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Mohs surgery for female genital Paget's disease: A prospective observational trial

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Abstract

Background: Extramammary Paget's disease recurs often after traditional surgical excision. Margin-controlled surgery improves recurrence rate for male genital disease but is less studied for female anatomy.

Objective: To compare surgical and oncologic outcomes of margin-controlled vs traditional surgical excision for female genital Paget's disease.

Study Design: We conducted a prospective observational trial of patients with vulvar or perianal Paget's disease treated with surgical excision guided by Mohs micrographic surgery

Clinical trial information: NCT03564483, study start date 2/19/2018 (https://clinicaltrials.gov/ct2/show/NCT03564483).

Presentations: These data were presented as an oral presentation at the Society for Gynecologic Oncology Winter Meeting in Whistler, BC, Canada on February 2–5, 2023.

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between 2018–2022. The multidisciplinary protocol consisted of office-based scouting biopsies and modified Mohs surgery followed by surgical excision with wound closure under general anesthesia. Modified Mohs surgery cleared peripheral disease margins using a moat technique with cytokeratin-7 staining. Medial disease margins (clitoris, urethra, vagina, anus) were assessed using a hybrid of Mohs surgery and intraoperative frozen sections. Surgical and oncologic outcomes were compared to a retrospective cohort of patients who underwent traditional surgical excision. The primary outcome was 3-year recurrence-free survival.

Results: Three-year recurrence-free survival was 93.3% for Mohs-guided excision (N=24, 95% confidence interval 81.5–100.0%) compared to 65.9% for traditional excision (N=63, 95% confidence interval 54.2–80.0%, p=0.04). Maximum diameter of the excisional specimen was similar between groups (median 11.3 cm vs 9.5 cm, p=0.17), but complex reconstructive procedures were more common with the Mohs-guided approach (66.7% vs 30.2%, p<0.01). Peripheral margin clearance was universally achieved with modified Mohs surgery, but positive medial margins were noted in nine patients. Reasons included intentional organ-sparing and poor performance of intraoperative hematoxylin and eosin frozen sections without cytokeratin-7. Grade three or greater postoperative complications were rare (0.0% for Mohs vs 2.4% for traditional, p=0.99).

Conclusions: Margin control with modified Mohs surgery significantly improved short-term recurrence-free survival after surgical excision for female genital Paget's disease. Use on medial anatomic structures (clitoris, urethra, vagina, anus) is challenging, and further optimization is needed for margin-control in these areas. Mohs-guided surgical excision requires specialized, collaborative care and may be best accomplished at designated referral centers.

Graphical Abstract

Mayo Clinic Multidisciplinary Surgery for EMPD

2	Gynecologic Oncology Consult	Study enrollment Age-specific cancer screenings
P	Dermatologic Surgery Consult	Office scouting biopsies
***	Multidisciplinary Consults	Urology Plastic surgery Colorectal surgery
	Mohs Surgery (Day 1)	Modified peripheral "moat" technique CK7 staining
×=	Surgical Excision (Day 2)	 Excision of Mohs-outlined tumor Examination of medial margins Wound closure and reconstruction
ф.	Follow-up and Surveillance	Post-op visit(s) Surveillance every 6 months

Keywords

Extramammary Paget's disease; vulvar Paget's disease; wide local excision; partial vulvectomy; skinning vulvectomy; radical vulvectomy; Mohs micrographic surgery; margin-controlled surgery; gender disparities; multidisciplinary surgery; cytokeratin 7 immunohistochemistry

1. Introduction

Extramammary Paget's disease (EMPD) is a dermatologic malignancy that typically presents as a red, pruritic plaque in the anogenital and axillary regions. Although rare, incidence in the US has increased more than two-fold since the early 1990s.¹ Clinical presentation is variable; while some lesions may be small or asymptomatic, others are very large, involve critical structures (e.g., clitoris, urethra, vagina, anus), and cause significant distress. EMPD is often limited to the epithelium (*in situ*) but does have the potential for invasion and metastasis.^{1–4} Several specialties treat EMPD, and until recently, there were no consensus guidelines regarding management.⁵ Because of this, there is a disparity in the treatment of female and male genital lesions.

Historically, gynecologic oncologists have treated female genital EMPD with wide local excision (WLE). Positive margins are common, as microscopic disease often exceeds gross visible disease.^{4,6,7} Recurrence rates after WLE are high, ranging between 0–58% with an aggregate rate of 37%.^{5,8–10} Increasingly, male genital EMPD is treated using a multidisciplinary approach that includes Mohs micrographic surgery (MMS) for margin control. Recurrence after MMS ranges between 0–33% with an aggregate rate of 11%.^{5,8,9} Even lower recurrence rates are reported with the use of cytokeratin-7 (CK7) immunohistochemical (IHC) stains during MMS.^{8,11,12} Given these data, recently published consensus guidelines propose margin-controlled surgery as recommended practice.⁵ Unfortunately, most of the cited studies reported primarily on male genital lesions. Few centers are performing MMS for female genital EMPD, and sample sizes in available literature are limited to fewer than fifteen.^{8,11,13–15} Female anatomy differs from male anatomy and includes areas that are technically difficult to assess in an outpatient setting.¹⁵ Thus, studies specific to female anatomy are needed to confirm effectiveness of a margin-controlled approach.

To address this disparity in management, we piloted a multidisciplinary treatment protocol for female genital EMPD that included modified Mohs surgery for margin control. We refer to our approach as MMS-guided WLE. The current study had two main objectives: to describe our initial experiences with MMS-guided WLE and to compare surgical and oncologic outcomes of MMS-guided WLE with traditional WLE. We hypothesized that MMS-guided WLE would result in superior recurrence-free survival (RFS) with acceptable morbidity.

2. Materials and Methods

This was a prospective observational trial approved by the Mayo Clinic Institutional Review Board and registered with the National Institute of Health (NCT03564483) prior

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to enrollment of the first study participant in 2018. All adult patients seen in consultation for histologically confirmed female genital EMPD were eligible for enrollment if they were willing and able to sign informed consent. Treatment approach was per patient and physician discretion and was not randomized. Trial enrollment included prospective collection of clinical data and tissue specimens. Participants who underwent the pilot approach of MMSguided WLE were included in the current analysis.

The MMS-guided WLE approach involved a multidisciplinary team including specialists from gynecologic oncology, dermatologic surgery, plastic surgery, colorectal surgery, urology, and internal medicine. The protocol began with preoperative consultations with surgical services pertinent to each patient's location and extent of disease (Figure 1). Officebased scouting (mapping) biopsies were performed to estimate disease borders, rule out invasion, and assess for involvement of functionally critical anatomy. Approximately four weeks later, a two-step surgical approach was undertaken that consisted of office-based MMS on day one followed by WLE with wound closure in the operating room on day two. A dermatologic surgeon performed MMS using a modified "moat" technique as previously described by our group.¹⁶ Negative peripheral margins were confirmed using sequential frozen pathology with CK7 IHC interpreted by the Mohs surgeon. The following day, a gynecologic oncologist and/or colorectal surgeon performed WLE to remove the bulk of the lesion. Perineal reconstruction was achieved using primary closure, flaps, or skin grafts with assistance from plastic surgery as needed. For lateralized lesions, 100% of disease margins were assessed using MMS (Figure 2). For lesions involving medial anatomic structures (i.e., clitoris, urethra, vagina, or anus), medial margins were assessed with a "hybrid" approach; MMS was used where feasible with local anesthesia, and visual inspection or intraoperative frozen section at the time of WLE was used for remaining medial margins (Figure 2). Frozen pathology at the time of WLE was performed with hematoxylin and eosin (H&E) staining alone given time constraints under general anesthesia (tissue processing with CK7 staining takes over an hour to complete per round of biopsies¹⁶). Surgical follow-up visits were conducted after 4-6 weeks, or earlier if perineal reconstruction was performed. Surveillance visits with thorough gynecologic examination were conducted every 4-6 months.

We compiled data from patients treated with MMS-guided WLE between 1/1/2018 and 06/30/2022. This prospective cohort was compared to a retrospective cohort of patients who underwent traditional WLE between 1/1/1990 and 12/31/2015. We included adult patients with a histologic diagnosis of primary or recurrent vulvar or perianal EMPD. Historic WLE patients were included only if sufficient information regarding surgery and pathology were available in the medical records. We excluded patients who declined research participation, who underwent surgery solely for palliation, and those with synchronous malignancies, including secondary Paget's disease associated with an adjacent invasive adenocarcinoma. Data for the MMS-guided WLE cohort were entered prospectively by research staff and validated by physician investigators (TPK, KHB). The WLE cohort was constructed from a previously published retrospective cohort at our institution.⁶ Clinical information from the original dataset was verified and augmented through chart review by the first author (KHB). WLE cases with documented dermal invasion were reviewed by a gynecologic pathologist to properly exclude cases with adjacent adenocarcinoma.

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The primary outcome was 3-year recurrence-free survival (RFS) analyzed using the Kaplan-Meier method. Secondary outcomes were overall survival (OS), operative time, surgical specimen size, type of wound closure, and postoperative complications. Operative time for final surgical excision was the time between incision and wound closure. Surgical specimen size was defined as the largest measurement of the excisional specimen by gross pathology. If the specimen was removed in two large portions, the excisional sizes were summed, but areas of iterative removal of small margin borders were not included. Wound closure type was grouped into four categories: primary closure (by either the primary surgical team or plastic surgery), advancement flap, rotational flap, or split-thickness skin graft. Patients who received both a flap and skin graft were included in the skin graft category. Postoperative complications within 30 days were graded based on the Expanded Accordion Scale.¹⁷ Grade 3+ complications involved repeat invasive procedures or organ failure. Minor complications (grade 1/2) included wound separations, surgical site infections, and urinary complications that required a maximum of wound packing or outpatient oral antibiotic treatment. Planned returns to the operating room for delayed skin grafting or anticipated wound cares (e.g. wound vac change) were not included as grade 3+ complications. Patient demographics, preoperative characteristics, and secondary outcomes were analyzed using the chi-square or Fisher's exact test for categorical outcomes and two-sample t-tests or nonparametric tests for continuous outcomes.

In addition to comparative analyses between MMS-guided WLE and WLE cohorts, we recorded descriptive statistics for the prospective cohort including Mohs stages, tumor measurements, and final margin status. We defined the number of Mohs stages as the number of iterations of margin excision and histologic examination required to obtain negative margins. Gross vs microscopic tumor size was the largest measurement of the lesion visible to the naked vs outlined by MMS. For patients with both measurements documented, we calculated the difference between gross and microscopic tumor size. Final margin status was defined by MMS with CK7 for peripheral margins and permanent surgical pathology with CK7 for medial margins. Test characteristics of intraoperative H&E frozen section were compared to the standard of CK7 permanent section.

3. Results

In the prospective cohort (MMS-guided WLE), 24 patients met inclusion criteria. In the retrospective cohort (WLE), 63 patients met inclusion criteria. Details of the full retrospective cohort were previously published.⁶ Demographic and preoperative characteristics of both cohorts are shown in Table 1. Patients who underwent MMS-guided WLE were younger than those who underwent WLE (mean age 65.2 vs. 70.3 years, p=0.04). Most patients were non-Hispanic White. The perianal skin was involved in approximately one third of patients. More patients in the MMS-guided WLE cohort were presenting for treatment of a recurrent lesion (25.0% vs 9.5%, p=0.04). One patient (4.2%) in the MMS-guided WLE cohort and three patients (4.8%) in the WLE cohort had microinvasive disease. A single patient in the MMS-guided WLE cohort had a diagnostic biopsy consistent with non-invasive disease but was found to have invasive disease on final excision (2 mm depth of invasion, classified as primary EMPD). Postoperative evaluation revealed an inguinal lymph node metastasis, which was successfully treated with primary radiation to the groin.

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81.5–100.0%). A single patient with non-invasive perianal disease experienced recurrence within three years of MMS. At the time of her initial surgery, negative anal margins were not pursued to preserve anal function. She recurred in the perianal area after 1.5 years and was treated with repeat MMS-guided WLE. Median follow-up duration for the remaining 23 patients without recurrence was 2.3 years (interquartile range, IQR, 1.0-3.3 years).

Three-year RFS in the WLE cohort was 65.9% (95% CI 54.2–80.0%). Eighteen patients experienced recurrence within three years of WLE (at a median of 1.6 years, IQR 0.7-2.1 years). Median number of recurrences was 2 with a range of 1 to 6. Recurrences were treated with surgery (14 patients), topical imiquimod (4 patients), carbon dioxide laser (2 patients), and observation (1 patient); some patients had recurrent treatments and/or multiple treatment modalities. Median follow-up duration for the remaining 45 patients without recurrence was 5.2 years (IQR 2.5–8.2 years). A Kaplan-Meier curve of RFS is presented in Figure 3. Three-year OS was 100% in both groups.

Secondary surgical outcomes are shown in Table 2. Median operative time for WLE and wound closure was not significantly different between groups. More patients in the MMSguided cohort had a perineal reconstructive procedure (66.7% vs 30.2%, p<0.01). One patient in the MMS-guided cohort required planned return to the OR for delayed skin grafting. One patient in the WLE cohort experienced a grade 3+ surgical complication (wound separation and infection after perianal WLE due to fecal incontinence that required a take-back operation for wound debridement and colostomy). Minor wound complications were observed in 66.7% of patients in the MMS-guided WLE cohort and were most often focal wound separations. A similar detailed description of minor events was not available for the WLE cohort.

We recorded and compared multiple measurements of lesion size in the MMS-guided WLE cohort (Table 3). Among 16 patients with all measurements, median gross visible size (determined by examination) was 3.5 cm (IQR 3.0-4.3 cm), and median microscopic size (determined by MMS) was 9.0 cm (IQR 7.0–11.9 cm). The median difference between gross visible and microscopic size was 5.6 cm (IQR 3.7–8.1 cm). The 8 patients who did not have both measurements tended to have larger tumors that were described but not measured on preoperative evaluation. Median microscopic tumor size among these 8 patients was 15.8 cm (IQR 12.5–20.9 cm, data not shown). In the WLE cohort, measurements of gross visible and microscopic lesion sizes were not available; therefore, the largest measurement of the main surgical specimen (determined by gross pathology) was recorded for comparison (Table 2). Surgical specimen size did not differ significantly between groups (MMS-guided WLE: median 11.3 cm, IQR 7.5-14.0 cm; WLE: median 9.6 cm, IQR 6.9-13.0 cm; p=0.20).

To contextualize final margin status, we categorized patients in the MMS-guided WLE cohort into two groups: lateralized vs medial lesions (Figure 2). Eight patients (33.3%) had lateralized lesions, whereas sixteen patient (67.7%) had medial lesions (Table 3). Final margins were negative in 8/8 and 7/16 patients with lateralized and medial lesions, respectively. Of the 9 patients with a positive medial margin, 4 were left intentionally positive to preserve organ function, whereas 5 were unexpected on final pathology and

largely due to the limitations in the performance of H&E frozen section without CK7 IHC. One patient underwent re-excision of an unexpected positive anal margin with a resultant complete negative margin. Given that positive margins were noted on final pathology despite frozen section assessment during surgical excision, test characteristics of H&E frozen section without CK7 were calculated. Among 15 patients who underwent frozen section, sensitivity was 28.5% and specificity was 100%. Positive and negative predictive values were 100% and 61.5%, respectively (data not shown).

Additional descriptive outcomes for MMS are shown in Table 3. Patients underwent a median of 13 scouting biopsies (IQR 7–17) for procedural planning. A median of two Mohs stages were required for margin clearance (range 1–5). Total time required for the MMS process was not easily quantifiable due to variations in lesion size and number of stages. A previous publication from our group estimated that each stage takes 15–90 minutes for tissue excision and mapping and an additional 1–3 hours for tissue processing and immunostaining¹⁶. Patients are made comfortable during tissue mapping, processing, and staining, but often spend a large portion of their day in the MMS suite.

4. Comment

Principal Findings

This prospective pilot study supports the effectiveness and safety of margin-controlled surgery for female genital Paget's disease. Three-year RFS after MMS-guided WLE was 93%, which was statistically superior to traditional WLE (66%, p=0.04). In patients with lateralized lesions, no recurrences were observed after MMS. In patients with medial lesions, only one recurrence was observed, which occurred in a patient with an anal margin that was left intentionally positive for preservation of function. Safety of the MMSguided approach was acceptable with no grade 3+ surgical complications. While surgical specimen size was similar to traditional WLE, MMS-guided WLE patients required more complex reconstructive procedures. Additionally, MMS-guided WLE required a multiday time commitment and significant interdisciplinary collaboration. Two-thirds of patients had medial lesions that could not be completely assessed using in-office MMS. This complexity may be reflective of our referral population, which disproportionately included recurrent disease and disease spanning large areas. Medial margins were assessed using intraoperative frozen sections with H&E staining, which failed to detect disease identified on final permanent sections with CK7. Optimizing evaluation and treatment of challenging medial anatomy (i.e., clitoris, urethra, vagina, and anus) may further lower recurrence rates.

Results in Context of What is Known

Our prospective results corroborate prior retrospective studies demonstrating superiority of a margin-controlled surgical approach for genital EMPD in male and mixed male and female cohorts.^{5,6,8,11,13,14,18–21} Our results highlight the efficacy of margin-controlled surgery in a female only, prospective cohort, strengthening the supporting evidence. Female anatomy includes medial structures that differ notably from male anatomy. In our study, there was a distinction between patients with lateralized and medial lesions. In the 8 patients with lateralized lesions requiring assessment of peripheral margins only, MMS was universally

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successful. Conversely, 16 patients with medial lesions required a hybrid assessment of medial margins due to limitations of office-based MMS; 9 were ultimately found to have a positive margin on final pathology. This was at times intentional to preserve organ function and at times a result of limitations of H&E frozen section without CK7. Superiority of CK7 staining has been previously documented and was confirmed in our study; thus, CK7 should be considered standard for pathologic evaluation of EMPD when feasible.^{5,8,11,12} We did not directly compare margin status between the MMS-guided and traditional excision cohorts given that historic surgical pathology used a "bread-loafing" sectioning technique without universal CK7 IHC that likely resulted in an indeterminable number of false negative results.⁶

Clinical Implications

Criticisms of using the margin-controlled approach for EMPD have included the hypothesis that this approach leads to larger excision size and higher morbidity compared to traditional excision.³ We found that surgical specimen size was not significantly different between MMS-guided and traditional WLE. One possible explanation is improved accuracy. In the past, surgeons performing WLE outlined a wide boundary in hopes of achieving negative margins around disease not grossly visible. In contrast, MMS precisely outlines disease margins, with excision of more tissue where disease is microscopically present and less tissue where disease is microscopically absent. It is important to note that our referral population likely included a higher percentage of large, complex, and recurrent lesions, which may have influenced this result. The MMS-guided WLE cohort did require significantly more reconstructive procedures for wound closure. Our reported rate (66.7%) was slightly lower than the rate reported in the urology literature (80%).⁸ It is unclear whether the increase in reconstructive procedures was due to the location or complexity of surgical defects after MMS or the integration of multidisciplinary care into the contemporary protocol.

Research Implications

Optimal evaluation of medial disease will be the basis for future investigation and protocol refinement at our institution. Is it also important to note that measures of morbidity in our study were limited to short-term surgical complications. More investigation is warranted to understand patient-reported outcomes (PRO) and long-term morbidity, as there is a paucity of data in the literature. One study in the urology literature reported high patient satisfaction with scar appearance and sexual function⁸, but no validated questionnaires nor qualitative methods were employed. As part of our prospective trial, participants completed multiple validated PRO questionnaires at various time points throughout their treatment course. These data, along with qualitative assessments of treatment impact, will be presented in forthcoming reports.

Strengths and Limitations

The implemented approach was a highly collaborative effort that included prospective data collection and detailed information about margin assessment and final margin status. The current study includes the largest prospective cohort of patients with female genital EMPD treated with MMS and the first to specifically address female anatomy. Additionally, our

approach incorporated a realistic balance of optimal histologic margin assessment, patient comfort, and technical challenges. We acknowledge several limitations. First, the study was conducted in a single hospital system with institutional support for collaborative care; therefore, results may not be easily generalizable. The intervention is resource intensive and may not be feasible in all centers. As is the case in all single institution studies of EMPD, sample size was limited by the rarity of diagnosis. This limited statistical analyses by precluding multivariable analysis to adjust for potential confounding variables. Additionally, referral patterns likely contributed to a more complex cohort than is likely to be found in community practice. Finally, we chose to evaluate early recurrence events (i.e., 3-year RFS) to evaluate and improve an ongoing pilot approach, but long-term follow-up will be important to understand risk of late recurrence and secondary malignancy.

Conclusions

Mohs surgery appears to be a safe and effective adjunct to traditional surgical excision for female genital Paget's disease. Use of CK7 IHC during MMS identifies significant occult disease through comprehensive peripheral margin assessment. Assessment of critical medial structures remains a challenge, and protocol adjustments will focus on optimizing margin assessment in these areas. Thorough preoperative counseling and assessment of patient priorities are essential, especially when critical medial structures are involved. Future investigations addressing patient reported outcomes may aid in understanding the full impact of this approach. Improved access to MMS may narrow the current gender disparity in EMPD outcomes, but consideration should be given to treatment at expert centers given the rarity of the diagnosis and specialized treatment approach.

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AJOG at a Glance:

Why was this study conducted?

- There is a sex-based disparity in surgical approach for genital Paget's disease.
- Studies on male genital disease suggest Mohs surgery improves cancer control.

What are the key findings?

- In a prospective cohort of patients with female genital Paget's disease, adding Mohs surgery to traditional surgical excision resulted in superior three-year recurrence-free survival.
- Microscopic (subclinical) disease extended significantly beyond gross visible disease (median difference >5 cm).
- CK7 immunohistochemical staining was superior to H&E staining alone for margin assessment.
- We identified unique challenges in the management of urethral, vaginal, and anal disease margins.

What does this study add to what is already known?

- Our results confirm that multidisciplinary surgical care inclusive of Mohs surgery is beneficial for female genital Paget's disease.
- Margin-control for female vs male genital disease is unique owing to the anatomy of natural orifices; optimal technique for medial disease requires further optimization.

Condensation:

Tweetable statement:

Surgery for vulvar Paget's disease is more effective when Mohs micrographic surgery is added for margin control.

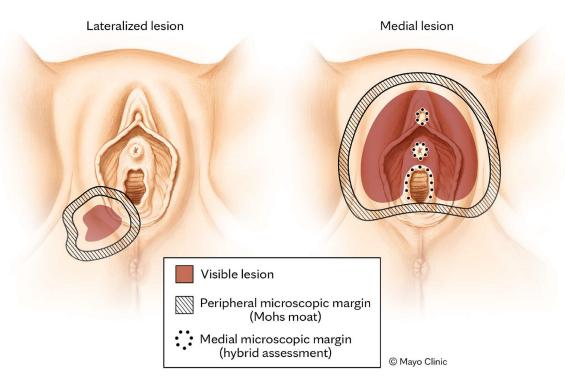


Figure 1. Title: Mohs-guided surgical excision multidisciplinary treatment pathway.

Legend: Abbreviations: MMS, Mohs micrographic surgery; WLE, wide local excision; CK7, cytokeratin 7; Post-op, postoperative.

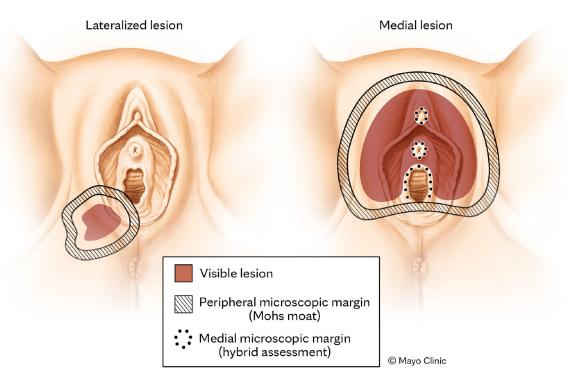


Figure 2. Title: Methods of margin control based on lesion location.

Legend: Mohs moat refers to modified peripheral Mohs micrographic surgery; hybrid assessment refers to an individualized combination of Mohs moat, intraoperative frozen sections at the time of wide local excision, and surgeon visual assessment.

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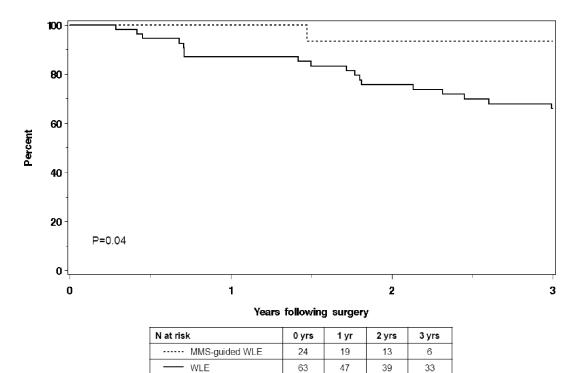


Figure 3. Title: Recurrence-free survival by surgical cohort.

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Legend: Abbreviations: MMS, Mohs micrographic surgery; WLE, wide local excision; yrs, years.

Table 1:

Demographics and preoperative characteristics

Characteristic	MMS-guided WLE N=24	WLE N=63	P [†]
Age at Page s surgery (years), mean (SD)	65.2 (9.5)	70.3 (10.5)	0.04
Race			0.06
Caucasian/White	22 (91.7)	60 (95.2)	
Asian Pacific Islander	2 (8.3)	-	
Unknown	-	3 (4.8)	
Ethnicity			< 0.0
Not Hispanic / Latina	24 (100.0)	41 (65.1)	
Unknown	-	22 (34.9)	
Smoking history			0.12
Never	20 (83.3)	44 (69.8)	
Former	3 (12.5)	12 (19.0)	
Current	1 (4.2)	-	
Unknown	-	7 (11.1)	
Primary site			0.51
Genital (vulvar, periclitoral, and/or vaginal)	15 (62.5)	44 (69.8)	
Perianal	3 (12.5)	10 (15.9)	
Genital and perianal	6 (25.0)	9 (14.3)	
Disease status at time of treatment			0.04
Primary	17 (70.8)	57 (90.5)	
Recurrent	6 (25.0)	6(9.5)	
Unknown	1 (4.2)	-	
Depth of invasion			0.32
No invasion (in situ)	22 (91.7)	60 (95.2)	
Superficial / focal (1 mm)	1 (4.2)	3 (4.8)	
Invasion (>1 mm)	1 (4.2)	-	

Abbreviations: ECOG, Eastern Cooperative Onco ogy Group; MMS, Mohs micrographic surgery; SD, standard deviation; WLE, wide local excision.

Results are N and % unless otherwise specified.

[†]T-test P value presented for age and chi-square or Fisher's exact test P value presented for the categorical variables.

Table 2:

Surgical outcomes

Characteristic	MMS-guided WLE N=24	WLE N=63	₽ [†]
Operative time for WLE & closure (minutes)			0.08
Median (IQR)	156(99, 219)	103 (80, 142)*	
Type of reconstructive procedure			0.01
None	8 (33.3)	44 (69.8)	
Advancement flap	9 (37.5)	12 (19.0)	
Rotational flap	4 (16.7)	4(6.3)	
Skin graft	3 (12.5)	3 (4.8)	
Grade 3+ surgical complication			0.99
No	24 (100.0)	40/41 (97.6)	
Yes	-	1/41 (2.4)	
Surgical specimen size (cm)			0.20
Median (IQR)	11.3 (7.5, 14.0)	9.6 (6.9, 13.0)*	

Abbreviations: IQR, interquartile range; MMS, Mohs micrographic surgery; SD, standard deviation; WLE, wide local excision.

Results are N and % unless otherwise specified.

 † Wilcoxon rank-sum P value presented for continuous variables and Fisher's exact test P value presented for the categorical variables.

* In the WLE cohort, 26 patients were missing operative time and 6 patients were missing surgical specimen size

Table 3:

Descriptive statistics for MMS-guided WLE cohort

Characteristic	N=24
Gross visible tumor size	
Ν	16
Median (IQR)	3.5 (3.0, 4.3)
Microscopic tumor size	
Ν	16
Median (IQR)	9.0 (7.0, 11.9)
Difference between gross and microscopic tumor size	
Ν	16
Median (IQR)	5.6 (3.7, 8.1)
Number of scouting biopsies, median (IQR)	13 (7, 17)
Number of MMS stages, median (IQR)	2 (1, 3)
Lesion location	
Lateralized	8 (33.3)
Medial	16 (66.7)
Type of surgical excision	
Partial vulvectomy/wide local excision	19 (79.2)
Radical vulvectomy	3 (12.5)
Other (vulvectomy with total vaginectomy)	2 (8.3)
Specialty surgeons involved in excision and closure (count)	
Gynecologic oncology	23
Plastic surgery	19
Colorectal surgery	4
Urology	1

Abbreviations: IQR, interquartile range; MMS, Mohs micrographic surgery.

Results are N and % unless otherwise specified.