

Mohs micrographic surgery: the experience of the dermatology unit of the university of Milan confirms the superiority over traditional surgery in high-risk non-melanoma skin cancers

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Abstract

The constant increase in the incidence of non-melanoma skin cancers (NMSC) makes their treatment a topic of paramount interest. Because most NMSC tend to develop in visible areas such as the head-neck area, it is a priority to choose the less destructive therapy and more appropriate reconstructive technique. Mohs Micrographic Surgery (MMS) represents the treatment of choice for skin tumors in critical sites, recurrent tumors and tumors with aggressive histologic features. We collected patients affected by NMSC who underwent MMS at the Dermatology Unit of IRCCS Fondazione Ca' Granda, Milan, in the period March 2017-December 2021. One hundred and fifty-nine patients were enrolled in this retrospective observational study. The excision margins were chosen based on a dermoscopic evaluation. The main histological diagnoses were basal cell carcinoma (145, 91.2%) and squamous cell carcinoma (10, 6.3%), in areas with high functional or anatomical value. 121 out of 159 surgeries did not require further enlargement after the removal of the clinically and dermoscopically visible lesion, but in 38 cases (23.9% of cases) the pathologist required at least one subsequent enlargement, due to the persistence of neoplasm at the bottom or at the margins of the lesion. Only one recurrence has been reported so far. MMS is a pathology-controlled surgery with high intrinsic value because of the low risk of recurrences and should be routinely adopted for high-risk NMSC.

Introduction

The constant increase in the incidence of non-melanoma skin cancers (NMSC)

makes their treatment a topic of paramount interest. In fact, from 1992 to 2012, there was a 100% increase in NMSC incidence in the Medicare population,¹ and, although the mortality rate is exceptionally low,² NMSC represent a significant economic burden on health services and also have significant morbidity, especially because most of them tend to develop in visible areas such as the head-neck area. The real incidence of NMSC is not quantifiable because it is not typically reported to cancer registries and it varies in different countries of the world; for example, in the US, in 2006, there were 3,5 million NMSC affecting 2,2 million patients, from 2002 to 2011 people affected by NMSC increased from 3,1 to 4,3 million, and in 2007 13 million patients had a history of NMSC, including 1 in 5 of 70 years or older. The management of NMSC is very expensive, just think that they are in fifth place among the most expensive cancers to treat in the United States, with an annual cost of therapeutic management of 4,8 billion from 2007 to 2012 and an increase in the number of procedures for NMSC by 14% from 1,918,340 in 2006 to 2,919,199 in 2012.³ Because the patient's quality of life can be negatively affected by a visible defect or lesion on the face, the goal of surgery is to choose the less destructive method and the more appropriate reconstructive technique. In the age of digital communication in which any information, even of a health nature, is easily accessible to everyone, patients are becoming *sophisticated consumers* of health service. The demand for high-quality skin cancer treatment and Mohs Micrographic Surgery (MMS) is likely to continue to rise.⁴ Although medical and physical treatment, such as topical imiquimod and 5-fluorouracil, and cryotherapy, can provide excellent results in some neoplasms, they are not indicated for histological types characterized by high risk of recurrences, *i.e.*, morpheiform and nodular.

Furthermore, such treatments do not provide neither the definitive histological diagnosis nor the confirmation of complete excision.^{5,6} Therefore, MMS is the treatment of choice for skin tumors in critical areas, recurrent tumors and tumors with aggressive histologic features:⁷ it is an approach to skin cancer removal that aims to achieve the highest rate of cure and to minimize the size of the surgical wound and consequent distortions at critical sites (eyes, ears, nose, and lips). In 2012 the American Academy of Dermatology in collaboration with the American College of Mohs Surgery, the American Society for Dermatologic Surgery Association and the American Society for Mohs Surgery estab-

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lished appropriate use criteria for MMS to minimize overuse of the procedure. The location on the body, patient and tumor characteristics should be taken into consideration when determining if MMS is appropriate.⁷ NMSCs, in particular basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), represent the main indications for MMS,^{8,9} although other tumors could be treated, such as lentigo maligna/melanoma,¹⁰ dermatofibrosarcoma protuberans, atypical fibroxantoma, leiomyosarcomas, extramammary Paget disease.¹¹ In particular, tumors with poorly defined margins, after previous removal or neoplasms

appeared on previously irradiated skin are considered at high risk. Regarding BCCs, the most aggressive histotypes are: morpheiform, fibrosing, sclerosing, infiltrating, perineural, metatypical, keratotic and micronodular patterns; about SCCs: sclerosing, basosquamous, small cell, poorly or undifferentiated, perineural, perivascular, spinkle cell, pagetoid, infiltrating pattern.⁷ According to the body area, skin neoplasms located in the so-called H area (facial center, eyebrow eyelids, peri-orbital area, nose, lips, chin, mandible, pre- and retro-auricular skin, temples, ears, genitals, hands and feet) are considered at high risk and deserving of MMS.⁷

Materials and Methods

MMS is a two-step, same-day surgical procedure aimed at the contextual pathological control of the margins of neoplasm before proceeding with the closure of the operative breach. An incisional formalin-embedded biopsy was required to confirm the clinical diagnosis and to discuss the best therapeutical approach with the patient. On the day of the procedure, clinical and dermoscopic pictures were taken and, according to the dermoscopic appearance, the drawing of the surgical margins was traced on the skin (Figure 1A,B). A stylized paper model showing the affected anatomical area was used for drawing the lesion and the surgical margins. The operating piece was marked with a reference point; its margins, then, coloured with different colours. The reference point and the colours were reported on the paper model, that was transferred with the surgical specimen in pathological department (Figure 2). There are different techniques of sample processing, chosen by the pathologist depending on the characteristics of the material, in order to perform a complete evaluation of surgical margins. According to classical MMS technique, the surgical specimen is divided into horizontal sections every 50 microns, starting from the deep plane until the material is exhausted. According to Mohs Tübingen, the technique consists in cutting the circumferential margins at full thickness from the specimen with saving of the central portion, proceeding also to dissect the deep margin. This technique has undisputed advantages: in addition to the traditional orientation of the sample and the increase of clinical indications that can be used in this intraoperative investigation, material is maintained for the definitive histological examination, useful for any immunohistochemical investigation, improved histological detail without

freezing artefacts.¹² In case of persistence of tumoral tissue, the pathologist, on the basis of the paper model, communicated the margin or fund concerned. The surgeon then proceeded to a further excision where indicated; the operating piece was again marked, oriented, marked with dyes and sent back to pathological anatomy for the extemporaneous histological examination. The process was repeated until both margins and bottom were free of neoplasm and the surgical breach could be closed. The suture of loss of substance could be direct, but often required cutaneous, myocutaneous flaps. Some characteristics, such as location of the loss of substance, depth of the wound, saving of the surrounding skin and quality of the surrounding tissues, were evaluated at the time of the reconstruction,

as they determined the success of the intervention, both functional and aesthetic.¹³

Results

From March 2017 to December 2021, 159 patients (74 males and 85 females) underwent MMS in our Dermatology Unit. Histological diagnosis was BCC in 145 cases (91.2%), 10 patients removed SCC (6.3%), 4 patients removed sebaceous carcinoma (2.5%). About anatomical locations, 142 patients removed a neoplasm on the face: 46 on the nose (nasal pyramid, tip of the nose, nasogenic sulcus), 20 on the ear (tragus, helix, hollow, pre- and retro-auricular), 16 on the periocular region (internal

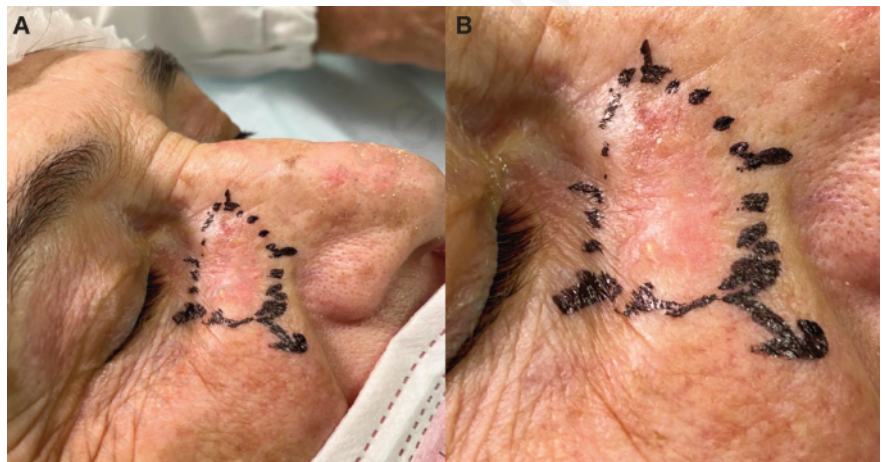


Figure 1. A,B): dermoscopic and surgical margins of the lesion and landmark.



Figure 2. Surgical piece marked with dyes and with landmark and stylized drawing.

canthus, eyelid). The remaining operations involved delicate sites such as the malar region (20), the eyebrows (8), the lips (15) or the frontotemporal region (17). The remaining 17 patients were operated on in highly functional sites, neck, instep, medial malleolus, or removed larger lesions with blurred margins located on the pectoral and on the leg. One female patient, 65-year-old, was affected by Gorlin-Goltz syndrome, a multisystemic autosomal dominant disorder with a high penetrance and variable expression. In her medical history, 14 BCCs were previously treated or removed; a BCC grew on the tip of her nose, thus requiring MMS. In our case series, 121 (76,1%) out of 159 surgeries did not require further enlargement after the removal of the clinically and dermoscopically visible lesion, but in 38 cases (23.9%) the pathologist required at least one subsequent enlargement, due to the persistence of neoplasm at the bottom or at a margin. Of these 38 enlargements, 15 were located on the nose, 5 on the ear and 4 on the eyelid. 34 enlargements were required on the head-neck area and 4 on the body (breast, instep, inguinal). In our case series, only in 1 case the enlargement process had to be carried out for more than 3 times, before proceeding with the reconstruction: the lesion was a sclerodermic BCC located in the auricular concha. No major surgical complications, *i.e.* major bleeding, infections, sepsis, were reported. The reconstruction was well tolerated by all patients: no major post-operative complications occurred. Minor post-operative complications, such as wound dehiscence, hematomas and small bleeds, were managed with local dressings, without requiring additional surgical interventions. Patients generally reported no or minor pain, managed with oral non-steroidal anti-inflammatory drugs. Only one recurrence has been reported so far.

Discussion

The main purpose of MMS is to check the margins of neoplasm before the closure of the operative breach. Despite the accuracy of drawing on the skin the margins of neoplasm visible on dermoscopic examination, procedure that is carried out routinely before a dermatological surgery intervention, in 25.2% of cases the margins of neoplasm exceeded the margins hypothesized with non-invasive techniques. We think that this observation confirms the superiority of MMS compared to traditional surgery in the radical removal of high-grade NMSC, in difficult sites and with particularly aggres-

sive histotypes. We did not consider a control group treated with traditional surgery because in that case the excision margins are >4-6 mm, while in our patients we considered the margins visible dermoscopically to save healthy tissue. In other centers where MMS is performed, the lesion is removed with excision margins >3-4 mm, obtaining a success rate comparable to ours.¹⁴ The number of MMS stages is believed to be related to some factors, among which: i) the anatomic site;¹⁵ ii) tumor histology, with some tumor histotypes such as morpheiform BCC having a wider-than-visualized lateral spread in the dermis; instead tumor size alone is not believed to predispose to more stages, and large, well-demarcated tumor can be removed in one or a few stages.¹⁶

Conclusions

Therefore, MMS is a method of surgical excision with high intrinsic value because it is cost effective if compared to traditional surgical excision. The quality of a surgical procedure is, in fact, determined by measuring some variables, such as the morbidity of procedure and tumor recurrence rates. MMS has many advantages that add to its value, not only to have smaller excisions, with a better aesthetic and functional result but, also, less risks of recurrences if compared with traditional surgery. In case of persistence of neoplasm, after the closure of the operative breach, traditional surgery requires further intervention and/or medical treatment or radiotherapy or close follow-up, which represents an additional cost in terms of money, time, patient distress and worst aesthetic outcome, because of the loss of more healthy tissue and for the difficulty of re-intervening on a surgical scar.^{17,18} According to a recent study that compares MMS and traditional surgery in the treatment of high-risk SCC, MMS is both less expensive and improves the quality of life in terms of quality-adjusted life years (QALY), confirming itself as the most cost-effective technique for treating high-risk NMSC.¹⁹ The higher cure rates provide a sense of security both in patient and physician and obviate the inconvenience and morbidity of repeated surgical procedures.¹⁸

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