

Barriers to Mohs Micrographic Surgery in Japanese Patients With Basal Cell Carcinoma

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PRACTICE POINTS

- Mohs micrographic surgery (MMS) is a safe and effective treatment method for nonmelanoma skin cancer. In some cases, this procedure is superior to standard wide local excision and repair.
- For the broader adaptation of this vital technique in Japan—where MMS is not well established—increased awareness of treatment outcomes among Japanese physicians is needed.

Mohs micrographic surgery (MMS) is a well-recognized treatment for nonmelanoma skin cancer worldwide, but Japan has lagged behind many other countries in adopting MMS. We present a series of 5 cases of MMS utilized in Japanese patients. All cases had a favorable outcome, each benefiting from MMS with a smaller final defect or a higher likelihood of cure than standard excision. Slow adaptation of MMS in Japan likely is due to a lack of familiarity with the technique, lack of a training pipeline for physicians, barriers to payment for the procedure, and misconceptions among Japanese physicians. Our case series demonstrates the utility of MMS in treating skin cancer among Japanese patients.

Margin-controlled surgery for squamous cell carcinoma (SCC) on the lower lip was first performed by Dr. Frederic Mohs on June 30, 1936. Since then, thousands of skin cancer surgeons have refined

and adopted the technique. Due to the high cure rate and sparing of normal tissue, Mohs micrographic surgery (MMS) has become the gold standard treatment for facial and special-site nonmelanoma skin cancer worldwide. Mohs micrographic surgery is performed on more than 876,000 tumors annually in the United States.¹ Among 3.5 million Americans diagnosed with nonmelanoma skin cancer in 2006, one-quarter were treated with MMS.² In Japan, basal cell carcinoma (BCC) is the most common skin malignancy, with an incidence of 3.34 cases per 100,000 individuals; SCC is the second most common, with an incidence of 2.5 cases per 100,000 individuals.³

The essential element that makes MMS unique is the careful microscopic examination of the entire margin of the removed specimen. Tissue processing is done with careful en face orientation to ensure that circumferential and deep margins are entirely visible. The surgeon interprets the slides and proceeds to remove the additional tumor as necessary. Because the same physician performs both the surgery and the pathologic assessment throughout the procedure, a precise correlation between the microscopic and surgical findings can be made. The surgeon can begin with smaller margins, removing minimal healthy tissue while removing all the cancer cells, which results in the smallest-possible skin defect and the best prognosis for the malignancy (Figure 1).

At the only facility in Japan offering MMS, the lead author (S.S.) has treated 52 lesions with MMS in 46 patients (2020-2022). Of these patients, 40 were White,

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5 were Japanese, and 1 was of African descent. In this case series, we present 5 Japanese patients who had BCC treated with MMS.

Case Series

Patient 1—A 50-year-old Japanese woman presented to dermatology with a brown papule on the nasal tip of 1.25 year's duration (Figure 2). A biopsy revealed infiltrative BCC (Figure 3), and the patient was referred to the dermatology department at a nearby university hospital. Because the BCC was an aggressive variant,

wide local excision (WLE) with subsequent flap reconstruction was recommended as well as radiation therapy. The patient learned about MMS through an internet search and refused both options, seeking MMS treatment at our clinic. Although Japanese health insurance does not cover MMS, the patient had supplemental private insurance that did cover the cost. She provided consent to undergo the procedure. Physical examination revealed a 7.5×6-mm, brown-red macule with ill-defined borders on the tip of the nose. We used a 1.5-mm margin for the first stage of MMS (Figure 4A). The frozen section revealed that the tumor had been entirely excised in the first stage, leaving only a 10.5×9-mm skin defect that was reconstructed with a Dufourmental flap (Figure 4B). No signs of recurrence were noted at 3.5-year follow-up, and the cosmetic outcome was favorable (Figure 4C). National Comprehensive Cancer Network guidelines recommend a margin greater than 4 mm for infiltrative BCCs⁴; therefore, our technique

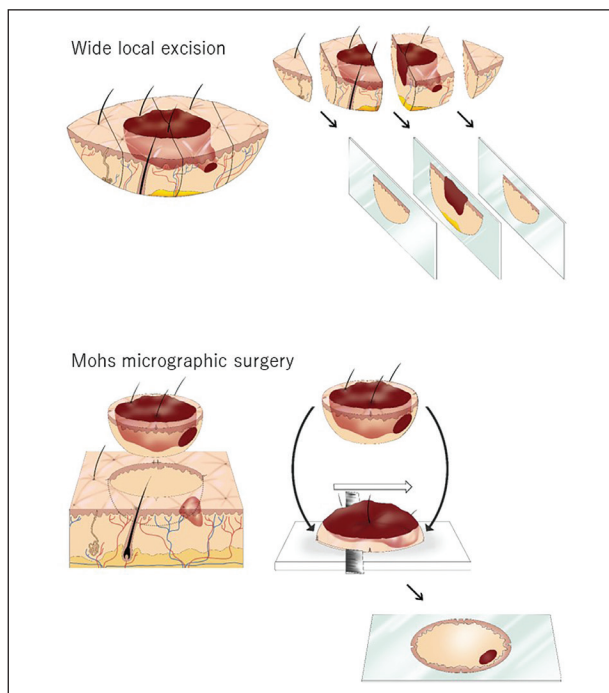


FIGURE 1. Illustration of conventional wide local excision and Mohs micrographic surgery (MMS) specimens. In wide local excision, the tumor is removed with a 3- to 10-mm margin of normal skin. The specimen is fixed with formalin and then vertically sectioned every 2 to 3 mm (bread-loafed) to create a thin representative slice. Each representative slice appears to show clear margins. In reality, the tumor remains between the second and the third slices, which leads to a false-positive interpretation. Even when positive markings are identified on pathology, lacking precision on the exact location of the residual tumor will require the surgeon to excise the entire scar, resulting in an unnecessarily large surgical defect. With MMS, the tumor is excised with a 1- to 2-mm margin of normal skin. There are small incisions at the 12-, 3-, 6-, and 9-o'clock positions to provide orientation. The specimen's entire cut surface is placed on a plane, frozen, cut, and mounted on a glass slide. It is stained with hematoxylin and eosin and evaluated by the Mohs surgeon, who examines the glass slide under a microscope to determine the presence of tumor cells and draws a map of any residual tumor location(s). In this example, tumor cells are seen as dark brown around the 4-o'clock position in the superficial to mid dermis. If any tumor cells remain at the margin, the process is repeated, with additional layers only taking residual tumor until the Mohs surgeon confirms that margins are clear. Once the tumor is excised entirely, the wound is repaired, usually by the same surgeon on the same day. Illustration courtesy of Moeno Watanabe.



FIGURE 2. A 50-year-old Japanese woman with a 7.5×6-mm brown papule with focally dense pigmentation on the tip of the nose that was confirmed via histopathology as an infiltrative basal cell carcinoma.

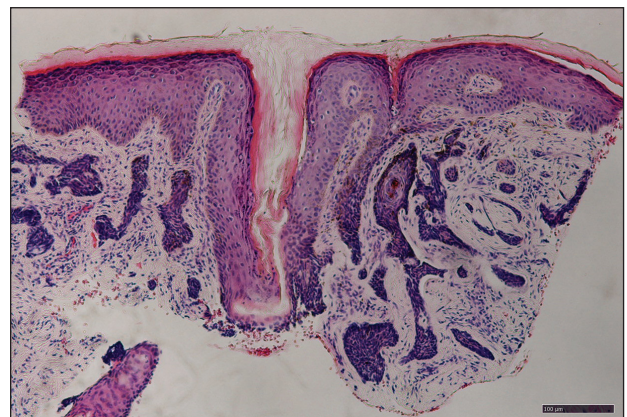


FIGURE 3. Histopathology of a lesion on the nose revealed infiltrative basal cell carcinoma (H&E, original magnification ×40). Reference bar indicates 100 μm.

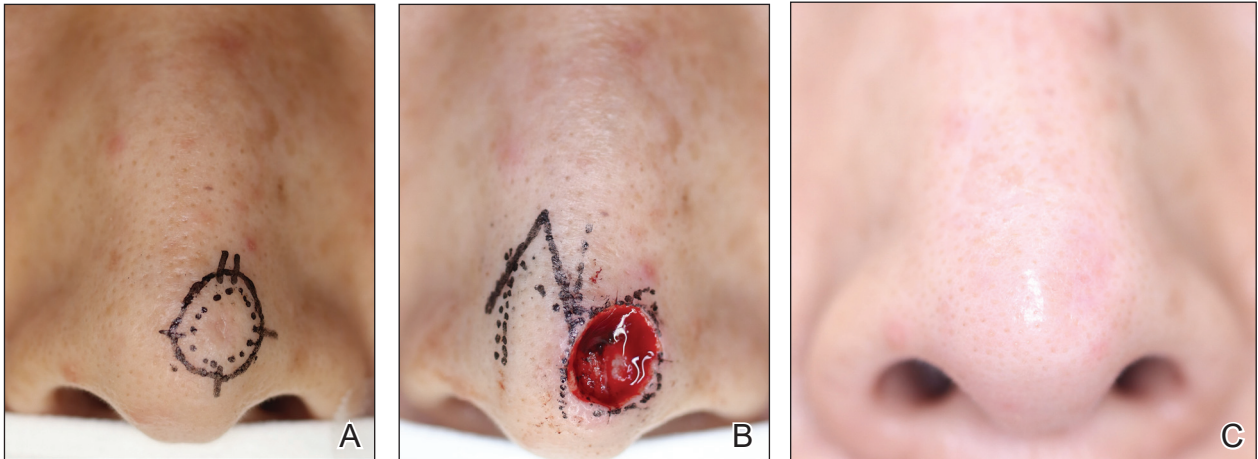


FIGURE 4. An infiltrative basal cell carcinoma was treated with Mohs micrographic surgery. A, A 1.5-mm margin was taken for the initial stage. B, A 10.5×9-mm skin defect was reconstructed with a Dufourmental flap. C, At 2.5-year follow-up, there were no signs of recurrence with a favorable outcome.

reduced the total defect by at least 4 mm in a cosmetically sensitive area. The patient also did not need radiation therapy, which reduced morbidity. She continues to be recurrence free at 3.5-year follow-up.

Patient 2—A 63-year-old Japanese man presented to dermatology with a brown macule on the right lower eyelid of 2 years' duration. A biopsy of the lesion was positive for nodular BCC. After being advised to undergo WLE and extensive reconstruction with plastic surgery, the patient learned of MMS through an internet search and found our clinic. Physical examination revealed a 7×5-mm brown macule on the right lower eyelid. The patient had supplemental private insurance that covered the cost of MMS, and he provided consent for the procedure. A 1.5-mm margin was taken for the first stage, resulting in a 10×8-mm defect superficial to the orbicularis oculi muscle. The frozen section revealed residual tumor exposure in the dermis at the 9- to 10-o'clock position. A second-stage excision was performed to remove an additional 1.5 mm of skin at the 9- to 12-o'clock position with a thin layer of the orbicularis oculi muscle. The subsequent histologic examination revealed no residual BCC, and the final 13×9-mm skin defect was reconstructed with a rotation flap. There were no signs of recurrence at 2.5-year follow-up with an excellent cosmetic outcome.

Patient 3—A 73-year-old Japanese man presented to a local university dermatology clinic with a new papule on the nose. The dermatologist suggested WLE with 4-mm margins and reconstruction of the skin defect 2 weeks later by a plastic surgeon. The patient was not satisfied with the proposed surgical plan, which led him to learn about MMS on the internet; he subsequently found our clinic. Physical examination revealed a 4×3.5-mm brown papule on the tip of the nose. He understood the nature of MMS and chose to pay out-of-pocket because Japanese health insurance did not cover the procedure. We used a 2-mm margin for the first stage,

which created a 7.5×7-mm skin defect. The frozen section pathology revealed no residual BCC at the cut surface. The skin defect was reconstructed with a Limberg rhombic flap. There were no signs of recurrence at 1.5-year follow-up with a favorable cosmetic outcome.

Patient 4—A 45-year-old man presented to a dermatology clinic with a papule on the right side of the nose of 1 year's duration. A biopsy revealed the lesion was a nodular BCC. The dermatologist recommended WLE at a general hospital, but the patient refused after learning about MMS. He subsequently made an appointment with our clinic. Physical examination revealed a 7×4-mm white papule on the right side of the nose. The patient had private insurance that covered the cost of MMS. The first stage was performed with 1.5-mm margins and was clear of residual tumor. A Limberg rhombic flap from the adjacent cheek was used to repair the final 10×7-mm skin defect. There were no signs of recurrence at 1 year and 9 months' follow-up with a favorable cosmetic outcome.

Patient 5—A 76-year-old Japanese woman presented to a university hospital near Tokyo with a black papule on the left cutaneous lip of 5 years' duration. A biopsy revealed nodular BCC, and WLE with flap reconstruction was recommended. The patient's son learned about MMS through internet research and referred her to our clinic. Physical examination revealed a 7×5-mm black papule on the left upper lip. The patient's private insurance covered the cost of MMS, and she consented to the procedure. We used a 2-mm initial margin, and the immediate frozen section revealed no signs of BCC at the cut surface. The 11×9-mm skin defect was reconstructed with a Limberg rhombic flap. There were no signs of recurrence at 1.5-year follow-up with a favorable cosmetic outcome.

Comment

We presented 5 cases of MMS in Japanese patients with BCC. More than 7000 new cases of nonmelanoma skin

cancer occur every year in Japan.³ Only 0.04% of these cases—the 5 cases presented here—were treated with MMS in Japan in 2020 and 2021, in contrast to 25% in the United States in 2006.²

MMS vs Other BCC Treatments—Mohs micrographic surgery offers 2 distinct advantages over conventional excision: an improved cure rate while achieving a smaller final defect size, generally leading to better cosmetic outcomes. Overall 5-year recurrence rates of BCC are 10% for conventional surgical excision vs 1% for MMS, while the recurrence rates for SCC are 8% and 3%, respectively.⁵ A study of well-demarcated BCCs smaller than 2 cm that were treated with MMS with 2-mm increments revealed that 95% of the cases were free of malignancy within a 4-mm margin of the normal-appearing skin surrounding the tumor.⁶ Several articles have reported a 95% cure rate or higher with conventional excision of localized BCC,⁷ but 4- to 5-mm excision margins are required, resulting in a greater skin defect and a lower cure rate compared to MMS.

Aggressive subtypes of BCC have a higher recurrence rate. Rowe et al⁸ reported the following 5-year recurrence rates: 5.6% for MMS, 17.4% for conventional surgical excision, 40.0% for curettage and electrodesiccation, and 9.8% for radiation therapy. Primary BCCs with high-risk histologic subtypes has a 10-year recurrence rate of 4.4% with MMS vs 12.2% with conventional excision.⁹ These findings reveal that MMS yields a better prognosis compared to traditional treatment methods for recurrent BCCs and BCCs of high-risk histologic subtypes.

The primary reason for the excellent cure rate seen in MMS is the ability to perform complete margin assessment. Peripheral and deep en face margin assessment (PDEMA) is crucial in achieving high cure rates with narrow margins. In WLE (Figure 1), vertical sectioning (also known as bread-loafing) does not achieve direct visualization of the entire surgical margin, as this technique only evaluates random sections and does not achieve PDEMA.¹⁰ The bread-loafing method is used almost exclusively in Japan and visualizes only 0.1% of the entire margin compared to 100% with MMS.¹¹ Beyond the superior cure rate, the MMS technique often yields smaller final defects compared to WLE. All 5 of our patients achieved complete tumor removal while sparing more normal tissue compared to conventional WLE, which takes at least a 4-mm margin in all directions.

Barriers to Adopting MMS in Japan—There are many barriers to the broader adoption of MMS in Japan. A guideline of the Japanese Dermatological Association says, MMS “is complicated, requires special training for acquisition, and requires time and labor for implementation of a series of processes, and it has not gained wide acceptance in Japan because of these disadvantages.”³ There currently are no MMS training programs in Japan. We refute this statement from the Japanese Dermatological Association because, in our experience, only 1 surgeon plus a single histotechnician familiar with

MMS is sufficient for a facility to offer the procedure (the lead author of this study [S.S.] acts as both the surgeon and the histotechnician). Another misconception among some physicians in Japan is that cancer on ethnically Japanese skin is uniquely suited to excision without microscopic verification of tumor clearance because the borders of the tumors are easily identified, which was based on good cure rates for the excision of well-demarcated pigmented BCCs in a Japanese cohort. This study of a Japanese cohort investigated the specimens with the conventional bread-loafing technique but not with the PDEMA.¹²

Eighty percent (4/5) of our patients presented with nodular BCC, and only 1 required a second stage. In comparison, we also treated 16 White patients with nodular BCC with MMS during the same period, and 31% (5/16) required more than 1 stage, with 1 patient requiring 3 stages. This cohort, however, is too small to demonstrate a statistically significant difference (S.S., unpublished data, 2020-2022).

A study in Singapore reported the postsurgical complication rate and 5-year recurrence rate for 481 tumors (92% BCC and 7.5% SCC). The median follow-up duration after MMS was 36 months, and the recurrence rate was 0.6%. The postsurgical complications included 11 (2.3%) cases with superficial tip necrosis of surgical flaps/grfts, 2 (0.4%) with mild wound dehiscence, 1 (0.2%) with minor surgical site bleeding, and 1 (0.2%) with minor wound infection.¹³ This study supports the notion that MMS is equally effective for Asian patients.

Awareness of MMS in Japan is lacking, and most Japanese dermatologists do not know about the technique. All 5 patients in our case series asked their dermatologists about alternative treatment options and were not offered MMS. In each case, the patients learned of the technique through internet research.

The lack of insurance reimbursement for MMS in Japan is another barrier. Because the national health insurance does not reimburse for MMS, the procedure is relatively unavailable to most Japanese citizens who cannot pay out-of-pocket for the treatment and do not have supplemental insurance. Mohs micrographic surgery may seem expensive compared to WLE followed by repair; however, in the authors' experience, in Japan, excision without MMS may require general sedation and multiple surgeries to reconstruct larger skin defects, leading to greater morbidity and risk for the patient.

Conclusion

Mohs micrographic surgery in Japan is in its infancy, and further studies showing recurrence rates and long-term prognosis are needed. Such data should help increase awareness of MMS among Japanese physicians as an excellent treatment option for their patients. Furthermore, as Japan becomes more heterogeneous as a society and the US Military increases its presence in the region, the need for MMS is likely to increase.

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