

# Modified Mohs Micrographic Surgery in Lentigo Maligna Treatment: A Series of Six Cases

Alexandra Zota, Anca Stanciu, Cecilia Enescu, Tiberiu Tebeica, Mihaela Leventer

Dr Leventer Centre, Bucharest, Romania

## Corresponding author:

Alexandra Zota, MD  
Dr. Leventer Centre  
Bucharest  
Romania  
alexandrav\_zota@yahoo.ro

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**ABSTRACT** The surgical approach to lentigo maligna is a challenge to dermatologists, given its clinical and histopathological particularities. Staged excision with paraffin-embedded, permanent sections for histopathological evaluation of surgical margins is an effective treatment of lentigo maligna because it enables complete excision of the tumor, at the same time preserving maximum amount of healthy tissue. We report a case series of 6 patients diagnosed with lentigo maligna who underwent this procedure in our Institution and we describe the procedure we used. Complete excision of the tumors was achieved with one to three levels, with margins of excision ranging from 2 to 8 mm. There were no local recurrences at the median follow-up of 16 months, obtaining 100% cure rate with this technique. These are comparable with the margins and number of levels of excision described in previous case series reported in the literature. The technique described herein for the treatment of lentigo maligna provides excellent cure rates for this type of cutaneous malignancy notorious for its challenging management.

**KEY WORDS:** modified Mohs micrographic surgery, lentigo maligna

## INTRODUCTION

Lentigo maligna is a cutaneous malignancy with increasing incidence and a significant risk of morbidity. It is defined as a subtype of melanoma *in situ* (therefore confined to the epidermis) associated specifically with chronic exposure to ultraviolet radiation, primarily affecting the head and neck region of elderly patients (1,2). It currently ranks as the most prevalent melanoma *in situ* subtype, accounting for 70% to 83% of all melanoma *in situ* tumors (3).

Although lentigo maligna falls into the category of melanoma *in situ*, its genetic background is different from other types of melanomas, as it is not associated with the propensity to form atypical nevi nor is it associated with significant rates of BRAF mutations. Instead, it is associated with a tendency to form solar lentiginos, advanced age, lighter skin types, cumulative sun exposure, and a higher incidence of p53 mutations (4-6).

Fortunately, when detected early, the disease is almost always curable (7).

Management of lentigo maligna is quite challenging and open to debate, due to a notable lack of randomized controlled trials and some shortcomings in the actual therapeutic options recognized even by the current guidelines and protocols in place for this tumor (1,3,4,7-11).

The treatment of lentigo maligna aims at completely removing the lesion in order to prevent recurrences and at the same time preserving the maximum amount of healthy tissue in order to maintain the cosmetic and functionality of the involved area. Different treatment modalities have been proposed to attain these goals, but some of them only with varying degrees of success.

Traditional wide local excision with 5 mm margins, the initial standard of care recommended for treating melanoma *in situ* including lentigo maligna, has been proved an unreliable method of treatment due to the difficulty in complete clearing of its margins (1,3,4,8,11-13).

Therefore, excision modalities that incorporate complete margin control have been recently advocated. These include Mohs micrographic surgery, staged excision with permanent vertical sections (slow-Mohs), the square method, perimeter technique, staged radial sections, and others (1,3,4,7,8,14).

At our institution, staged excision with rush en-face permanent sections, also known as slow-Mohs, is the treatment of choice for lentigo maligna.

Slow-Mohs surgery is a variation of Mohs surgery, primarily introduced by Breuninger *et al.*, with the aim of overcoming the inconveniences associated with interpreting the frozen tissue sections of this technique for particular types of skin tumors such as lentigo maligna, while maintaining its advantage of providing 100 percent margin assessment. As in with Mohs surgery, Slow-Mohs surgery involves the excision and orientation of the tumor with marker dyes and color-coded diagrams, but the tissue specimens are en-face sectioned and embedded in paraffin, with the possibility of IHC staining. The histopathological margins assessment following this technique is more reliable, considering the difficulty of differentiation between healthy and tumoral tissue on the frozen section.

Therefore, this technique is particularly useful for the management of lentigo maligna, as it enables margin-controlled excision, while at the same time providing accurate interpretation of the morphology of the tumor through classic and immunohistochemical stains, which is notorious for the difficulty in identifying its periphery, which may be represented only by small nests or single melanocytes.

## METHODS

Since 2017, we have treated lentigo maligna with serial excisions in a staged fashion using the slow-Mohs technique.

Before treatment, a positive histologic diagnosis is established in all patients. We used deep shave biopsies from the most darkly pigmented or thickest parts of the lesion.

The procedure was performed in an outpatient setting under local anesthesia, with additional oral sedation as needed.

The first step was to identify and mark the clinically apparent borders of the lesion, taking into account the clinical and dermoscopic examination.

After identifying and marking the clinical borders of the lesion, a margin of 1 to 5 mm of clinically normal surrounding skin is marked around the outlined lesion and then the first layer of the Mohs procedure

is excised at 90 degrees as a single piece down to the subcutaneous fat.

The explanation of this slightly different approach from traditional Mohs surgery lies in the fact that the 45 degree scalpel beveling used in traditional MMS is not appropriate for LM because it diminishes the melanocyte density in the sections and thereby impedes histological interpretation.

The depth of the excision should be down to the deep subcutaneous fat to ensure it is beneath the hair follicles.

Precise mapping of the specimen and excision site is performed by following the orientation of the face of a clock (the 12 o'clock position is scored on the specimen and sutured onto the patient).

The excised specimen is placed in formalin and sent to the pathologist. During histopathologic processing, the accompanying drawing is reviewed and the margins of the specimen are color-coded to maintain orientation. Depending on its size, the specimen may be divided into subsections and then processed with permanent/paraffin-embedded, hematoxylin and eosin stained, with en-face vertical sections at 2-3 mm intervals for complete margin evaluation. The slides are then examined by the pathologist.

Immunohistochemical stains are used at our institution to aid in diagnosis.

After histopathological and immunohistochemical interpretation, a surgical map is drawn that outlines the orientation and color-coding of the individual subsections of the specimen, which will help the surgeon in the event that residual tumor is identified.

If warranted, a partial closure is performed to obtain hemostasis and simplify wound care for the patient while awaiting histological evaluation of the margin status.

The second stage of slow Mohs is performed if the lateral surgical margins are positive.

In stage 2, the patient will return for a second level of slow-Mohs excision.

The surgeon analyzes the slides and documents areas that show tumor infiltration. Then, the second layer of normal-appearing tissue with a 1 to 5 mm margin laterally is taken only around the positive area, thereby sparing excision of normal tissue.

The specimen is again oriented with color-coded inked margins or suture, placed in formalin, and sent to the pathologist.

The entire process is repeated as indicated until histologically tumor-free margins are obtained.

After the tumor is completely cleared, the patient returns for surgical wound repair.

The initial diameters of the clinically apparent the lesions were measured so, the final defects.

The final defects are often large and complicated due to the subclinical spread of lentigo maligna and require more complex reconstruction techniques such as skin flaps or skin grafts.

With regard to the histopathological analysis of subsection margins, nests, and contiguous melanocytes, as well as a large number of single melanocytes with markedly atypia, are interpreted as evidence of disease. The challenge of this process was to differentiate atypical melanocyte of lentigo maligna from mildly atypical melanocytes seen in sun-damaged skin.

### Data collection

Data collected included patient details, location, history of previous treatment, size of the preoperative tumor and postoperative surgical defect, number of stages required for complete excision, margins of excision at each level, the method of surgical reconstruction, and outcomes at the last clinical follow-up visit. The outcome of interest was local recurrence. A biopsy is indicated if clinical recurrence is suspected. Secondary questions of interest were the relationship between lesion size and the number of stages of excision and the total margin required to clear the tumor.

### RESULTS

Six patients, two women and four men, underwent staged surgical excision for lentigo maligna between 2017 and 2020.

The age range of the patients at the initial presentation was 52 to 77 years, with an average of 55.5.

All lesions were pigmented lentigo maligna, except one case of amelanotic lentigo maligna involving the temporal area.

All tumors were primary lentigo maligna.

The site of involvement was the head and neck area (forehead, scalp, cheek, nose). The most common sites of involvement were the forehead (2 patients) and cheek (2 patients), followed by the scalp and nose.

With our technique, we take an initial margin of 2 to 5 mm around the visible tumor, depending on the site and the aspect of the lesion.

For all lesions, the average number of levels required for complete excision was 1.64 (range 1-3 levels). This is comparable to the average stages of excision reported in the literature.

Two lesions required only one level of excision with margins of 2 mm and 5 mm, while the rest of the lesions were completely excised with two or

three levels, with margins at each level ranging from 2 to 5 mm. For all lesions, the total margin of excision ranged from 2 mm to 8 mm from the clinically apparent tumor.

Lesions ranged in size from 5/10 mm to 40/45 mm before treatment (recorded as minimum × maximum diameter). The final postsurgical defect after complete histologic clearance ranged from 15/17 mm to 50/55 mm. Both the initial lesions size and postoperative defect size were similar to those reported in the literature previously.

In our cases, we found no correlation between lesions size and total margins of excision.

The size and location of the final defect determined the method of surgical reconstruction, which included direct closure and flap repair (advancement flap, transposition flap).

We achieved a 100% cure rate of lentigo maligna during an average follow-up of 16 months.

### DISCUSSION

#### Diagnosis of lentigo maligna

Early recognition of lentigo maligna is of paramount importance, but it can be quite challenging as its clinical presentation can be subtle and varied (3,4,15). Diagnosis of lentigo maligna relies on a high clinical suspicion index aided by dermoscopy, Wood's lamp examination, and, when available, reflectance confocal microscopy. Histological evaluation with immunohistochemistry staining remains the gold standard for the confirmation of the diagnosis.

In clinical terms, lentigo maligna commonly presents as a slowly-growing pigmented macular lesion in chronically sun-damaged skin, which can be irregular and asymmetric, tends to have an ill-defined border, and displays color variegation from light brown to black (3,4,8). It exhibits slow radial growth, and as the lesion enlarges, it may develop skip areas with a patchy, non-contiguous pattern (16). If vertical growth happens, invasive melanoma (lentigo maligna melanoma) is diagnosed and a papular or dermal component may be felt.

The timeframe of progression of lentigo maligna to lentigo maligna melanoma varies widely from 10 to 50 years, while the lifetime risk is estimated to be greater than 5% (17).

Dermoscopic features of lentigo maligna include the following: asymmetric pigmented follicular openings, dark rhomboidal structures, slate-grey globules, annular-granular pattern, black dots, and streaks (18,19). Notably, these dermoscopic features can be shared with other similar lesions, necessitating the



inclusion of pigmented actinic keratosis, solar lentigo, pigmented seborrheic keratoses, and lichen planus-like keratoses in the differential diagnosis (20).

Wood's lamp examination is a useful tool in assessing the margin delineation of lentigo maligna and the depth of melanin, given the fact that lesions possessing an increased concentration of epidermal melanin will appear darker and fluorescent under Wood's light.

Reflectance confocal microscopy is a noninvasive imaging technique that can detect characteristic histological features related to lentigo maligna through evaluation of tissue architecture at the nuclear and cellular level without performing a biopsy (21,22).

However, the gold standard for the diagnosis of lentigo maligna is excisional biopsy.

In theory, excisional biopsy removes the whole clinical lesions with a 1-3 mm margin down to the subcutaneous fat (4). This procedure enables a complete evaluation of the depth and peripheral involvement of the lesion. However, the large size of lentigo maligna, its indistinctive clinical borders, and location in cosmetically sensitive areas make this procedure unfeasible and quite impossible to perform. In such cases, scouting biopsies can be performed which should include samples from the darkest and most concerning part of the lesion as well as from the periphery in order to minimize the sampling error and delineate the peripheral margin involvement (4).

Histopathologic diagnosis of lentigo maligna can be quite difficult due to the fact that it is difficult to distinguish lentigo maligna from sun-induced melanocytic hyperplasia that is naturally present on sun-damaged skin (23).

Microscopic features of lentigo maligna consist of atypical melanocytic hyperplasia at the dermo-epidermal junction, a confluence of atypical melanocytes, angulated nuclei replacing the basal layer, and nesting of atypical melanocytes with occasional pagetoid spread (24).

Immunohistochemistry with MART-1/Melan-A, HMB-45, tyrosinase, MITF, Sox10, and S100 may aid in diagnosis (25).

### Treatment of lentigo maligna

The actual therapeutic options for lentigo maligna vary from standard wide local excision to margin control surgery and other alternatives like imiquimod, cryotherapy, and radiotherapy. However, surgery is the treatment of choice.

Initially, the standard of care proposed for treating melanoma *in situ*, including lentigo maligna, was wide local excision with 5 mm margins (1,4,8,12,26,27). However, taking into consideration cumulative evidence from multiple studies over recent years, the conclusion that has been reached is that the aforementioned technique is not the optimal treatment

**Table 1.**

Sex	Age	History of previous treatment	Localization	Size of preoperative tumor	Size of surgical postoperative defect	Number of levels of excision	Margins of excision at each level	Total margin of excision	Method of reconstruction	Outcome of the last clinical follow-up
Female	68	No previous treatment	Nose	10/11mm	20/21 mm	2	2,2	4	Transposition flap	No recurrence at 5 months
Male	52	No previous treatment	Right cheek	30/15mm	30/45 mm	2	5, 2	7	Advancement flap	No recurrence at 10 months
Male	68	No previous treatment	Temporal region	8/10mm	15/17 mm	1	5	5	Direct Closure	No recurrence at 10 months
Male	77	No previous treatment	Right cheek	5/10mm	14/20 mm	2	5,3	8	Direct Closure	No recurrence at 13 months
Male	69	No previous treatment	Scalp	40/45cm	50/55 mm	1	2	2	Direct Closure	No recurrence at 27 months
Female	70	No previous treatment	Forehead	8/12 mm	14/20 mm	2	1, 2	3	Direct Closure	No recurrence at 31 months

option for lentigo maligna due to the difficulty in completely clearing its margins.

Numerous studies as well as the National Comprehensive Cancer Network, a consensus group that develops evidence-based practice guidelines, have addressed the potential need for >5 mm margins in lentigo maligna and stated that techniques with a comprehensive histologic assessment of the margins may need to be considered in such cases (1-4,8,14,15).

It is well known that lentigo maligna has an asymmetric peripheral growth pattern and exhibits imprecise clinical borders with significant subclinical spread. That is why the 5 mm margins recommended for wide local excision of lentigo maligna are inadequate for curing this lesion and can be both insufficient and excessive for the same lesion (6).

By definition, traditional wide local excision with histopathological specimens processed by standard bread loaf techniques with transverse vertical sections does not allow complete margin control of lentigo maligna, which is essential for these kinds of lesions that, as previously noted, are notorious for their clinically indistinctive borders and unpredictable subclinical extension. In fact, this technique allows histologic examination of only 0.1% to 5% of the total margin, making it less than ideal for the complete cure of lentigo maligna (4,15,28).

Consequently, routine surgical excision may lead to incomplete removal of the lesion with high recurrence rates and with the cost of unnecessary tissue loss.

In this context, dermatologic surgeons have tried to overcome the issues associated with traditional surgery by turning to excision modalities that incorporate margin control.

Mohs micrographic surgery has emerged as a superior surgical option for treating lentigo maligna, as suggested by a growing body of literature (2,7,31-40). Mohs is a specialized surgical excision technique ideally used for the treatment of a variety of cutaneous neoplasms that grow in a contiguous fashion and are located in cosmetically sensitive areas or areas with a high risk of recurrence. It offers excellent cure rates for this type of tumors, by offering complete and immediate assessment of the entire peripheral and deep margins of the skin cancer, at the same time preserving the maximum amount of healthy tissue. Being a tissue-sparing technique, Mohs micrographic surgery may be particularly suited for the treatment of lentigo maligna, which are lesions notorious for their large diameters, localization in areas where tissue preservation is critical either for cosmetic or functional reasons, and, above all, that have clinically

indistinctive borders with unpredictable subclinical extension.

Therefore, with Mohs micrographic surgery, the complete excision of the lesions is achieved with the maximum amount of normal tissue preserved because the surgical margins are tailored to what is found histologically. However, when it comes to treating melanocytic lesions by Mohs micrographic surgery, there are well-documented difficulties in accurately interpreting the histopathology of these lesions on the frozen tissue section (8). There are two major difficulties in evaluating melanocytic lesions on frozen sections. On one hand, these sections can be plagued by freeze artifact, tissue folding, and keratinocyte vacuolization, resembling melanocytes that can lead to false positives. On the other hand, there is a great difficulty in determining the peripheral margins of lentigo maligna in the context of background melanocytic hyperplasia occurring in chronically sun-damaged skin from the edge of the lesion (29,30). All these inaccuracies make Mohs micrographic surgery unreliable for accurately interpreting the histopathology of lentigo maligna.

Therefore, neither traditional wide local excision nor Mohs micrographic surgery are the best-suited treatment modalities for the management of lentigo maligna.

In order to overcome the pitfalls associated with these techniques, a modified Mohs surgery technique using staged excision with permanent rush-processed paraffin embedded sections (slow-Mohs) was developed. Its name stems from the longer time involved in the processing and evaluation of its permanent paraffin sections, which may require several days to achieve clear margins. This technique maintains the principal advantage of standard Mohs micrographic surgery of providing a complete histological assessment of tumor margins and avoids the pitfalls related to Mohs micrographic surgery frozen sections. Despite their time-consuming nature, permanent sections are considered the gold standard for evaluation of melanocytic lesions, as melanocytes retain their pericytoplasmic vacuolization with this method, allowing them to be more readily identified.

As with standard Mohs micrographic surgery, slow-Mohs surgery involves excision and orientation of the tumor with marker dyes and color-coded diagrams, but it differs from standard Mohs micrographic surgery in the way the sections are prepared, cut (vertical sections), and examined (en-face) (5).

We reported early cure rates in a series of six patients with lentigo maligna treated with slow-Mohs with permanent sections in which complete excision



with no recurrence was achieved in all patients with margins of 2 to 8 mm and levels of excision which varied from one to three. These are comparable with the margins and number of levels of excision described in previous case series reported in the literature.

Although there is no consensus on the initial margins of excision that should be used during staged excision, the majority of reports suggested margins of 2-3 mm at each level of excision. However, the initial margin may be anywhere from 2 to 10 mm around the clinical borders, depending on the size of the lesion, anatomic location, or functional considerations (7). In our case series, there were three cases with initial margins of 5 mm, two cases with 2 mm, and one case with 1 mm.

Our small series adds to the growing body of literature that has addressed the potential need for larger than 5 mm margins of excision to achieve complete cure of lentigo maligna.

In fact, a number of studies have demonstrated that the standard margin of 5 mm recommended for melanoma *in situ* was inadequate for the complete excision of more than 30% of lentigo maligna and are associated with recurrence rates of 9% to 20% (4,42).

In our case series, the largest lentigo maligna lesions treated measured 40/45 mm and required only one level of excision with 2 mm margins.

The smallest lesion measured 5/10 mm and required two levels of excision with 5 mm and 3 mm margins, the total margin of excision being 8 mm.

The rest of the lesions required 1 to 3 layers of excision with total margins ranging from 2 mm to 8 mm. This observation may point to the fact that the margins necessary for the complete clearing of lentigo maligna are not related to the dimensions of the lesions but rather to the subclinical spread.

Our results also suggest that margins of excision of 2 to 8 mm can be safely employed with numbers of excision varying from one to three, achieving smaller postoperative defects without compromising early cure rates, which is comparable with reports of previous case series described in the literature.

The use of standard surgical excision for lentigo maligna is linked with both unnecessary loss of healthy tissue and also incomplete excision of the tumor, which leads to high rates of local recurrence.

Furthermore, this tumor is located in a critical sensitive area with cosmetical and functional implications, so maximum tissue conservation is of the utmost importance. This calls into question the effectiveness of this procedure to accurately cure this kind of cutaneous neoplasia.

That being said, margin-controlled surgery techniques are more appropriate for treating this tumor.

## CONCLUSION

Lentigo maligna presents diagnostic and treatment challenges due to its clinical mimicry of benign lesions, its occurrence on background sun-damaged skin, thus confounding histopathologic differentiation between true tumor and benign melanocytic hyperplasia, and its occurrence in cosmetically and functionally sensitive areas (11). Thus, maintaining clinical diligence and choosing the ideal treatment modality that ensures optimal outcomes (which entails complete excision of the tumor confirmed by histopathological assessment of margins with maximum preservation of healthy tissue) is of paramount importance to minimize morbidity and mortality in patients.

Surgical excision with histologically clear margins is the current standard of care for the treatment of lentigo maligna. Staged excision with paraffin-embedded, permanent sections for histopathological evaluation of surgical margins is a reliable method for excising lentigo maligna because it enables complete excision of the tumor with complete margin control and at the same time avoids some of the pitfalls related to Mohs micrographic surgery frozen sections.

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