KATARZYNA MACKENZIE

PLASTIC SURGEON

Malignant Melanoma

Malignant melanoma (MM) is less common than non-melanoma skin cancers, but it is one of the most dangerous forms of skin cancer. It can develop from existing mole, but it more often appears as a new mole on the skin. The highest reported rates of melanoma in the world are in Australia and New Zealand. In New Zealand, the most common site in men is the back (around 40% of melanomas in men), and the most common site in women is the leg (around 35% of melanomas in women).

If melanoma is recognized and treated early, it is almost always curable, but if it is not, the cancer can advance and spread to other parts of the body, where it becomes hard to treat and can be fatal.

Length of surgery	30-90 minutes
Anaesthesia	General or local anaesthetic
Hospital stay	Day case
Risks/complications of surgery	Frequent: Swelling, bruising Infrequent: Infection, unsightly scarring, bleeding (haematoma), wound healing problems, permanent numbness, incomplete excision, flap/graft loss
Recovery	5 days facial sutures removed 2 weeks body sutures removed 2-4 weeks until swelling disappears 2-4 weeks until return to gym and other strenuous activities 12 weeks until final result – scars continue to improve over the next 12 months
Driving	1-7 days
Follow up	2 weeks, 6 weeks, 3 months
Duration of results	Permanent unless recurrence

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What is malignant melanoma?

Melanoma is a malignant tumour of melanocytes. Melanocytes are cells that produce the dark pigment, melanin, which is responsible for the color of skin. Melanoma is described as:

- In situ, if the tumour is confined to the epidermis
- Invasive, if the tumour has spread into the dermis
- Metastatic, if the tumour has spread to other tissues

What are the risk factors for malignant melanoma?

The main risks factors for developing MM are:

- Cumulative sun exposure
- Older age
- Previous invasive MM
- Previous non-melanoma skin cancer (BCC, SCC)
- Many melanocytic naevi (moles)
- Multiple (>5) atypical naevi
- Strong family history of melanoma with 2 or more first-degree relatives affected
- Tanning beds
- Genetic risk factors-BRAF and p53 mutation

Who is more likely to develop MM?

The following groups of people are at greater risk of developing the MM:

- Immunosuppressed patients
- Organ transplant patients
- People who have had significant cumulative ultraviolet light exposure
- People susceptible to sunburn
- Family history of MM
- Familial Atypical Multiple Mole Melanoma Syndrome
- People with many (more than 50) ordinary moles

What are the clinical features of MM?

MM can vary in the appearance, but most usually it appears as:

- Unusual looking freckle or mole
- Variety of colours, including no pigment
- Can be flat or raised
- Can be itchy or tender
- New mole or an existing one that is growing, changing colour (either becoming lighter or darker) or becoming irregular in some way

Most melanomas have characteristics described by the Glasgow 7-point checklist or by the ABCDE's of melanoma. Not all lesions with these characteristics are malignant. Not all melanomas show these characteristics. People should be referred if they have a suspicious pigmented skin lesion with a weighted 7-point checklist score of 3 or more.

Weighted Glasgow 7-point checklist:

Major features of the lesions (scoring 2 points each):

- Change in size
- Irregular shape
- Irregular colour

Minor features of the lesions (scoring 1 point each):

- Largest diameter 7 mm or more
- Inflammation
- Oozing
- Change in sensation

Some physicians also use the ABCDE guide which is also be helpful for patients when teaching them in self-examination.

ABCDE guide:

- Asymmetry
- Border irregularity
- Colour variation
- Diameter over 6mm
- Evolving (enlarging/changing)

When should the patient be referred to a specialist?

Dr Mackenzie would recommend referring any patient for which the following are present:

- Recent history of change (although this can sometimes be over months)
- Score of 3 or more on the Glasgow 7 point checklist
- Signs that fit with the ABCDE rule
- High risk factors such as atypical mole syndrome (AMS) or family history of melanoma
- Examination – 'ugly duckling sign' (pigmented moles that look different from patient's other moles) or dermoscopic changes
- Can't exclude melanoma

What are the subtypes of MM?

Melanomas are described according to their appearance and behavior. The subtypes include:

Superficial spreading melanoma

- Most common type of melanoma
- Occurs at sites of intermittent, intense sun exposure, especially on the trunk in males (40%) and the legs in females (also 40%)
- Slow growing and flat
- Usually>0.5cm
- Variegated colour pattern–blue, black, brown, pink
- Irregular shape
- Palpable +/- nodules

Lentigo maligna melanoma

- Arise in Hutchison's Melanotic Freckle
- Early form of melanoma
- Usually face or UV exposed skin
- >60years
- Flat macule, irregular outline
- Irregular pigment, brown, black, loss of pigment
- Can be very large

Acral lentiginous melanoma

- Soles, palms, nailbed
- High incidence in dark skinned people

- Starts as a slowly-enlarging flat patch of discoloured skin
- Brown – black stain, amelanotic, ulceration
- Late diagnosis – poor prognosis

Nodular melanoma

- 15% of melanomas
- Palpable nodule
- Ulceration
- Uniform colour – blue, grey, black, pink, amelanotic
- Worse prognosis

Desmoplastic/neurotropic melanoma

- Fibrous MM with tendency to grow down nerves
- 1% of melanoma in Australia and New Zealand
- Presents as a slowly growing lump within the skin
- Usually lacks the ABCD melanoma warning signs
- More locally aggressive with an increased tendency for local recurrence but less likely for nodal or distant metastases

What is Breslow thickness?

The Breslow thickness is reported for invasive melanomas. It is measured vertically in millimetres from base of superficial ulceration to the deepest point of tumour involvement. It is a strong predictor of outcome; the thicker the melanoma, the more likely it is to spread.

What is staging of MM?

Melanoma staging means finding out if the melanoma has spread from its original site in the skin. Most melanoma specialists refer to the American Joint Committee on Cancer (AJCC) cutaneous melanoma staging guidelines (2009). In essence, the stages are:

Stage 0-in situ melanoma
Stage 1-thin melanoma<2mm in thickness
Stage 2- thick melanoma > 2 mm in thickness
Stage 3- melanoma spread to involve local lymph nodes
Stage 4- distant metastases have been detected

How is MM diagnosed?

- History
- Examination
  - ABCDE
  - Dermoscopy
- Biopsy
  - Dependent on size of lesion and patient
  - Excisional biopsy, 2mm margin
- Patient counselling
- Imaging maybe considered
- SLNB maybe considered

Diagnosis of MM is based on clinical features. Any changes to the skin can be a concern, but growing size, changing shape, developing new colours, bleeding, pain, crusting, red around the edges or itching. The ABCDE system tells you some of the things to lookout for (see above).

To confirm the diagnosis, a small piece of the abnormal skin (a biopsy), or the whole area (an excision biopsy), is removed under a local anaesthetic and sent to a pathologist to be examined.

Following confirmation of the diagnosis, wide local excision is carried out at the site of the primary melanoma. The extent of surgery depends on the thickness of the melanoma and its site.

REMEMBER - IF IN DOUBT, CHECK IT OUT!

How can MM be treated?

Three quarters of the people who have a melanoma removed will have no further problems. However, the larger and deeper a tumor grows, the more dangerous and potentially disfiguring it may become, and the more extensive the treatment must be. The thinner the melanoma is when it is removed; the better is the survival rate. In a small minority of people, the melanoma may have spread but further surgery or chemotherapy can often help to control this.

Surgery

Surgery is usually the recommended treatment. This involves removing the suspicious mole with a 2mm margin of normal skin around it, using a local anaesthetic. The skin is then closed Once the Breslow thickness is determined a wide local excision is usually undertaken. The width of excision size is determined by the depth and stage of the melanoma. It is important this is performed by a team experienced in melanoma excision that is part of the skin cancer Multi-Disciplinary Team (MDT) team.

Dependent on stage, a patient may also be offered a Sentinel Lymph Node Biopsy (SLNB) to check if the cancer has spread to local nodes. This is carried out under general anaesthetic at the same time as the wider excision. A positive result means that cancer has started to spread. In New Zealand, many surgeons recommend sentinel lymph node biopsy for melanomas thicker than 1 mm, especially in younger persons. However, although the biopsy may help in staging the cancer, it does not offer any survival advantage. The necessity for sentinel node biopsy is controversial at present.

Radiotherapy

Radiotherapy is not commonly used to treat melanoma which generally is not radiosensitive but there are some instances when it can be useful; including treatment of brain metastases and bony metastases. It is generally only used for advanced disease. Radiotherapy does have side effects, and these vary depending on the site of the treatment. Patients may experience reddening of the skin or feel sore and fatigued during the treatment period but this usually starts to disappear within a fortnight of treatment ending.

Chemotherapy

Chemotherapy for melanoma is rarely curative and aims instead to control symptoms in cases of advanced melanoma. The most common chemotherapy drug used to treat melanoma is dacarbazine (DTIC).

Isolated limb perfusion

Isolated limb perfusion (ILP) is a specialized surgical technique for the treatment of cancers in limbs, commonly melanomas and sarcomas. Melanoma can spread with multiple outbursts of tumour progressing gradually higher up the limb before progressing to the lymph nodes.

ILP delivers high doses of a combination of anti-cancer drugs directly to a limb at concentrations too high for the vital organs to tolerate. To prevent organ damage, the limb's blood supply is isolated from the rest of the body during the operation via a tourniquet. The limb is connected by the main artery and vein to a cardiac bypass machine to oxygenate the blood while the chemotherapy is delivered, together with a protein called Tumour Necrosis Factor which interacts with both the drugs and the cancer cells to make the treatment more effective. This combination circulates through the limb for an hour, before the drugs are washed out and the limb is reconnected to the normal circulation.

This can be curative in some cases but usually offers extension of life and improved quality of life by avoiding amputation.

Immunotherapy

Immunotherapy is an emerging treatment that harnesses the body's immune response to target and destroy cancer cells. Using synthetic, mass-produced versions of natural immune system proteins, or by inhibiting receptors that block the immune system, immunotherapies boost the body's ability to fight disease. New agents are adding years to many patients' lives. Some of the immunotherapy drugs include Ipilimumab, Pembrolizumab, Nivolumab, Interleukin -2.

Targeted therapy

Targeted therapies, among the most revolutionary treatments for advanced melanoma, use drugs or other substances to identify and attack specific types of cancer cells, or to block the action of certain genes, enzymes, proteins or other molecules that promote the growth and spread of cancer cells. This allows the cancerous cells to be treated without killing healthy cells. The most common drugs include Vemurafenib, Dabrafenib, Trametinib, Cobimetinib.

What is involved in the operation?

Usually this surgery is carried out under local anaesthesia or under general anaesthesia if it is more extensive or in a difficult location. The procedure can take between 30 and 90 minutes depending on the extent of surgery.

The skin lesion is removed as an excisional biopsy with a 2mm margin. The lesion will be sent away to be examined by pathologist.

The skin is usually stitch together directly a skin graft is required to reconstruct the defect. The skin graft is then stitched into its new position. Where it is taken from (the donor site) is either stitched together or allowed to heal from the remaining bottom layer of skin depending which type of skin graft is used. Once the Breslow thickness is determined by a pathologist a wide local excision is usually undertaken. The width of excision size will be determined by the depth and stage of the melanoma.

Dr Mackenzie will apply a dressing to the operation site, which will need to be left in place for a few days. You will be given additional dressings as required, and any appropriate post-operative medication will be prescribed.

What can you expect after the operation?

As the local anaesthetic wears off, the operation site may feel sore. Painkillers such as paracetamol will help.

You should take it easy for the first few days and take special care not to bump or knock the operation site. If you have had a lesion removed from your face, it may be helpful to sleep using some extra pillows as this will help to reduce swelling and bruising. If the skin lesion was on your arm or leg, it is best to try to elevate the limb as much as possible for the first few days.

You should not apply make-up to the operation site until you have had your stitches removed.

You need to keep the wounds dry for 48 hours. You can shower then and gently dab the wounds dry. You may use a hairdryer on a cool setting to speed up drying. In the face, stitches will need to be removed between 5 and 7 days following surgery. When possible elsewhere on the body, Dr Mackenzie uses absorbable sutures, which do not need to be removed. If she has to use non-absorbable sutures, they will need to be removed between 10 and 14 days following surgery. It is usual to have some swelling and bruising in the area in the early stages.

A skin graft will usually be left undisturbed for 5 to 7 days and will have a dressing on it that will need to be kept clean and dry until then. If you had a split thickness skin graft, a well-padded dressing will be placed on the donor site as this may ooze for a few days. Unless problematic, this dressing should be left undisturbed until your follow up appointment.

It is usually possible to return to light activities the next day but strenuous activities will need to be avoided for about 2-4 weeks.

The area is usually healed in 2 to 3 weeks but the scar will continue to strengthen and then to soften and fade for 12 to 18 months afterwards.

Once the Breslow thickness is determined by a pathologist a wide local excision is usually undertaken. The width of excision size will be determined by the depth and stage of the melanoma:

- When there is an in situ melanoma, Dr Mackenzie excises 0.5-1 centimeter of the normal skin surrounding the tumor and takes off the skin layers down to the fat
- In removing an invasive melanoma that is 1 mm or less in Breslow's thickness, the margins of surrounding skin are extended to 1 cm and the excision goes through all skin layers and down to the fascia (the layer of tissue covering the muscles)
- If the melanoma is 1.01 to 2 mm thick, a margin of 1 to 2 cm is taken
- If the melanoma is 2.01 mm thick or greater, a margin of 2 cm is taken

These margins all fall within the range of what is called "narrow" excision. When you consider that until recently, margins of 3 to 5 cm (wide excision) were standard, even for comparatively thin tumors, you can see how dramatically surgery has changed for the better. Physicians now know that even when melanomas have reached a thickness of 4 mm or more, increasing the margins beyond 2 cm does not increase survival.

What is the follow up for MM?

Follow-up appointments are vital to detect recurrence or spread of melanoma as early as possible, but it also offers an opportunity to diagnose a new primary melanoma. A second invasive melanoma occurs in 5–10% of melanoma patients, and a new melanoma in situ is diagnosed in more than 20% of melanoma patients.

The frequency and longevity of follow-up appointments varies according to the stage of melanoma. Early stage melanomas may only require a year's follow-up but later stage cancers may require follow-up for up to five years. Follow-up intervals are preferably six-monthly for five years for patients with stage 1 disease, three-monthly or four-monthly for five years for patients with stage 2 or 3 disease, and yearly thereafter for all patients.

Follow-up appointments may include:

- A check of the scar where the primary melanoma was removed
- A feel for the regional lymph nodes
- A general skin examination
- A full physical examination
- In those with many moles or atypical moles, baseline whole body imaging and sequential macro and dermatoscopic images of melanocytic lesions of concern

Regular imaging scans may also be required to detect spread of the melanoma in more advanced patients so that treatments can be started early.

Tests are not worthwhile for patients with stage 1 or 2 melanoma unless there are signs or symptoms of disease recurrence or metastasis. No tests are necessary for healthy patients who have remained well for 5 years or longer after removal of their melanoma.

Patients are taught what signs and symptoms to look out for and it is vital that they return to their specialist if they experience:

- Skin changes or changes to a mole
- Swollen or painful lymph nodes
- Persistent bone pain
- Frequent headaches
- General symptoms of feeling unwell such as fatigue, unexplained weight loss or loss of appetite

What are the complications of skin cancer surgery?

In general, this operation is safe. Nevertheless, no surgery is without risk
All general anaesthetics carry risks such as deep vein thrombosis and chest infection but with modern anaesthetic techniques, these are minimised. The most common complications include:

- Bleeding- holding firm pressure for 10 to 15 minutes with a clean towel or tissue is usually sufficient to stop this. If this is more than expected, please contact the hospital or clinic so that you can be advised or assessed
- Delayed wound healing
- Infection-if inflamed or ulcerated, Dr Mackenzie will prescribe antibiotics
- Poor scaring- they may be red or raised or lumpy or stretched than expected and further treatments will be recommended
- Partial or complete loss of a skin graft or skin flap- if part or all of the transferred tissue is lost, it may mean a longer time with dressings on the wound or occasionally further surgery to remedy the problem and heal the wound quicker
- Incomplete excision-we can see the cancer cells with a bare eye. Sometimes microscopically there are some cancer cells at the edge of the skin cancer excised. Dr Mackenzie will normally recommend a further procedure in this instance to completely treat the skin cancer and reduce the risk of it recurring

What is the outlook for patients with melanoma?

Melanoma in situ is cured by excision because it has no potential to spread round the body.

The risk of spread and ultimate death from invasive melanoma depends on several factors, but the main one is the Breslow thickness of the melanoma.

Metastases are rare for melanomas < 0.75 mm and the risk for tumours 0.75–1 mm thick is about 5%. The risk steadily increases with thickness so that melanomas > 4 mm have a risk of metastasis of about 40%.

How can MM be prevented?

Sun protection and being sun-smart reduces the risk of MM and is especially vital for high risk patients. The following preventative measures will help to reduce the risk of MM:

- Always wear sunscreen- at least SPF30+, should be broad spectrum (blocking both UVA and UVB radiation). Should be applied 15-30 minutes before going outside and then again

immediately before going outside. Sunscreen needs to be reapplied regularly during the day (2-hourly in sunny weather, otherwise 3 to 4-hourly)

- Daily application to the face and hands regardless of your intended activities should be considered
- Avoid sun exposure-remain indoors or in shade during the middle of the day, between 11 am and 4 pm, when UV radiation levels are at their highest
- Cover up well- protect your skin with clothing, and don't forget to wear a hat that protects the face, neck and ears, and sunglasses
- Sunbeds and sunlamps should be avoided
- Don't get sunburn
- Keep newborns out of the sun
- Regularly checking your skin for signs of skin cancer can help lead to an early diagnosis and increase your chances of successful treatment
- It's also important to be aware that if you've had a non-melanoma skin cancer, your risk of developing another one in the future is increased therefore regular skin check-ups are recommended