## Document history:

<table>
<thead>
<tr>
<th>Version number</th>
<th>Date of revision</th>
<th>Summary of changes</th>
<th>Amended by</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>August 2013</td>
<td>First guideline version</td>
<td>David Chao</td>
</tr>
<tr>
<td>2.0</td>
<td>August 2019</td>
<td>To include updates from NICE, BAD and the Melanoma Focus Meeting Consensus guidelines</td>
<td>FI, SH &amp; AS</td>
</tr>
</tbody>
</table>
1 Contents
1. Introduction .......................................................................................................................... 4
2. Screening and surveillance .................................................................................................. 4
3. Management in primary care .............................................................................................. 4
4. Assessment and Management in Secondary Care .............................................................. 5
   4.1 Management of adult patients .................................................................................... 5
   4.2 Management of TYA patients ...................................................................................... 5
5. Staging ................................................................................................................................ 6
6. Surgical Management ......................................................................................................... 7
   6.1 Primary excision ........................................................................................................... 7
   6.2 Sentinel lymph node biopsy (SNB) ............................................................................. 7
   6.3 Lymphadenopathy ....................................................................................................... 8
   6.4 Lymph Node Dissection (LND) .................................................................................. 8
7. Histopathology and molecular profiling ............................................................................ 9
   7.1 Minimum dataset ........................................................................................................... 9
   7.2 Molecular testing .......................................................................................................... 9
8. Vitamin D ............................................................................................................................ 10
9. Imaging ................................................................................................................................ 10
10. Adjuvant Treatment of completely resected stage 3 melanoma ....................................... 10
11. Management of advanced or metastatic disease ............................................................... 11
12. Follow up management ...................................................................................................... 12
13. Appendices ......................................................................................................................... 14
Table 1 ................................................................................................................................... 14
1. Introduction

The North Central and East London Cancer Alliance (NCELCA) guidelines for the management of malignant melanoma are the result of the merger of the previous 2013 guidelines, which have been updated to incorporate the following:

- Melanoma Focus Meeting Consensus guideline May 2018.

2. Screening and surveillance

The system will adopt the 2010 BAD guidelines for both screening and surveillance.

3. Management in primary care

Patients may present to their general practitioner with a new or changing pigmented lesion. The weighted 7-point checklist has been recommended by NICE for routine use in UK general practice and may be helpful in assessing pigmented lesions.

**Major features** 2 points
- Change in size
- Irregular shape
- Irregular colour

**Minor features** 1 point
- Largest diameter 7mm or more
- Inflammation
- Oozing
- Change in sensation

Suspicion is greater for lesions scoring 3 points or more. However, any one feature is adequate to prompt an urgent referral if the concerns about cancer are strong. Biopsy or attempted excision should not be carried out in primary care.

At this stage, the GP can do one of the following:
- Reassure the patient and discharge.
- Reassure the patient, but point out signs to look for which may represent malignant change and advise patient to return if change is noted.
- Reassure the patient, but take a clinical photograph and advise to return if change is noted.
- Refer to local Dermatology Unit via the urgent suspected cancer route/two week rule (TWR). NCELCA has a Suspected Skin Cancer referral form with all dermatology units listed.
4. Assessment and Management in Secondary Care

4.1 Management of adult patients

Patients are referred in via the TWR and should be seen by a Dermatologist. In clinic the following model is used:

- A full history is taken.
- The patient is asked to undress and examined thoroughly in bright light with a dermoscope – in accordance with NICE guidance, all pigmented skin lesions referred for assessment in secondary care should be done so using dermoscopy carried out by healthcare professionals trained in this technique.
- For a clinically atypical melanocytic lesion that does not need excision at first presentation in secondary care, use baseline photography (preferably dermoscopic) and review the clinical appearance of the lesion, and compare it with the baseline photographic images, 3 months after first presentation to identify early signs of melanoma.
- If the lesion is deemed suspicious it should be excised.
- Where possible the clinic will offer immediate biopsy service. If not possible, the biopsy will be performed as soon as possible.
- Biopsy is an excision biopsy (excising the lesion with a 2mm margin). If excision is not possible due to site/size of lesion, then an incision biopsy is acceptable.
- When biopsy is undertaken, care is given to orientation of scar with view to future excisions.
- The pathology request form will give the following details - name, age, gender, DOB, hospital number, site, brief history, differential diagnosis and orientation stitch if necessary.
- Patients are requested to return in 2-3 weeks for the results. Patients should be encouraged to request their results if they do not hear within 4 weeks.
- If the pathology records melanoma, then patients are requested to return to the appropriate clinic to be given their diagnosis in person.

If the patient may be managed by the LSMDT (Stage 0 or stage IA melanoma) then definitive treatment may be carried out at that hospital and surgical margins are given in section 6.1. However, for patients under 18y or 18-24y additional guidance is available (see section 4.2).

For patients with stage IB – IIC melanoma with a Breslow thickness of more than 1mm, the option of Sentinel Lymph Node Biopsy (SLNB) should be considered. This staging procedure is offered by the two main SSMDTs at the Royal Free Hospital and the Royal London Hospital. It is stressed that co-morbidities and informed patient choice are vital determinants for this procedure, and patients should be given verbal and written information about the advantages and disadvantages (See Appendix A, Table 1 taken from NICE guidelines, July 2015).

4.2 Management of TYA patients

UCLH is the designated Principal Treatment Centre for The North Thames Teenage and Young Adult (TYA) Network, which includes organisations affiliated with NCELCA. The Royal
Free Hospital (RFH) has been awarded TYA Designated Hospital status for patients with skin cancer acknowledging the specific expertise for managing skin cancer at this Trust.

There are 3 distinct groups of young patients with skin cancer to be considered under this guidance.

1) All patients 18y and under: These patients must be referred to Adolescent Dermatology at UCLH and discussed at the Skin Cancer SSMDT at the Royal Free Hospital. If it is deemed appropriate then patients should undergo their further surgical treatment at the RFH. Follow up should take place back at UCLH.

2) Patients aged 19 to 24y with melanoma under Breslow thickness 1mm and no other poor prognostic markers, such as ulceration or mitotic activity: There is a conflict here between the TYA and Skin Cancer Improving Outcomes Guidance (IOG). Under TYA IOG such patients should be offered treatment at the Principal Treatment Centre (in this case UCLH) or the designated TYA centre (in this case RFH) only, but it must be recognised that this is generic guidance. Under Skin Cancer IOG such patients are dealt with locally by the LSMDT and do not require referral onwards to the SSMDT. Discussion at the Skin Cancer Pathway Board has highlighted that for this good prognosis group of patients mandatory referral to the SSMDT would only lengthen treatment and travelling times, potentially compromising outcome. Therefore the pragmatic compromise will be that these patients will be offered the choice between further surgery at the site of the LSMDT or to be referred to the SSMDT. Those patients who stay with the LSMDT for further treatment will be provided with a TYA information pack detailing appropriate support services for them and the LSMDT will be required to complete a form on each patient which will be forwarded directly to the TYA MDT. Those requiring further support will be contacted by the designated TYA CNS.

3) Patients aged 19 to 24y with melanoma of Breslow thickness 1mm or greater, with or without other poor prognostic markers: This patient group is currently obliged to be referred to the SSMDT for further treatment under Skin Cancer IOG. These patients will be provided with an information pack detailing appropriate support services for them and the Skin Cancer CNS will dial into the TYA MDT on Wednesday afternoons on alternate weeks to discuss these patients. Those requiring further support will be contacted by the designated TYA CNS.

5. Staging

Staging for melanoma is based on the American Joint Commission on Cancer (AJCC) and the current working version is the 8th edition 2018\(^1\).

---

\(^1\)[https://cancerstaging.org/references-tools/deskreferences/pages/default.aspx]
6. Surgical Management

6.1 Primary excision

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (In-situ)</td>
<td>at least 0.5cm*</td>
</tr>
<tr>
<td>1</td>
<td>at least 1cm</td>
</tr>
<tr>
<td>2</td>
<td>at least 2cm</td>
</tr>
</tbody>
</table>

*Imiquimod for stage 0 melanoma – consider imiquimod to treat stage 0 melanoma in adults if surgery to remove the entire lesion with a 0.5cm clinical margin would lead to unacceptable disfigurement or morbidity. Consider a repeat skin biopsy for histopathological assessment after treatment with topical imiquimod to check whether it has been effective.

6.2 Sentinel lymph node biopsy (SNB)

- SNB is indicated for patients with primary cutaneous melanoma pT2a (≥1.0mm Breslow thickness) and above. All tumours of ≥1.0mm should be referred to the appropriate surgeons at the Royal Free Hospital or Royal London Hospital.

- Patients with a pT1b primary melanoma should be considered for SNB, particularly where the primary tumour displays either of the following features:
  a. Lymphovascular invasion
  b. Mitotic rate≥2/mm²

- SLNB cannot be carried once a wide local excision has already been completed and therefore all dermatologists/surgeons who perform primary excisions must be aware of the guidelines.

- SLNB must only be carried out by experienced surgeons using a dual technique (lymphoscintigraphy and blue dye), who are core members of the SSMDT and meet NICE IOG criteria. There must be adequate dermatopathology support for this service.

All patients with positive SLNB (stage III) must have CT or MRI head plus CT Chest/Abdo plus pelvis +/- neck where appropriate or PET-CT prior to any further oncological or surgical treatment. MSLT2 has demonstrated no benefit in elective lymphadenectomy over enhanced observation in patients with positive sentinel nodes.

Completion lymph node dissection (CLND) should not be recommended routinely for patients who have a positive sentinel node biopsy. Patients deemed at high risk should be considered for adjuvant therapy. A lymph node dissection should be considered for those patients who subsequently present with node ONLY recurrence.
In line with the Melanoma Focus Consensus Statement, CLND could be considered for those patients with features identified in their SNB that indicate a high risk of regional relapse, namely:

- Extracapsular spread
- ≥3 involved sentinel nodes
- Dewar criteria (multifocal or extensive)

AND

- Who are unsuitable for adjuvant therapy, either due to medical co-morbidities or where geographical constraints may limit access to routine follow-up at a regional cancer centre

SLNB gives valuable prognostic information and identifies patients who are at higher risk of relapse to be considered for adjuvant treatment or clinical trial. It is the recommendation of the Pathway Board that SLNB continues to be the standard of care for these reasons, and that patients should be offered the option of having SLNB with proper counselling.

Enhanced surveillance for sentinel node positive patients will include routine ultrasound of the draining nodal basin(s) to allow early detection of nodal recurrence in the interval between six-monthly full staging.

6.3 Lymphadenopathy

- Patients who present with suspicious lymphadenopathy should be investigated with fine needle aspiration cytology (FNAC) or core biopsy (which is preferred), with or without imaging guidance. If the FNAC or core is negative and clinical suspicion is high then open biopsy should be considered but referral to the SSMDT is strongly recommended at this point. It is vital that if open biopsy is performed then the incision must be such as to allow subsequent complete block dissection of the regional nodes without compromise.

- All patients should have blood tests, MRI head together with CT thorax/abdomen/pelvis +/- neck if appropriate or PET scanning prior to lymphadenectomy.

6.4 Lymph Node Dissection (LND)

Radical lymph node dissections (LND) should only be performed by a designated core member of the SSMDT at the Royal Free Hospital or Royal London Hospital. Pre-operative staging investigations should be carried out as listed previously. The decision as to whether or not surgery should proceed prior to scanning should be made after SSMDT discussion with an informed patient. The block dissection specimen should be marked and orientated for the pathologist.

Axilla

It is recommended that axillary LND should include all nodes in levels I – III, and this may require either resection or division of pectoralis minor.
Inguinal
The management of inguinal lymph node metastases is controversial. A superficial inguinal lymph node dissection should be considered in the presence of:
- A single clinically involved node in the femoral triangle.
- Medical co-morbidities which would increase the risk associated with more extensive surgery.
- A positive superficial inguinal sentinel node.

A pelvic lymph node dissection of ileo-obturator nodes should be considered:
- If there is >1 clinically palpable subinguinal node.
- If there is U/S and/or CT evidence of pelvic node involvement.
- If pathological review of the superficial specimen shows multiple microscopically/macroscopically involved nodes.

Cervical
Cervical nodal disease should be reviewed and treated by either surgeons in the SSMDT with expertise in head and neck skin cancer including melanoma, or by a Head and Neck MDT with a special interest in melanoma. Some LSMDT have core members who are Head and Neck surgeons and dissections may take place locally if in the best interests of the patient and only after discussion with the SSMDT.

A comprehensive and not a selective neck dissection should be performed. The term comprehensive allows either:
- A radical dissection of levels 1-5.
- Modified radical – the above, sparing spinal accessory nerve, internal jugular vein and sternocleidomastoid muscle.
- Extended radical – Radical dissection including parotid and/or posterior occipital chain.

The risk of recurrence is high (up to 28%) despite comprehensive surgery and so surgery may be combined with adjuvant radiotherapy. This is the only nodal group shown to have improved local recurrence rate with post-operative radiotherapy (Guadagno BA et al)\(^2\). If extra-capsular spread is noted, then the management should be discussed at the SSMDT.

7. Histopathology and molecular profiling
7.1 Minimum dataset
All pathology departments should be reporting the minimum dataset as stipulated by the Royal College of Pathologists (Updated Feb 2019). Staging should be according to the 8\(^{th}\) edition AJCC staging 2018; the full text can be found on: https://www.rcpath.org/uploads/assets/uploaded/a04ea9a6-7d0a-4cfb-bb336b2ea538a215.pdf

7.2 Molecular testing
If targeted systemic therapy is a treatment option, offer BRAF testing using:
- A secondary melanoma tissue sample if there is adequate cellularity, or

\(^2\) Lancet Oncol 2009; 10: 409–16
- A primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.
- BRAF testing should be performed on all patients with stage 3 and 4 disease.

Do not offer BRAF testing of stage IA – IIB primary melanoma at presentation except as part of a clinical trial.

Consider BRAF testing of stage IIC primary melanoma who are at high risk of relapse if insufficient tissue is available from nodal deposits or in-transit metastases, consider genetic testing of the primary tumour for people with stage III melanoma.

Consider C-kit testing in mucosal and acral melanoma.

BRAF testing from the RFH is sent to Manchester (St Mary’s University) and from the RLH is done in-house

8. Vitamin D
NICE guidance recommends measurement of Vitamin D levels at diagnosis in secondary care in all people with Melanoma.

9. Imaging
Offer CT staging to people with Stage IIC melanoma who have not had SLNB and to people with Stage III, or suspected stage IV melanoma.

Include the brain as part of imaging for people with suspected stage IV melanoma – MRI is the modality of choice where possible.

Consider whole-body MRI for children and young people (birth to 24 years) with stage III or suspected stage IV melanoma

While CT imaging is considered the standard of care PET scans may be used instead depending upon availability and physician preference. PET scans may also be used if there is concern on CT imaging where the PET scan would influence clinical management and it may also be considered for occult primaries

10. Adjuvant Treatment of completely resected stage 3 melanoma
Recent trials have demonstrated significant benefits with the use of adjuvant systemic therapy in stage 3 disease establishing a new standard of care. Treatment may either be with dabrafenib and trametinib in BRAF mutant disease or immunotherapy with either pembrolizumab or nivolumab in BRAF mutant and wild-type disease and are now NICE approved. There are no randomised data directly comparing the 2 approaches in patients with BRAF mutant disease and decisions about which therapy to use should be made on an individual basis according to patient preferences, relative toxicities and co-morbidities. Trials are ongoing examining the use of combination immunotherapy in the adjuvant setting as well as in stage 2 disease but are not currently standard of care. Radiotherapy does not
have an established role in the adjuvant setting but may be considered in individual cases following discussion in MDT.

11. Management of advanced or metastatic disease
The treatment algorithms for advanced melanoma have evolved at a tremendous pace. The treatments presented below are for licensed and/or NICE approved therapies. For most patients with advanced disease immunotherapy is now established as standard of care either with combination or single agent checkpoint inhibitor therapy. Patient with a BRAF mutation have an additional line of therapy available and whether or not to treat such patients with upfront immunotherapy or BRAF inhibitors should be discussed on an individual basis according to individual patient preference, disease burden/metastatic site and disease tempo. Where possible patients should be considered for entry into clinic trials. All such patients must be discussed with the appropriate SSMDT and both SSMDTs operating in London Cancer must be fully aware of the clinical trial portfolio available within London Cancer which should include Phase I trials. Where there is a gap in the portfolio the Lead for Research should see if there are relevant trials available at other institutions in and around London.

Patients with brain metastases should where possible be considered for stereotactic treatment and discussed at the neuro-oncology MDT if appropriate.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Off study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin metastases</td>
<td>Excision</td>
</tr>
<tr>
<td></td>
<td>Isolated limb perfusion (^1)</td>
</tr>
<tr>
<td></td>
<td>Radiotherapy</td>
</tr>
<tr>
<td></td>
<td>ECT (^2)</td>
</tr>
<tr>
<td></td>
<td>(T)-VEC (Talimogene laherparepvec)</td>
</tr>
<tr>
<td>Visceral disease</td>
<td>Metastectomy for solitary disease if stable</td>
</tr>
<tr>
<td></td>
<td>Immunotherapy :</td>
</tr>
<tr>
<td></td>
<td>Ipilimumb and Nivolumab in combination</td>
</tr>
<tr>
<td></td>
<td>Pembrolizumab or Nivolumab monotherapy</td>
</tr>
<tr>
<td></td>
<td>Ipilimumab monotherapy</td>
</tr>
<tr>
<td></td>
<td>(BRAf) mutation inhibitors: in combination with MEK inhibitors :</td>
</tr>
<tr>
<td></td>
<td>Dabrafenib and trametinib</td>
</tr>
<tr>
<td></td>
<td>Encorafenib and binimetinib</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy</td>
</tr>
</tbody>
</table>
CNS disease | Metastectomy for solitary disease
| Stereotactic Radiotherapy
| Whole brain Radiotherapy

Bone metastases | Bisphosphonates
| Radiotherapy

1. Patients need to be referred to the Royal Marsden Hospital for this procedure (think this may also be done at St Georges)

2. Electro-Chemo Therapy is NICE approved (IPG446) and available at the Royal London Hospital and the Royal Free Hospital

12. Follow up management

These guidelines follow NICE’s recommendations:

Perform a full examination of the skin and regional lymph nodes at all follow-up appointments.

Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).

Provide psychosocial support for the person with melanoma and their family or carers at all follow-up appointments.

All local follow-up policies should include reinforcing advice about self-examination and health promotion for people with melanoma and their families, including sun awareness, avoiding vitamin D depletion and NICE guidance on smoking cessation.

Follow-up after stage 0 melanoma
Discharge people who have had stage 0 melanoma after completion of treatment and provide advice

Follow-up after stage IA melanoma
For people who have had stage IA melanoma, consider follow-up 2–4 times during the first year after completion of treatment and discharging them at the end of that year. Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stage IA melanoma.

Follow-up after stages IB–IIB melanoma or stage IIC melanoma (fully staged using sentinel lymph node biopsy)
For people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years. Do not routinely offer screening investigations (including imaging and
blood tests) as part of follow-up to people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy.

**Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma**

For people who have had stage IIC melanoma with no sentinel lymph node biopsy, or stage III melanoma, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years.

Consider surveillance imaging as part of follow-up for people who have had stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:
- There is a clinical trial of the value of regular imaging or
- The specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging 6-monthly for 3 years is identified.

Take into account the possible advantages and disadvantages of surveillance imaging and discuss these with the person

**Follow-up after stage IV melanoma**

Offer personalised follow-up to people who have had stage IV melanoma.

**Follow up for occult primary**

This group of patients should be followed up as per Stage III
13. Appendices

Table 1

Advantages and Disadvantages of SLNB (taken from NICE guidelines)

<table>
<thead>
<tr>
<th>Possible advantages of sentinel lymph node biopsy</th>
<th>Possible disadvantages of sentinel lymph node biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>The operation helps to find out whether the cancer has spread to the lymph nodes. It is better than ultrasound scans at finding very small cancers in the lymph nodes.</td>
<td>The purpose of the operation is not to cure the cancer. There is no good evidence that people who have the operation live longer than people who do not have it.</td>
</tr>
</tbody>
</table>
| The operation can help predict what might happen in the future. For example, in people with a primary melanoma that is between 1 and 4 mm thick:  
- around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative  
- around 3 out of 10 die within 10 years if the sentinel lymph node biopsy is positive. | The result needs to be interpreted with caution. Of every 100 people who have a negative sentinel lymph node biopsy, around 3 will subsequently develop a recurrence in the same group of lymph nodes. |
| People who have had the operation may be able to take part in clinical trials of new treatments for melanoma. These trials often cannot accept people who haven’t had this operation. | A general anaesthetic is needed for the operation. |
| | The operation results in complications in between 4 and 10 out of every 100 people who have it. |