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Overview

Current Concepts in the Surgical Management of Non-melanoma Skin Cancers

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Abstract

The surgical management of non-melanoma skin cancers has seen some significant changes over the past 20 years, as a result of developments in three equally important and overlapping specialties that deal with this specific pathology: plastic and reconstructive surgery, surgical oncology and dermatological surgery. Better understanding of vascular and particularly microvascular anatomy, coupled with technological advances in operating microscopes, microsurgical instrumentation and preoperative planning via advanced imaging, allows functional and aesthetic restoration of any radical oncological skin and soft-tissue surgery defect from head to toe. As reconstruction has practically lost its technical boundaries, resectional surgery can be executed without compromising on surgical margins, thus reducing rates of local recurrences and metastatic spread. The increasing use of Mohs surgery and its several advantages for difficult high-risk non-melanoma skin cancer in facial sites especially, offers optimal cure rates while reducing functional impairment and optimising cosmetic outcomes. Advances in preoperative planning utilising computed tomography and magnetic resonance imaging scans can help to predict the degree of resectability and tailor further treatments, including radiotherapy, accordingly. From the reconstructive point of view, these techniques provide a roadmap to select the best blood supply for the transplanted flap, thereby reducing complications and increasing success rates. The focus of skin cancer surgery has therefore shifted from pure cancer clearance and flap survival, to a high degree of functional and aesthetic reconstruction.

Key words: Mohs; reconstruction; skin cancer surgery

Introduction

Non-melanoma skin cancer (NMSC) is the most common cancer among Caucasian populations. Its incidence is increasing worldwide [1,2]. In 2015, over 142 101 cases of NMSC were newly diagnosed in the UK, which represents a significant underestimate due to incomplete recording by cancer registries [2,3]. Skin cancer in the UK is projected to cost the National Health Service over £180 million by 2020 [4] and imposes significant demands on primary and secondary care services [5].

About 74% of NMSC are represented by basal cell carcinoma (BCC) and 23% by cutaneous squamous cell carcinoma (cSCC), with other rarer tumours making up the rest [3]. Risk factors include fair skin type (Fitzpatrick skin types I and II), ultraviolet radiation exposure, genetic susceptibility, older age, male gender, prior history of skin cancer and immunosuppression [6,7]. Over 80% of NMSC occur on sun-exposed sites, predominantly on the head and neck, and are associated with significant morbidity. Lesions insidiously invade surrounding tissue, causing local tissue destruction, functional impairment and cosmetic disfigurement [8,9]. Most NMSC are treated surgically, at times requiring complex reconstructive efforts.

Management of Non-melanoma Skin Cancer

There are several approaches to the management of NMSC. The primary goal of treatment is complete tumour eradication with maximal preservation of normal function

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and cosmesis. In clinical practice, the choice of management is dependent on the risk stratification of the tumour, patient preference and suitability, and availability of local services [10,11]. The features of high-risk NMSC are summarised in Table 1. The eighth edition of Tumour, Node and Metastasis has been implemented in the UK for skin cancer staging since January 2018 [12–14].

The British Association of Dermatologists has published multidisciplinary guidelines for the management of BCC and cSCC [15,16]. Surgery is the mainstay of treatment. Other treatments can be broadly categorised into physical destruction, chemical destruction, immunomodulation and systemic therapies. The value of multidisciplinary working relationships in the management of high-risk NMSC is very important.

Surgical excision is the treatment of choice for NMSC, with superior cure rates compared with all non-surgical treatment options [15–18]. The concept of margins is central in the surgical treatment of cutaneous tumour. In patients who are not candidates for surgery due to patient choice, significant comorbidities, and/or those with widespread metastasis, non-surgical treatment options can be considered.

Standard Resectional Surgery

NMSC resectional surgery, as with any other oncological surgical field, aims to achieve tumour-free margins that would reduce the chances of local recurrence and potential metastatic spread. In patients where regional lymph nodes are already affected by the disease, surgery will include removal of diseased lymphatic basin via axillary, inguinal or neck lymphadenectomies, more commonly known as dissections. These are usually extensive resections carried out under general anaesthesia by specially trained plastic and reconstructive surgeons or surgical oncology specialists. The adequacy of margins is dictated by the original pathology and can vary from a few millimetres for low-risk BCC to 3 cm for Merkel cell carcinoma (MCC). For difficult, usually facial, NMSCs, particularly BCC and cSCC with certain features and characteristics (see Table 1), Mohs surgery may offer optimal treatment with the highest cure rates. The technique enables precise mapping and tracking of such tumours and can enable the preservation of tissue in certain anatomically and functionally sensitive areas (periorbital, perinasal, peri-oral and peri-auricular). The adequacy of margins remains a controversial topic in NMSC surgery. Despite a large number of papers published on this subject, there is no universal consensus in terms of the adequacy of margins, particularly for high-risk tumours such as MCC and dermatofibrosarcoma protuberans [18]. One of the recent studies on 1296 cSCC excised from the skin [19] found no local recurrence if the margin was 3.5 mm or greater, but a significantly higher recurrence rate (6%) in poorly differentiated tumours removed with more narrow margins (1.3 mm). This highlights the importance of re-excision or additional postoperative radiotherapy in patients where wider or deeper re-excision is not feasible due to anatomical constraints or comorbidities. From the practical point of view, one should also consider the difference between the measured surgical margin before excision and the one measured by pathologist after excision, which is always smaller, due to a degree of skin retraction. Most studies agree that most recurrences appear within the first 2 years from the completion of surgical treatment [20]. As a result, skin cancer guidelines generally recommend tight 3-monthly follow-up in the first few years after initial surgery.

Basal Cell Carcinoma

Standard recommended margins for BCC are 4–5 mm for primary relatively low-risk lesions and 6 mm or more for

Table 1
Features of high-risk basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC)

Feature	High-risk BCC	High-risk cSCC
Sites	Nose and paranasal folds Periocular Ears Scalp and temples Lips	Lip, ears, non-sun-exposed sites, e.g. penis, scrotum and soles of feet In areas of previous injury, e.g. burns, irradiation, scar and chronic ulcers
Histological subtype	Morphoeic – linear groups of cancer cells with surrounding scarring Infiltrative – like morphoeic but with less scarring Micronodular – very small groups of cancer cells Basosquamous carcinoma – with both basal and squamous elements	Moderate or poor differentiation
Histological features	Perineural invasion Invasion below dermis – lymphovascular invasion	Perineural invasion Depth greater than 4 mm or extending to subcutaneous tissue (Clark level 5)
Tumour size	Greater than 2 cm	Greater than 2 cm
Other factors	Immunosuppression Previously treated lesion Genetic disorders such as Gorlin's syndrome	Immunosuppression Previously treated lesion

recurrent or ill-defined lesions [15,17,18]. Features of high-risk BCC have been summarised in Table 1.

High-risk BCC managed by standard resection may require staged resection and delayed reconstruction after fast paraffin turnover for results or are more ideally cleared using Mohs surgery (see below), enabling definitive histologically-confirmed tumour clearance before reconstructive surgery [21]. The decision on whether surgery is carried out under local or general anaesthesia depends on the size of the tumour, the depth of invasion, the specific anatomical location as well as the complexity of reconstruction and patient choice. Smaller lesions, in most instances, can be removed under local anaesthesia as day case procedures. However, larger ones with deep-tissue invasion will probably require general anaesthesia.

Squamous Cell Carcinoma

The recommended margin for resection of SCC is 6 mm for high-risk lesions, although in well-defined, low-risk tumours, a 4 mm margin will achieve histological clearance in over 95% of cases [16–18]. The features of high-risk cSCC have been summarised in Table 1.

When there is a suspicion of perineural or bony invasion or nodal metastases, imaging (magnetic resonance imaging or computed tomography) should be carried out as a part of staging. In patients with clinically involved nodes, fine needle aspiration should be carried out, with or without ultrasound guidance, to confirm or exclude regional metastasis. Once regional metastatic disease is established, a positron emission tomography-computed tomography scan is carried out to rule out distant metastasis, before a final decision on treatment is made. In high-risk head and neck cSCC, due to patterns of lymphatic drainage, parotid lymph nodes and subsequently parotid glands are often the site of metastases that require surgical ± radiotherapy treatment (Figure 1a). Although the overall metastatic rate for all skin cSCC is only 5%, high-risk lesions exhibit much higher rates of regional metastases. For example, tumours with reported perineural invasion can spread to regional lymph node basins in as many as 47% of patients [22]. The extent of surgery is dictated by the size and the location of the primary tumour, involvement of the regional nodal

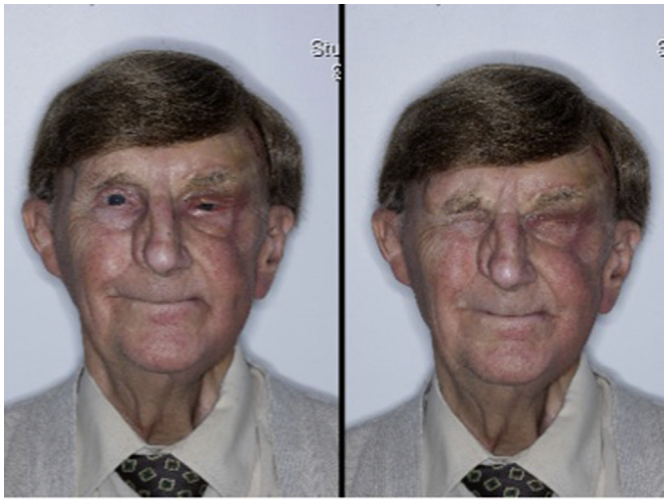

Fig 2. Complete functional facial nerve recovery 9 months after surgery and postoperative radiotherapy despite advanced age.

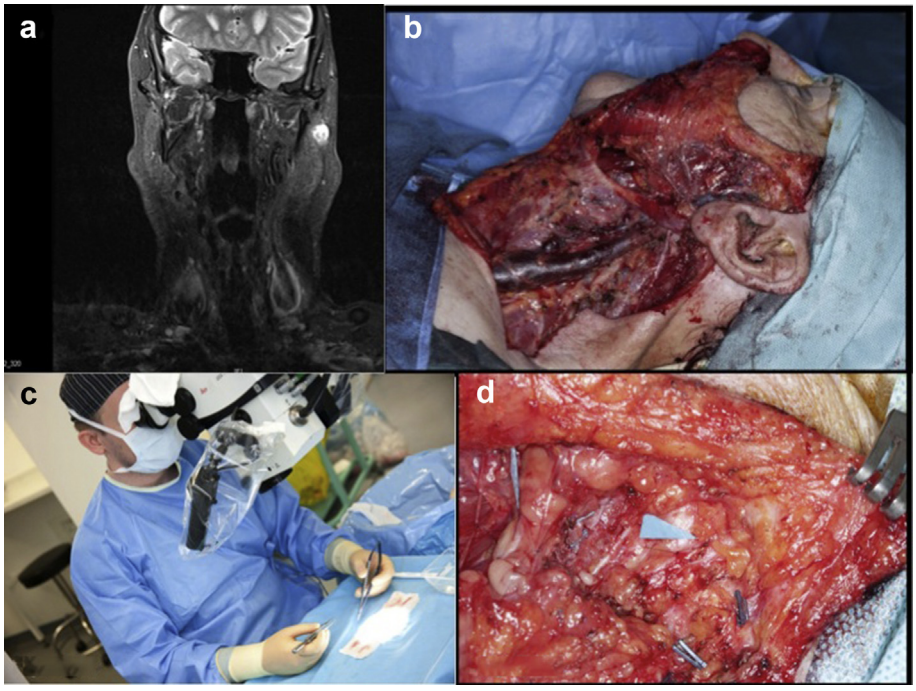

Fig 1. (a) Cutaneous squamous cell carcinoma (cSCC) metastases into the parotid gland; (b) total parotidectomy and radical neck dissection for metastatic cSCC; (c) use of high-power operating microscope to prepare nerve grafts for micronerve grafting of facial nerve defects; (d) grafts sutured between two ends of resected facial nerve branches using microsurgical techniques.

basin and surrounding structures. As most advanced primary cSCC are located in the head and neck area and many involve the parotid, superficial or total parotidectomy with (sometimes) sacrifice of the facial nerve may be required in conjunction with neck dissection (Figure 1b). This leads to significant morbidity for the patient, as subsequent facial palsy interferes with eye closure, brow movement, speech and impairs social interactions. However, modern reconstructive surgery using microsurgical nerve reconstruction (Figure 1c,d) can successfully restore both function and cosmesis, even in elderly patients (Figure 2a,b). Studies have shown improved survival rates and regional control in patients with nodal disease with extracapsular spread (which is found in up to 70% of patients after lymph node dissection for metastatic cSCC) when postoperative radiotherapy is carried out after radical surgery [23].

Merkel Cell Carcinoma

MCC is, unlike BCC and SCC, fairly rare and therefore best treated at tertiary cancer centres within a multidisciplinary team environment. Similar to cSCC, surgery is the mainstay of treatment. A wide margin local excision in three dimensions (as per often significant vertical growth), with sentinel lymph node (SLN) biopsy, is the recommended treatment of choice. Recommended margins for primary MCC lesions are at least 3 cm. However, due to the fact that 50% of these tumours are found in the head and neck area, the site would often not allow such a wide margin. In these situations, a 1 cm margin with postoperative radiotherapy to the primary site after flap reconstruction is an alternative option. Achieving adequate negative margins is associated with significantly

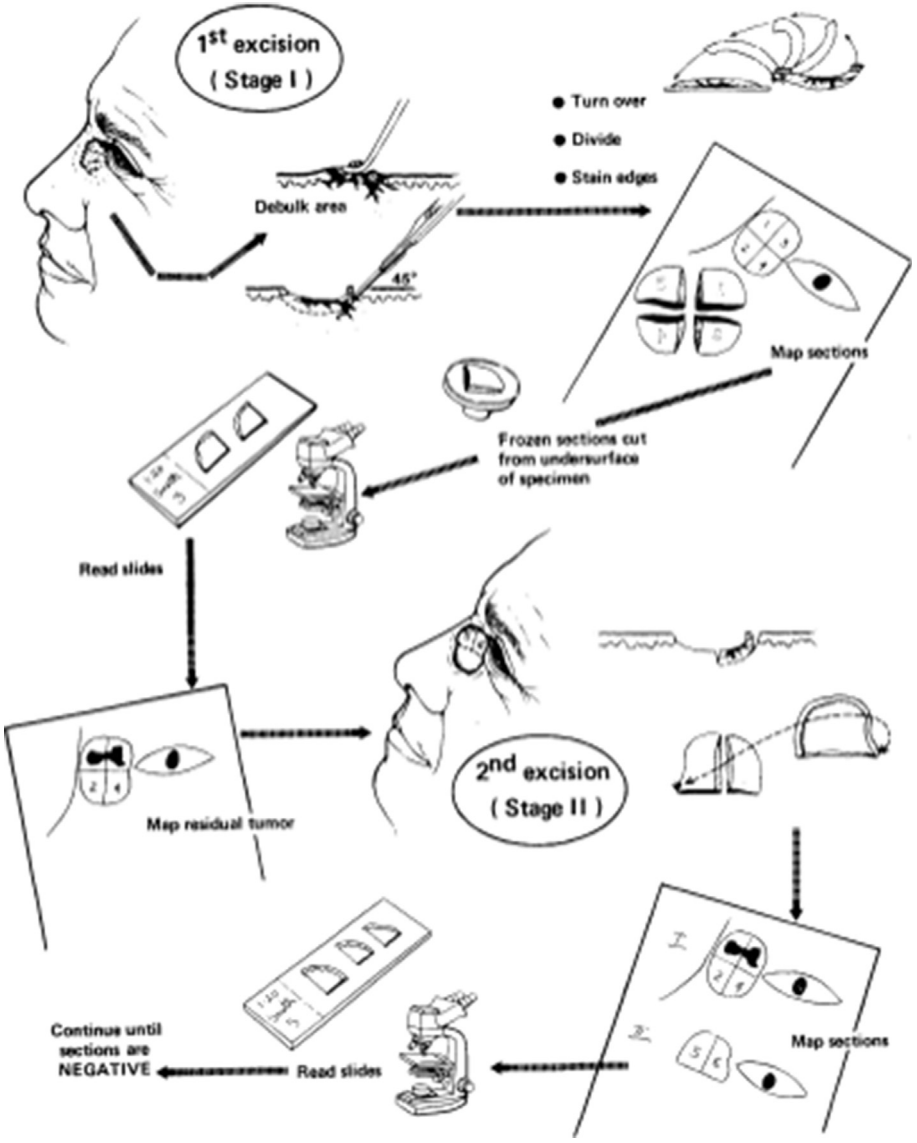

Fig 3. Illustration of the Mohs surgery technique. (Taken from Swanson NA, Grekin RC, Baker SR. 'Mohs surgery: techniques, indications, and applications in head and neck surgery', Head Neck Surg. 1983 Nov-Dec;6(2):683-92.)

improved overall survival and disease-free survival [24]. If the SLN biopsy is positive, a lymph node dissection of the affected regional basin should be carried out, unless the patient is unfit for general anaesthesia; then regional radiotherapy can be given. Adjuvant radiotherapy is frequently used after surgery, particularly for large MCC. For small MCC following Mohs surgery, there is a small but statistically insignificant difference after clear margins are achieved [25]. Postoperative radiotherapy is usually well tolerated and effective to minimise recurrence. As occult micro-metastases occur in over 30% of patients with the clinically negative lymph node basin, a SLN biopsy is the mainstay procedure carried out to correctly stage the disease and proceed with regional treatment, either lymph node dissection or radiotherapy, depending on the patient's medical status or fitness for major surgery. MCC is also known for local recurrences and studies have shown improved outcomes in patients who underwent radiotherapy after radical surgery to both the primary site and the regional nodal basin [26]. The accuracy of the SLN biopsy in MCC depends on the localisation of the primary site. The lowest is in the head and neck area, where literature reports almost 7% of non-localisations of SLN [27] as well as a similar percentage of primary lesions draining into the contralateral neck (crossover) [28]. This is followed by the trunk and limbs. Due to the requirement for wide margins and subsequent reconstruction, most MCC surgeries are carried out under general anaesthesia by plastic and reconstructive surgeons. In certain areas of the head and neck, there may be a role for Mohs surgery for resectional stage, followed by reconstruction.

Mohs Micrographic Surgery

Mohs micrographic surgery was developed by Frederic Mohs in the 1930s [29]. It is a highly precise technique that combines staged resection of the tumour with a comprehensive histological examination of the entire surgical margin (peripheral and deep), thus allowing maximal preservation of normal skin and tissue [15], with, simultaneously, the most optimal tumour clearance rates.

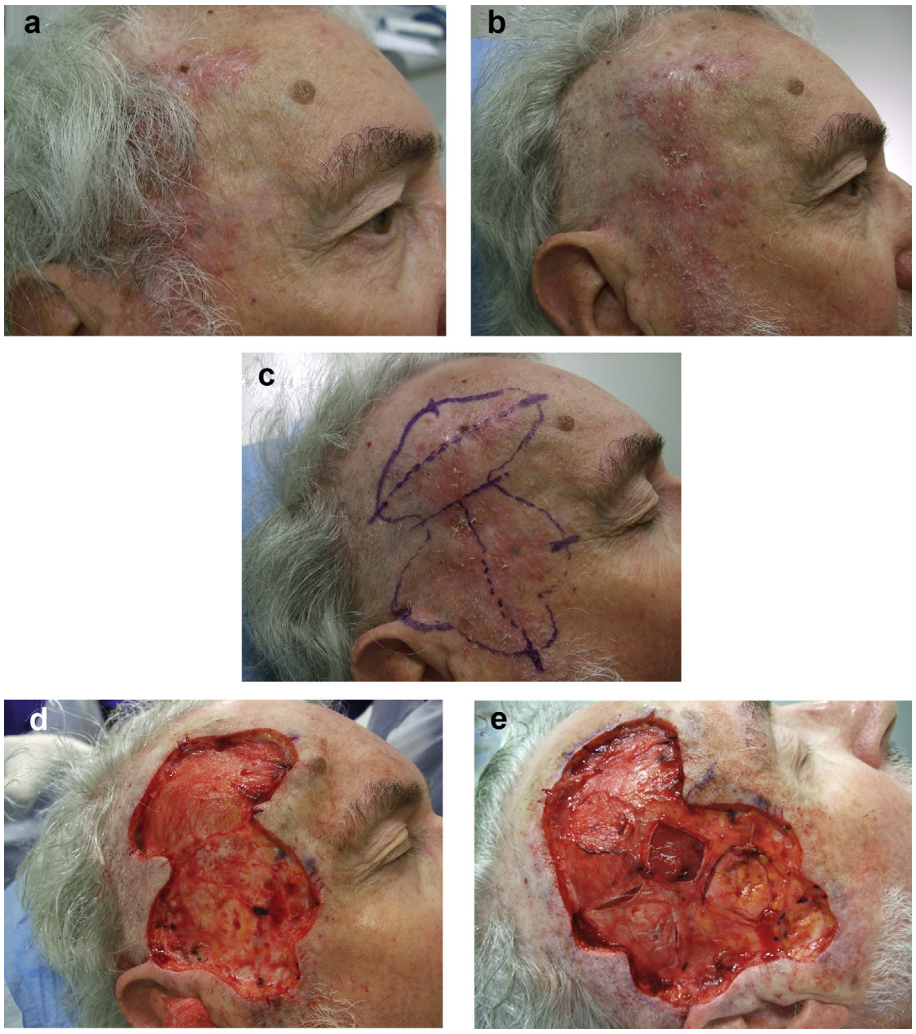

Fig 4. 71 year-old male patient with extensive recurrent BCC right temple after failed photodynamic therapy and standard excision over 10 years earlier. Images before, during and after complete resection with 2 layers of Mohs surgery.

The Technique

Mohs surgery takes place in a day case/outpatient setting under local anaesthesia. The tumour is marked and the area infiltrated with local anaesthetic (e.g. 1% lignocaine with 1:80–100 000 adrenaline). Adjunctive use of 0.25% bupivacaine helps to prolong the duration of the anaesthesia for 4–6 hours [30]. The tumour is first de-bulked, often with a Volkmann spoon/curette. A saucer-shaped 'layer' of tissue, peripheral and deep to the de-bulked tumour, is then removed with a clinically narrow margin (typically 2–3 mm). Nicks are made on the tissue to maintain its orientation, and subsequently inked with coloured dyes to enable precise mapping of the tumour. The entire cut surface of the specimen is then flattened, frozen in a cryostat and sectioned horizontally. This method enables 100% visualisation of the peripheral and deep margin in a single section, which is then examined microscopically by the Mohs surgeon in real-time (the processing of layers typically taking 30–60 minutes). Any residual tumour is mapped and further layers are taken using the same process. The process is repeated until all margins are free of tumour (see Figures 4 and 5). Once complete clearance is achieved, the defect can be repaired by various methods, including secondary intention ('natural') healing, direct closure, local skin flap or skin graft. Most defects are reconstructed by the Mohs surgeon immediately after tumour clearance. Complex, large or deep defects, such as those involving bone, or defects in particular sites, such as around or involving the eyelid margin, may require a separate reconstructing surgeon for repair under sedation or general anaesthesia as in Figure 4. Mohs surgeons regularly work with oculo-plastics, ear, nose and throat, plastic and maxillofacial surgeons as part of multidisciplinary teams to deliver the best patient outcomes. An overview of the Mohs procedure is shown in Figure 3 [31,32].

Mohs surgery is primarily recommended for the management of high-risk NMSC, as summarised in Table 1. Tumours in high-risk facial sites, such as the central face, those of aggressive histological subtypes, such as infiltrative and micronodular BCC or those displaying perivascular and perineural invasion (PVI), and larger tumours, may extend significantly more extensively and deeply than clinically anticipated. Mohs surgery enables the full extent of the tumour to be revealed before a more complex reconstruction, e.g. flap repair. Equally, in cosmetically sensitive facial areas, such as around the eyes, ears, nose and lips, Mohs surgery may enable tumour clearance with smaller, more conservative margins and thus a more optimal reconstruction with better cosmetic and functional outcomes.

In addition to BCC and cSCC, Mohs surgery can also be used to treat other rarer skin cancers, including dermatofibrosarcoma protuberans, microcystic adnexal carcinoma and lentigo maligna [33,34]. Dermatofibrosarcoma protuberans is a locally invasive, soft-tissue sarcoma that usually presents as a nodular lesion on the trunk or extremities that can invade widely and deeply. Lentigo maligna (melanoma *in situ*) occurs usually on the head and neck or upper arms of elderly patients. The atypical melanocytes of lentigo maligna can spread significantly beyond the clinical markers of the tumour and be difficult to identify in fresh-frozen tissue. 'Slow' Mohs surgery may therefore be undertaken, where the technique of Mohs surgery remains the same with horizontal sectioning, but tissue is fixed in paraffin and stages taken typically every 48 hours to allow

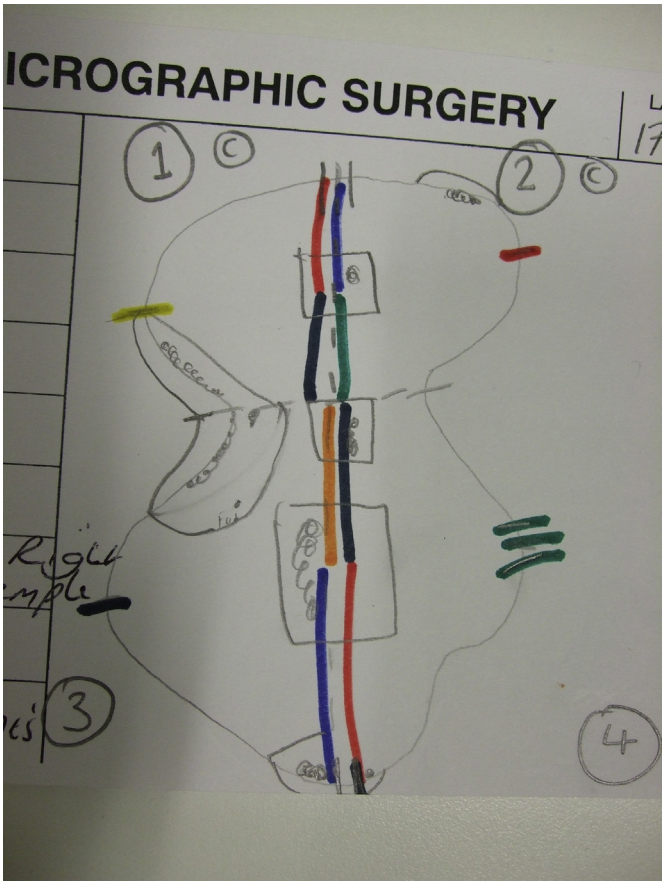

Fig 5. Corresponding Mohs surgery map.

Table 2
Indications for Mohs micrographic surgery [15,42]

Tumour size > 2 cm in diameter
Tumour located in areas where the risk of local recurrence is high (i.e. high-risk sites, especially central face, around the eyes, nose, lips and ears)
Tumour located in areas where tissue preservation is important for maintenance of function and physical appearance
Tumours with aggressive histological subtypes (micronodular, infiltrative and morphoeic basal cell carcinoma, basosquamous carcinoma and poorly differentiated squamous cell carcinoma)
Tumour with indistinct clinical margins
Recurrent or incompletely excised tumour
Tumour with perineural or perivascular involvement
Tumour in immunocompromised patients
Tumour arising in irradiated skin or in chronic scar

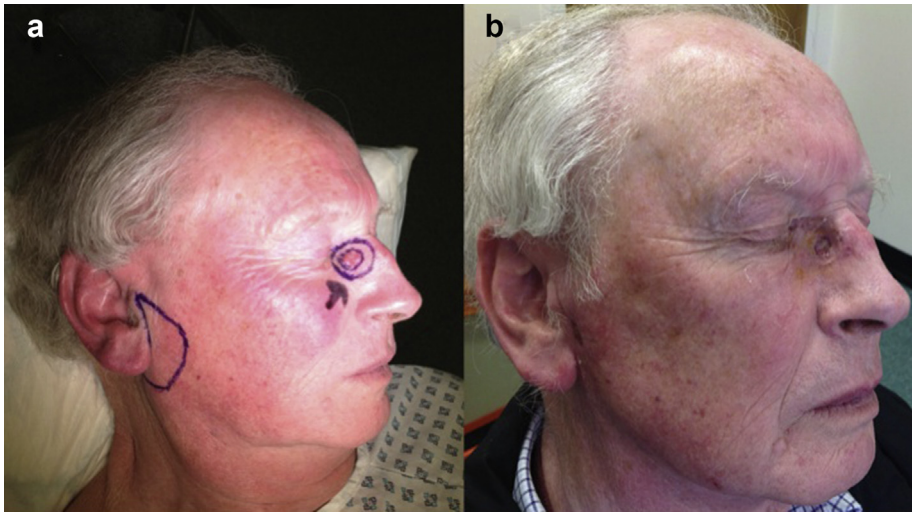

Fig 6. (a) Planned excision of medial canthal basal cell carcinoma and full-thickness skin graft harvest from the preauricular area; (b) partial skin graft failure requires prolonged wound healing.

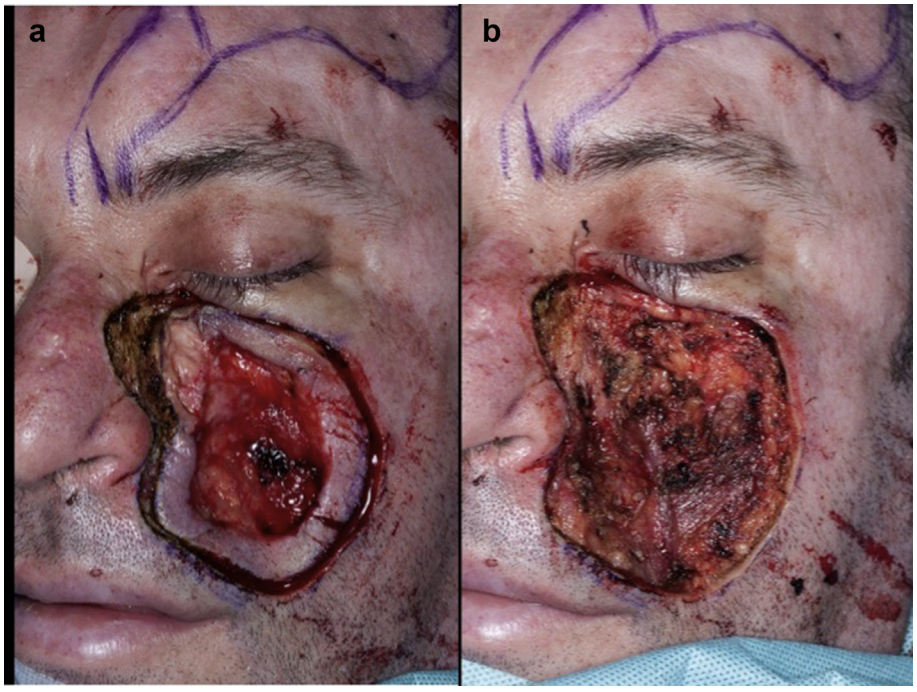

Fig 7. Extensive basal cell carcinoma after failed Mohs surgery required further excision down to maxilla and reconstruction.

for increased required processing time. Microcystic adnexal carcinoma is a rare eccrine sweat gland tumour that classically occurs over the central face. It can spread far beyond its surface appearance and does optimally with margin-controlled techniques such as Mohs surgery [34,35]. The use of Mohs surgery for melanoma is still to be established, but is on the rise, particularly in the USA [36].

Mohs Micrographic Surgery versus Wide Local Excision

Standard resectional surgery or wide local excision provides an effective, well-tolerated treatment option for most NMSCs [37]. Standard tissue excision is processed vertically using a classic histopathology technique known as 'bread loafing', in which tissue is sectioned in a vertical orientation at intervals, typically three to five cuts through the tissue block. However, bread loafing examines less than 1–2% of the total histological margin depending on the specimen size and can result in false-negative results. Sampling error may occur if the intervals of the sections miss extensions of tumour, especially in tumours of more aggressive subtypes (e.g. micronodular, infiltrative, or morphoeic BCC) or those displaying PVI. Equally, as discussed above, undertaking wide local excision in NMSCs in cosmetically sensitive facial

Fig 8. Forehead flap based on supratrochlear vessel. Pedicle used to resurface the mid-face defect, forehead donor site left to heal by secondary intention.

sites may result in suboptimal functional and cosmetic outcomes, as well as inferior tumour clearance rates and Mohs surgery should then be considered.

In Mohs surgery, the fresh tissue technique and horizontal sectioning allow for complete 100% examination and immediate microscopic control of all margins – peripheral and deep. Skin tumours with asymmetrical growth patterns can thus be identified and removed. The fresh-frozen technique allows for real-time microscopy with results available within 30–60 minutes rather than 1–2 weeks for standard histology. The removal of healthy unaffected tissue is minimised during Mohs surgery, enabling maximal preservation of normal skin and deeper tissues, sparing unaffected nerves and muscle. In addition, no reconstruction occurs until the patient is clear of cancer, thus minimising the risk of a second costly and disruptive procedure that can occur with standard excision if the initial excision is incomplete. Mohs surgery often leads to smaller, less deep defects and thus simpler reconstructive options, less cosmetic disfigurement and better functional outcome. It offers the best cure rates for the most difficult high-risk NMSCs and is thus the 'gold standard' treatment for such lesions [17,18]. Mohs surgery combines surgical excision, anaesthesia, pathology and usually reconstruction in one single day case/outpatient procedure, obviating the requirements for further procedures and, hence, is a cost-effective procedure when used appropriately. Reported 5-year cure rates with Mohs surgery include: primary BCC (98–99%), recurrent BCC (92.2–96%), primary cSCC (92–99%) and recurrent cSCC (90–94%) [15,38–40] (Figure 5).

Relative Contraindications of Mohs Surgery

Absolute contraindications to Mohs surgery are few. The technique is a staged procedure and thus time-consuming, requiring specialised expertise and equipment [41]. Appropriate patient and tumour selection for Mohs surgery is therefore important. Indications for Mohs surgery for NMSC are summarised in Table 2. Patients should be able to tolerate local anaesthetic surgery over a relatively prolonged period, typically 4 hours including reconstruction. Patients who require general anaesthesia, for example high-risk tumours invading bone or the orbit, or patients with psychological or mental capacity issues, will generally be unsuitable. Patients not suitable for Mohs surgery can be considered for wide local excision or radiotherapy.

Reconstructive Surgery

Reconstructive surgery for patients with advanced skin cancers has changed dramatically in the past 30 years, following advances in imaging for planning resections and reconstructions, as well as instrumentation for microvascular surgical procedures and operating microscopes. In addition, a better understanding of vascular and microvascular anatomy, including the invention of perforator flaps, allowed the harvest of various flaps from head to toe in order to replicate what was lost as a result of cancer removal with minimum morbidity for the patient. This shift reduced the use of skin grafts to certain anatomical locations and patients otherwise not fit for more sophisticated and better quality flap reconstructions. Unlike flaps, grafts have no blood supply of their own, requiring a well-vascularised bed and avoidance of sheer-forces, which could prevent the 'graft take' during the first week of graft revascularisation from the undersurface. This is often not possible due to preoperative radiotherapy, the need to cover bone, joints, tendons, nerves or major blood vessels, where flaps are indicated. Hence, healing after skin grafts is often unpredictable and partial or total graft failures followed by a longer periods of delayed healing by secondary intention are common (Figure 6a,b). A multitude of flaps – composite tissues with a blood supply – now exist and can be harvested from almost any area of the body where a blood supply can be found and incorporated into the flap design.

Various flap classifications have been described according to the type of blood supply (random pattern flaps; axial; perforator), the type of tissue flaps are made of (fascio-cutaneous; musculo-cutaneous; osteo-cutaneous; osseous; muscle; fascial and various combinations of the

Fig 9. The same patient as in Figure 8, 9 months after division of the pedicle with excellent aesthetic outcome.

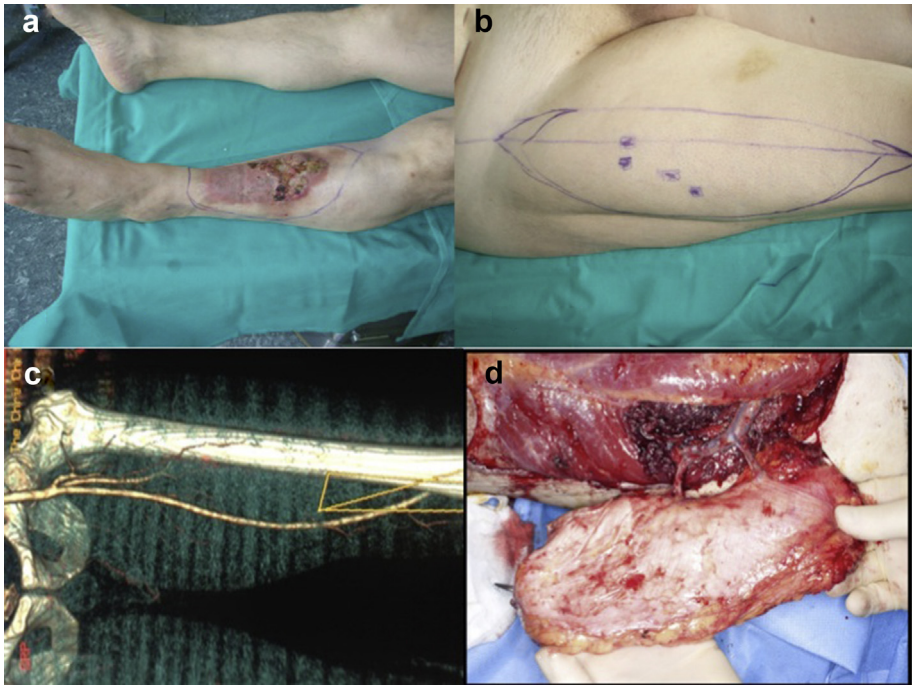

Fig 10. (a) A large cutaneous squamous cell carcinoma (cSCC) in the pretibial area requiring excision down to the bone and free flap reconstruction; (b) free microvascular antero-lateral thigh (ALT) perforator flap planned based on perforators coming off the descending branch of lateral circumflex femoral vessels; (c) preoperative flap planning with a three-dimensional computed tomography angiogram improves the accuracy and safety of flap harvest and reduces complications; (d) intraoperative ALT perforator location corresponds to computed tomography angiogram.

above), as well as pedicled (Figures 7–9) or free (microvascular) flaps, depending on whether the flap's main blood supply stays connected (pedicled) or is disconnected during the flap harvest, to be reconnected using microvascular techniques with microsurgical instruments and a high-power operating microscope (Figure 1). The last two decades have seen great advances providing more tailored and sophisticated reconstructions using

Fig 11. Flap following microvascular anastomosis used to resurface the bone after cutaneous squamous cell carcinoma removal.

perforator flaps. These flaps rely on perforating vessels that travel through the muscle and subsequently pierce the fascia to enter fat and skin. The technique, which requires tedious and technically challenging dissection under loupe magnification with special instruments, allows the harvest of skin flaps all over the body, sparing underlying muscles and thus reducing functional morbidity and improving cosmesis to flap donor sites (Figure 10a–d, 11). Perforator flaps have become more reliable, safer and faster with the use of computed tomography-angiogram and magnetic resonance imaging scans, which cannot only locate the best blood supply for the flap (Figure 10c,d), but also give preoperative information on the intramuscular course, branching and intra-flap vascular architecture – all very important for successful dissection, reduced complications and more predictable significantly improved outcomes [43]. Most free tissue transfers nowadays have success rates above 95%, which is, despite the complexity and time required for surgery, still better than many skin grafts or pedicled flaps (Figure 11). Despite these advances, there are still ancient techniques that have survived the test of time, frequently used for head and neck resurfacing. For example, the oldest plastic surgery described in history, the forehead flap, has undergone few technical modifications, but it is still for many a treatment of choice for smaller to medium nasal and mid-face lesions (Figure 7a,b, 8, 9a,b).

Conflict of interest

The authors declare no conflicts of interest.

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