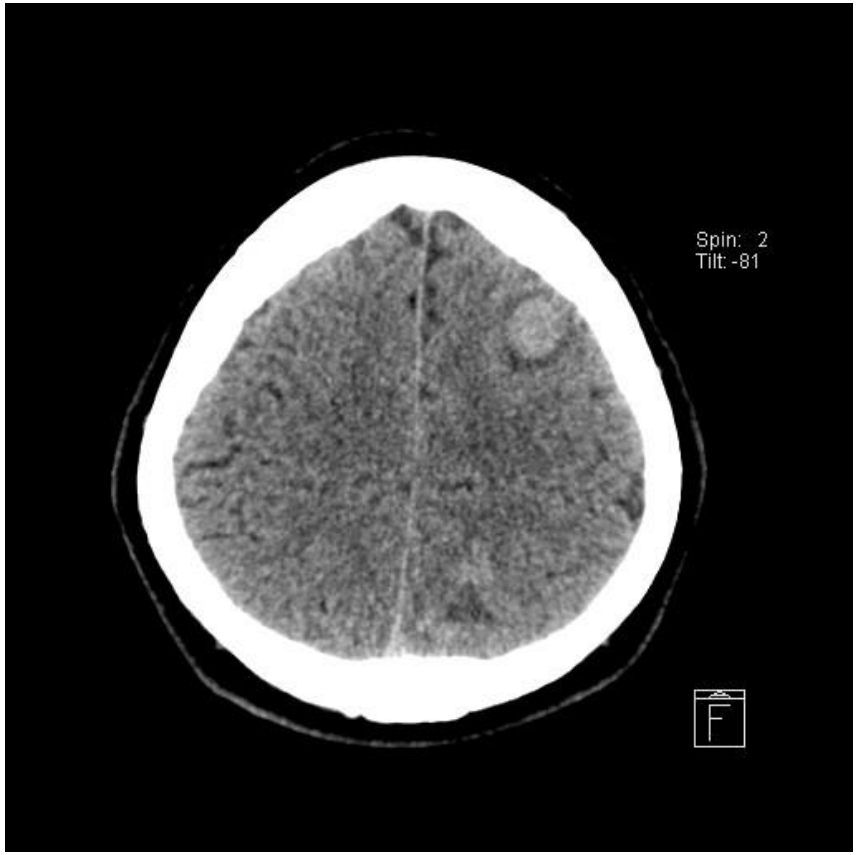
Combination immune checkpoint inhibitors

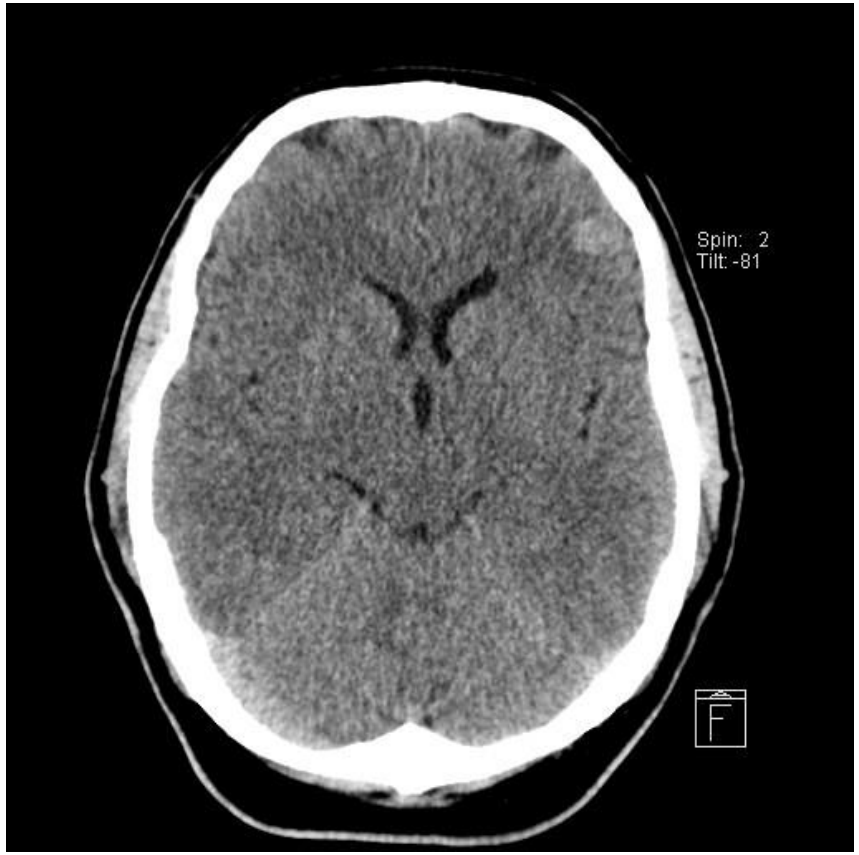
- 60 year old man
- Developed lesion under the nail of the left third finger, diagnosed as melanoma.
- Nov 2010 Treated with amputation and left axillary clearance with nodal involvement.
- Apr 2011 Underwent further axillary surgery for recurrent melanoma. This was in spite of the use of a vaccine on an adjuvant basis to try and prevent recurrence (DERMA study). Since then developed transit lesions in the left upper limb and received radiotherapy to the left axilla. Developed distant metastasis left upper posteromedial thigh, treated with resection mid-2012. Further in-transit disease left arm.
- 25/09/2012 Subsequent discovery of a large left adrenal metastasis on PET CT. Lesions from the limb resected.
- Mid-2013 Underwent right adrenalectomy. He has para-aortic disease as well as palpable left axillary and left thigh deposits.
- Jul 2014 Episode of syncope ± seizure activity, thought to be due to hypoadrenalism (hypophysitis due to ipilimumab)
- Jan 2017 CT - Ongoing complete response.
- Feb 2017 Patient choice to stop treatment

Pembrolizumab non-responder

- 45 year old Maori man
- 2010 1.3mm melanoma, non-ulcerated, involving posterior left upper arm treated with excision biopsy. Declined wider excision and sentinel node biopsy.
- Jan 2016 Presented with a 7 cm left axillary mass that had been growing over the last three months. Fine needle aspiration confirmed melanoma.
- Feb 2016 CT-PET scan showed an 8 x 7 cm mass left axilla, smaller mass involving right axilla, multiple lung metastases ranging up to 2.1 cm and subcutaneous and bone metastases present (widespread).
- Feb 2016 Core biopsy left axilla confirmed melanoma, BRAF mutation present.
- Mar 2016 Commenced dabrafenib and trametinib
- Oct 2016 Progressive disease confirmed with lung lesion of 12 mm and progression in left axillary nodal disease. Changed to second line pembrolizumab.

November 2016 (after 2 cycles pembro)



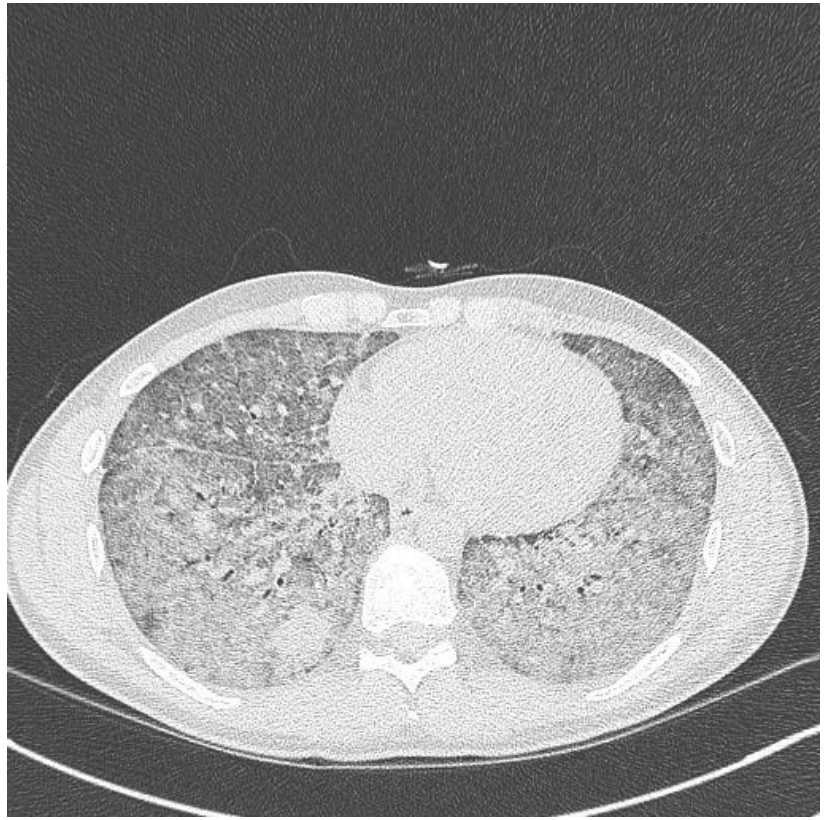


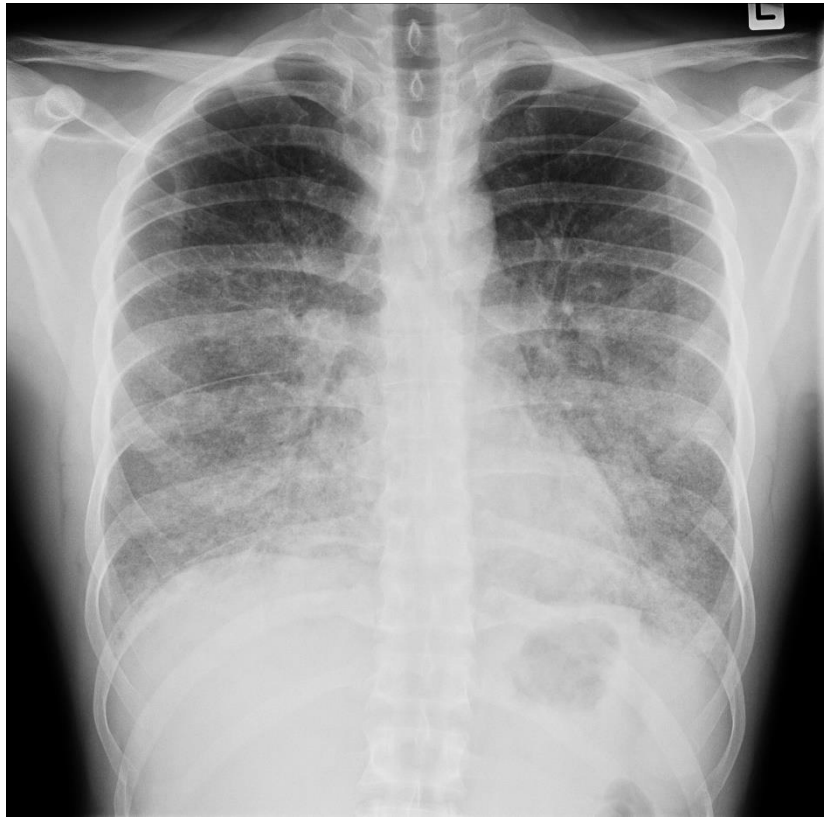
Non-responder: progress

- PD in brain and axilla
- Completed whole brain RT Dec 2016
- Received 4 cycles pembro
- Treatment stopped early Feb 2017
- Died late Feb 2017

Toxicity from pembrolizumab

- 30 year old male
- Metastatic melanoma to lungs, nodes
- Presented with dry cough after cycle 3 pembrolizumab
- Progressive axillary node
- Not hypoxic, no respiratory distress on admission





Pneumonitis

- Treated with high dose corticosteroids
- CPAP in intensive care
- Treated with infliximab
- Deteriorated and died despite treatment, 10 days after admission