“Better health with the best cosmetic result, no one can ask more from a surgical procedure in the 21st century.”(1) This phrase was used in the journal of Cutaneous and Aesthetics surgery in 2012 to describe Mohs Micrographic Surgery (MMS).

Since its inception in 1930s by Dr Frederic Edward Mohs, who had already completed majority of the basic research on the technique as a medical student, (2) MMS has gained popularity and is now regarded as the gold standard technique for removing non-melanoma skin cancer (NMSC) due to its healthy tissue preservation, low complication rates, cost effectiveness and low recurrence of NMSC when treated by this technique. (3,4)

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the two most common subtypes of NMSC. (5) In the UK, BCC is the most common cancer among Caucasians and the rate of incidence of BCC is increasing by approximately six fold compared to mainland Europe. (6) NMSC is projected to cost the NHS £180 million by 2020 (7), which has major economical implications in today’s NHS where demands are far exceeding the resources and therefore provision of cost-effective care is paramount. (8)

So what is MMS?

MMS involves a combination of surgery and microscopic examination, during which local anaesthetics is administrated and the cancerous tissue is excised in horizontal manner to the skin and examined under the microscope, allowing for observation of 100% of the surgical margin. The excised tissue is then orientated, separated into four quadrants, and embedded for the cryostat thin sectioning. This technique is known as the fresh-tissue technique, which allows for considerably quicker analysis of the excised tissue whilst the patient is in the waiting room compared to the original technique

described in Dr Mohs' landmark article in the Archives of Surgery in 1941. (9) This procedure is repeated until clear surgical margin is observed. The use of MMS has increased significantly over years and between 1995 to 2009 it was estimated to have increased by 400% and currently 1 in 4 skin cancers is being treated with MMS in the US. (10) In the UK however, these numbers are considerably lower due to provision of MMS through the NHS as oppose to private insurance companies, and the fewer number of MMS when compared to the US. (11)

Why is MMS the gold standard for NMSC?

MMS has been shown to be safe, with low rate of major complications and superior 10-year cure rates and better healthy tissue preservation when compared to Standard Surgical Excision (SSE), which divides the specimen vertically. (12,13) The results of a 10-year follow up randomised control trial of BCC in the Netherlands, comparing the two techniques, showed a 7.6% less cumulative recurrence rates when resecting primary BCC (pBCC) and 9.6% less when excising recurrent BCC (rBCC) using MMS. (14) Additionally, the study showed a substantial proportion of recurrences occurred after more than 5 years post-treatment: 56% for pBCC and 14% for rBCC. This confirms that although MMS is the superior surgical technique there is a need for a long-term follow-up. And this need is most felt in the UK since prospective randomised studies are rare. It is evident that a long-term follow up study, evaluating recurrence rate, cost-effectiveness, and patient life quality comparing MMS to surgical excision as well as other interventions for NMSC in the UK is needed.

In addition, a systematic review of observational studies assessing the efficacy of treatment for SCCs highlighted the lack of prospective studies and suggested that when compared to SSE or external radiotherapy, MMS is not superior in reducing the

recurrence rate. (15) Although the outcomes of this review must be interpreted with caution, it could be argued that MMS might not be the most suitable treatment option for all patients specially when considering the cost compared to SSE. This is more so, when excising small size lesions from low risk areas such as the extremities and the trunk.

When considering the cost of MMS, it is vital to include both the immediate and long-term costs. Although the immediate cost is much higher than the standard surgical excision, it has been shown that given the reduced future costs incurred due to less subsequent procedures, MMS is the more cost effective technique. (16,17) In addition, MMS preserves more healthy tissues and involves smaller reconstructions and flaps, which allows for fewer complications and better aesthetic outcomes. This is very useful for the patient as NMSC occurs mainly on sun-exposed sites, with 80% of BCCs appearing on the head and neck. (18)

On balance, MMS is considered as the gold standard treatment for complex or recurrent NMSC due to its safety, reduced complications, lower recurrence rates, and better aesthetic outcomes for the patient. Although there are a number of studies that highlight its cost-effectiveness in the US compared to other techniques, it is still unclear whether this is the case in UK.

What are the indications for MMS?

A 2012 report published by The American College of Mohs Surgery and the American Academy of Dermatology detailed the appropriate use criteria (AUC) for the MMS. (19) This report offers guidelines for the first time, for 270 scenarios for which MMS is frequently considered and was agreed upon by several dermatological associations,

determining which skin cancers should be treated with this technique. The guidelines are based on location, subtype and size of the lesion. Cost was also implicitly considered as an additional factor the evaluation of the AUC.

Based on these guidelines, appropriate use of MMS includes primary BCC or SCC (regardless of subtype, size, or depth), if the lesion is arising in prior radiated skin, a traumatic scar, areas of osteomyelitis, areas of chronic inflammation/ulceration, or in patients with genetic syndromes. MMS is also the preferred treatment option for all high-risk SCC such as keratoacanthoma cases as well as all forms of BCC including recurrent, primary aggressive, primary nodular and primary superficial in area H of the body. Fig 1 highlights the different areas of the body for MMS considerations.

In addition, this guideline highlights 44 clinical scenarios in which it is inappropriate to use MMS and 24 scenarios where it is uncertain to be beneficial for treatment of NMSC. Figure 1 highlights these clinical scenarios as well as describing different location areas for MMS consideration. When MMS is deemed inappropriate, there are a number of other treatment modalities that can be considered. These include physical destruction such as (radiotherapy (20), curettage and cautery (21), and cryotherapy), or chemical destruction (photodynamic therapy (22)) and immunomodulatory therapy (23) (topical Imiquimod). Table 1 summarises the evidence for each treatment modality and compares the cure rate between them. However, there is a lack of long-term randomised clinical trials comparing all these treatment options to MMS in the UK in terms of efficacy, recurrence rates or cost-effectiveness.

Inappropriate for BCC if in Zone L and one of the following:

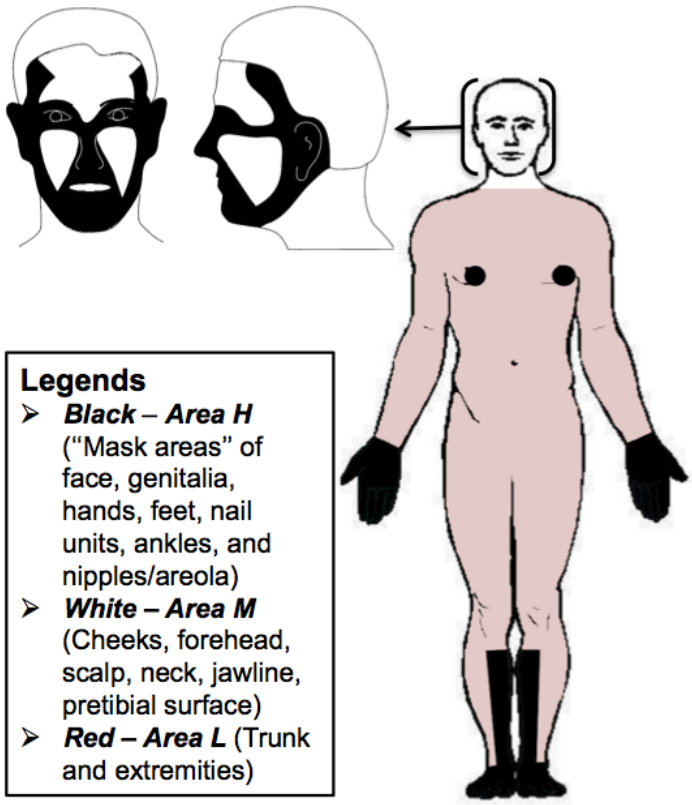
A. Primary superficial BCC of any size
B. Superficial Recurrent BCC of any size
C. Primary aggressive BCC of size ≤0.5cm
D. Primary nodular BCC of size ≤2cm in healthy and size ≤1cm in immunosuppressed patients

Inappropriate for SCC if:

A. Primary AK with focal SCC in situ; Bowenoid AK;SSC in situ, AK type of any area

In Zone L and one of the following

B. Primary SCC without aggressive histological finding (i.e. <2 mm or Clark level ≤ IV) and of size ≤2cm
C. Primary SCC of KA type of size ≤1cm in healthy and size ≤0.5cm in immunosuppressed patients
D. Primary in situ SCC/Bowen disease of size ≤2cm in healthy and size ≤1cm in immunosuppressed patients



Legends

- ***Black – Area H*** ("Mask areas" of face, genitalia, hands, feet, nail units, ankles, and nipples/areola)
- ***White – Area M*** (Cheeks, forehead, scalp, neck, jawline, pretibial surface)
- ***Red – Area L*** (Trunk and extremities)

Fig 1. Definitions of different areas of the body for MMS considerations. The diagram also highlights the clinical cases where it is inappropriate to use MMS.
SCC (squamous cell carcinoma), BCC (Basal Cell Carcinoma), AK (Actinic keratosis), KA (keratoacanthoma)

Table 1. Summary of evidence for different treatment modalities for NMSC

Therapy	Author	Year	No of participants	Cure rate (%)	Follow up period for data (years)
Primary BCC					
MMS	Eva van Loo et al.	2014	408	96.6	10
Standard Surgical Excision	Eva van Loo et al.	2014	408	87.8	10
Radiotherapy	Chassagne et al.	1997	862	92.5	4
Curettage and cautery	Rudriquez-Vigil et al.	2007	257	79.4-98	5,3
Imiquimod	Quirk et al	2010	169	80.4	5
Photodynamic therapy	Basset-Sequin	2008	60	78	5
Primary SCC					
MMS	Leibovitch et al.	2005	1263	97.4	5
Standard Surgical Excision	Rowe et al	1992	124	91.9	5
Radiotherapy	Rowe et al	1992	160	90	5

Case Studies

This case study is an excellent example of a clinical scenario where MSS is inappropriate. Although all the systematic reviews and clinical trials seem very academic, this case study shows how they can be used in clinical practice to benefit the patient.

Fig 2.

Mrs BM, a 54-year old Italian female was referred to skin cancer assessment clinic for a lesion behind her right ear that she had noticed growing in size for the last 4 months. Mrs BM grew up in Italy for most of her life and has had excessive sun exposure. She is skin type 1 according to Fitzpatrick skin type chart. On examination, there was a 0.9 x 1.2 cm pearly papule with rolled edges on the right ear in the area where the skin is contact with her spectacles. On further exposure of the patient, there was a 4 x 6 cm lesion on the right shoulder. Only on further questioning, Mrs BM admitted that the lesion had been growing in size over the last 5 years. Histological punch biopsies were taken from both lesions. The lesion behind the ear was consistent with spectacle frame acanthoma, otherwise known as granuloma fissuratum for which the patient was advised to modify her reading glasses. The lesion on the shoulder however was a BCC. Given the growth is size and ill-defined nature of the lesion, Mrs BM would benefit from excision of the BCC. However, given the location as well as patient choice, she underwent a SSE as oppose to MMS.

In conclusion - ‘To have or not to have’

MMS is arguably the most revolutionary dermatosurgical technique of the last century and it continues to be the mainstay. According to most recent literatures, MMS is the gold standard for the treatment of NMSC, which has an increasing incidence and present a huge financial and logistical challenge to the NHS, particularly as our population ages.

However, when decisions are made about which patients benefit from the procedure most, it is of most importance to understand patient's needs, severity of disease, location and patient comorbidities. We must use the method wisely and according to the proper clinical indications taking into account the extra cost of the procedure over the simpler standard surgical excision. This technique should be reserved for more complex and recurrent NMSC and therefore, there is no rationale for performing MMS on a primary BCC on the extremities or the trunk, for example. Expanding the use of this method for inappropriate indications raises the cost of medical expenses to the NHS.

When MMS is deemed inappropriate there are other evidence based treatment options that can be offered. In addition, recent developments of novel molecular hedgehog pathway inhibitors for high-risk BCC (including oral vismodegib and sonidegib) may represent a paradigm shift towards medical management of NMSC. (24) Knowledge of available and emerging therapies will be helpful in improving patient outcomes. In addition, prevention strategies such as reduced sun exposure are of equal importance.

The patient autonomy, and proper consent is the key to any medical procedure and the ultimate decision regarding the appropriateness of MMS should be determined by the expertise and clinical experience of the clinician together with the patient.

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