Original Article

A retrospective review of Mohs micrographic surgery trends over more than 10 years in Saudi Arabia

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ABSTRACT

الأهداف: دراستنا لمراجعة عمليات موس الدقيقة التي أجريت في المملكة العربية السعودية. جراحة موس الدقيقة هي تقنية جراحية دقيقة أثبتت أنها تتمتع بأعلى معدل شفاء مع الحفاظ على الأنسجة الطبيعية لأقصى درجة. يعتبر من أفضل الطرق الجراحية لإزالة سرطانات الجلد غير الميلانيني، وخاصة ذات لأنسجة العدوانية ، والأورام الموجودة في المناطق عالية الخطورة أو حيث يكون الحفاظ على الأنسجة أمرًا ضروريًا.

المنهجية: تم إجراء دراسة حشدية متعددة المراكز على المرضى الذين خضعوا لجراحة موس الدقيقة بين يناير 2010م وسبتمبر 2022م. تم استخلاص المعلومات من قاعدة بيانات المدينة الطبية بجامعة الملك سعود ومدينة الأمير سلطان العسكرية الطبية في المملكة العربية السعودية.

النتائج: تم تسجيل ما مجموعه 70 مشاركًا في هذه الدراسة. ثلثا (67%) الأورام التي تم علاجها باستخدام جراحة موس الدقيقة كانت سرطانات الخلايا القاعدية، 18.6% كانت سرطانات الخلايا الحرشفية، 5.7% كانت سرطانية دهنية ، 4.3% كانت ساركومة ليفية جلدية، و 1.4% كانت أورام نادرة مثل سرطان مخاطي أولي. كان النوع الأكثر شيوعًا من عمليات الترميم هو الإغلاق الأولي في أكثر من نصف المرضى. لم تكن هناك آثار جانبية باستثناء ورم دموي في مريض واحد وعدوى جرح في مريضين.

الخلاصة: على الرغم من أن جراحة موس الدقيقة لا تزال غير منتشرة بشكل عام في المملكة العربية السعودية ، فقد زاد استخدامها في العقد الماضي.

Objectives: To review Mohs micrographic surgery (MMS) trends in Saudi Arabia.Mohs micrographic surgery is a precise surgical technique that has been proven to have the highest cure rate with maximum normal tissue preservation. It is the treatment of choice for non-melanoma skin cancer (NMSC), especially the aggressive histopathological forms, and tumors located in high-risk regions or where tissue preservation is a mandate.

Methods: A multicentric retrospective study was performed on patients who underwent MMS between January 2010 and September 2022. The information was extracted from the database of King Saud University Medical City and Prince Sultan Military Medical City in Saudi Arabia.

Results: A total of 70 participants were enrolled in this study. Two-thirds (67%) of the tumors that were treated using MMS were basal-cell carcinomas (BCC), 18.6% were squamous cell carcinomas (SCC), 5.7% were sebaceous carcinoma, 4.3% were dermatofibrosarcoma protuberans (DFSP), and 1.4% were rare tumors such as primary mucinous carcinoma. The most common type of reconstruction used to repair post-MMS defect was primary closure in more than half of the patients followed by secondary intention healing (20%). There were no side effects apart from a hematoma in one patient and wound infection in two patients.

Conclusion: Although MMS is still generally underutilized in Saudi Arabia, its use has increased in the last decade.

Keywords: retrospective, review, Mohs, micrographic, surgery, MMS, skin cancer, BCC, SCC, DFSP, sebaceous carcinoma, basosquamous carcinoma, mucinous carcinoma, Riyadh, Saudi Arabia, KSA

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Non-melanoma skin cancer (NMSC) is considered to be the most common skin malignancy globally. According to estimates, one in 5 Americans will get skin cancer at some point in their lifetime (more than 95% of which will be NMSC). The treatment of NMSC carries a significant economic burden. The average annual cost of treating skin malignancies increased by 126.2% in the United States of America in less than 10 years, whereas the cost of treating all malignant diseases increased by 25.1%.[1]

The treatment of choice for NMSC is surgery. From surgical interventions, Mohs micrographic surgery (MMS) has been proven to have the highest cure rate with maximum normal tissue preservation. The reported high cure rate of MMS in comparison to regular wide excision is due to the fact that in regular wide surgical excision, arbitrary margins are designated followed by vertical sectioning of the skin specimen, which allows only examination of 1% of the tumor margin.[2] On the other hand, MMS enables excision with clearly defined thin margins, and then specimens are cut into horizontal pieces in stages afterward, enabling instantaneous and close-up evaluation of 100% of the peripheral and deep margins. Therefore, most studies report that MMS has a cure rate of 97% to 99.8% for primary basal-cell carcinoma (BCC) and 94% for recurrent BCC.[1] Mohs micrographic surgery is also commonly used for squamous cell carcinoma (SCC) with a cure rate of 97%.[3] It has been used in the removal of melanoma in situ with a cure rate range of between 77% and 98% depending on the surgeon.[4]

In many developed countries such as the USA, Canada, New Zealand, Great Britain, and the Netherlands, MMS is considered to be the standard surgical treatment for NMSC. Mohs micrographic surgery is performed by a board-certified dermatologist who has been through a specialized training program to acquire the necessary cutaneous histopathological knowledge and surgical skills. With regard to Europe, Prickett et al[5] reported that the countries with the greatest incidence rates of NMSC are the Netherlands, Switzerland, and Belgium, where they have 117 Mohs surgeons who have earned certification from the European Society for Micrographic Surgery (ESMS).[5] In Saudi Arabia, MMS is rarely performed, despite having been introduced in the country more than a decade ago. In Saudi Arabia, MMS is performed mainly in 2 medical institutes: King Saud University Medical City (KSUMC) and Prince Sultan Military Medical City (PSMMC).

Studies reviewing trends in MMS are limited. Our search in the medical literature in the English language did not reveal any published study in the middle east. Therefore, we aim to examine the clinical and histological features of the cutaneous malignancies that were treated with MMS in Saudi Arabia and evaluate the outcome of the procedure.

Methods. A multicentric retrospective study was performed on the data of those patients who underwent MMS in 2 large medical centers in Riyadh (KSUMC and PSMMC), Saudi Arabia between January 2010 and September 2022. This study complies with the Declaration of Helsinki and it was approved by the Institutional Review Board of King Saud University's research ethics committee (No. E-22-6834). We included all cases of skin cancer who underwent MMS without any exclusion. The information extracted into Microsoft Excel from the databases of KSUMC and PSMMC in Riyadh includes histopathological results and patient charts. The data is classified according to the histopathological diagnosis of the tumor (BCC, SCC, and other tumor types), the status of the tumor (primary or recurrent), its location, the number of MMS stages, the reconstruction type that was undertaken, and the surgical outcomes of the procedure, which include short-term sequels such as postoperative hemorrhage/hematoma, wound infection, wound dehiscence, skin graft or skin flap necrosis and long-term sequels such as recurrence of the treated tumor.

The procedure followed was that, first, a skin biopsy was performed in order to confirm the diagnosis. Following that, a preoperative discussion with the attending physician was carried out to assess whether MMS was appropriate. All patients provided specific preoperative information, including a general medical history, a review of systems, medications, and allergies, as well as relevant social and family histories. Due to their potential effects on platelet aggregation and bleeding tendency, patients who were using non-steroidal anti-inflammatory drugs (NSAID) were advised to pause taking them 3 to 4 times the length of the drug's half-life before the surgery day. Two days after the MMS, patients were told to resume taking their medications again. In most cases, the tumor was removed using the standard MMS technique. Most tumors were excised at a 30-45 degree angle with a 1-2 mm margin, while a wider margin of 3-5 mm was used to remove more aggressive histopathologic classifications of BCC (micronodular, infiltrating, sclerosing), Bowen disease, and lentigo maligna. A nick on the specimen and the skin was made to mark at 12 and 6 o'clock positions. Additional markings were placed for larger tumors. The tumor was brought to the MMS laboratory, where a

map was created and the tissue was marked with ink and flattened. After that, the tissue was clamped to a metal chuck, coated with optimal cutting temperature compound (OCT), placed in the microtome, and prepared as 6-8 μm horizontal tissue wafers that were placed on 2 slides. Hematoxylin and eosin (H&E) staining was used to color the slides, and they were then examined. The MMS map was marked with any positive margins. In the event that a tumor was discovered, the patient was brought back to the operating theater, the layer matching to the positive area was removed, and the tissue was processed in accordance with the first stage. The stages were repeated until the clearance of the tumor. The skin defect was repaired when the entire tumor had been excised. The entire surgery was carried out under local anesthetic in an outpatient minor operation room on the same day. An electrosurgical device was used to meticulously accomplish intraoperative hemostasis to help minimize postoperative hemorrhage. Following surgery, all patients closed the wound by using conventional pressure dressings. Pressure dressings were constructed with a layer of non-adherent material overlaid by absorbent cotton gauze, secured with high-tensile-strength adhesive tape. Patients were advised to avoid engaging in intense activities for a few days following surgery in order to reduce the possibility of postoperative hemorrhage and edema. The assigned dermatologic surgeon performed the whole tumor excision procedure. The surgical reconstruction was usually done by a dermatologic surgeon or a plastic surgeon. There were many measures taken to reduce the risk of postoperative wound infection. First of all, the procedure was performed in a clean environment with the surgeons, nurses, and assistants wearing surgical masks. The tumor removal was performed after preparing the surgical site with povidone, using sterile instruments, sterile paper drapes, and sterile surgical gloves. Patients were bandaged with sterile, dry dressings between surgical stages. To improve wound healing in patients, delicate operative techniques were implemented and all patients were requested to limit cigarette smoking before surgery and for the immediate postoperative period (1-2 weeks).

In order to reduce the likelihood of anesthetic-related postoperative complications, local anesthetic, typically 1% or 2% lidocaine hydrochloride with epinephrine, was used for MMS cases. No patients were given intravenous sedatives. Preoperative and postoperative vital signs were taken as part of regular patient monitoring. Oral anxiolytics (lorazepam) were prescribed for some patients. When lorazepam was used, the doses were 1 mg on the night before the procedure and 1 mg on the day of the procedure. After completion of the surgical procedure, the attending physician gave the patients post-procedure instructions for dressing and wound care, which included retention of the original dressing for 24 hours post-surgery with avoidance of contact with water followed by the application of an antibiotic or petrolatum ointment and a nonstick dressing. Before suture removal, the patients were instructed to adhere to wound care standards. Depending on the surgical site and type of wound, sutures were removed between 5 and 14 days after the procedure.

Results. The total number of patients treated by MMS in Saudi Arabia has increased gradually, from only one patient in 2015 to 26 patients in 2020 (Table 1). In total, 70 patients underwent MMS in the period between 2010 and 2022, although we found no evidence of any patients prior to 2015. The majority of the treated tumors were BCC (67%) (Figures 1 & 2), followed by SCC (18.6%). Other tumoral types benefiting from MMS are sebaceous carcinoma (5.7%), dermatofibrosarcoma protuberans (DFSP) (4.3%), and rare tumors such as primary mucinous carcinoma (1.4%) (Figure 3 & Table 2).

The indications for MMS were documented. These indications included aggressive histopathological

Table 1 - Demographic data of the 70 records.

Characteristics	n	%
Age		
20-29	2	2.9
30-39	2	2.9
40-49	5	7.1
50-59	8	11.4
60-69	16	22.6
70-79	15	21.4
80-89	16	22.6
90-99	6	8.6
Gender		
Male	44	63
Female	26	37
Nationality		
Saudi	69	98.6
Non-Saudi	1	1.4
Number of Mohs per year		
2015	1	1.4
2016	2	2.9
2017	12	17.1
2018	8	11.4
2019	12	17.1
2020	26	37.1
2021	7	10
2022	2	2.9

Figure 1 - Mohs micrographic surgery for pigmented basal-cell carcinomas over the forehead. **A**) Pigmented basal-cell carcinomas over the forehead. **B**) Immediate post-first stage of Mohs surgery. **C**) one-week post-Mohs surgery. **D**) Two weeks post-Mohs surgery.

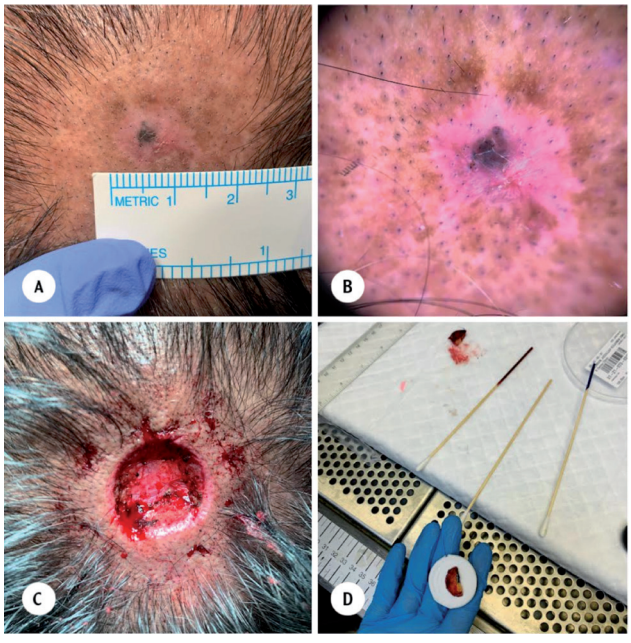

Figure 2 - Mohs micrographic surgery for pigmented basal-cell carcinomas over the scalp. **A**) Pigmented basal-cell carcinomas over the scalp. **B**) Dermoscopic findings show the absence of a pigment network; there are white, pink, gray, and light-brown stroma, with sharply defined, fine linear, and branching arborizing vessels. **C**) Immediate first stage post-MMS. **D**) Coloring the specimen for the frozen section.

Figure 3 - Mohs micrographic surgery for primary mucinous carcinoma. **A**) Primary mucinous carcinoma of the skin over the left temporal area. **B**) Dermoscopic findings show a whitish network and light-brown globules with branching serpentine vessels. **C**) Skin biopsy specimen revealed a dermal mass composed of glands and solid nests of epithelial cells which appear to be floating in copious mucin (Hematoxylin and Eosin staining). **D**) Complete healing by secondary intention.

subtypes such as invasive variant (2.9%), morpheaform variant (1.4%), and micronodular variant (1.4%); tumors that were located in high-risk areas, such as the H-zone of the face (51.4%); tumors that were located in surgical areas where tissue preservation is critical, such as hands (2.9%); recurrent tumors (10%); and tumors over a long-standing scar (1.4%). Three-quarters of the tumors treated with MMS in our study were high-risk tumors (Table 2).

The majority of patients underwent MMS under local anesthesia only. Only 4 patients required oral sedation (5.7%). Almost all the patients (98.6%) underwent MMS in a single day and the frozen-section tissue-processing technique was employed. Only one case of DFSP was treated with the "slow" MMS method, which needs more than one day to be completed. The mean number of stages required in order to obtain complete removal of the tumor was 1.76. All tissue that was excised and prepared was read and interpreted by both the Mohs surgeon and the dermatopathologist in all patients in our study.

After completion of MMS, the reconstruction of the surgical defect was undertaken by the Mohs

surgeon in more than 90% of patients; only 6 patients required a plastic surgeon to complete the repair of the surgical defect. Regarding the technique of surgical defect closure that was implemented, in the majority of patients (53%) primary closure was performed by the Mohs surgeon (Figure 1). The final defect was left to heal by secondary intention in 20% of the patients (Figure 3). One-fifth of the surgical defects were repaired using skin flaps different types of flap were used, including an advancement flap (10%), a rhombic transposition flap (2.9%), a unilateral rotation flap (1.4%), an O to Z flap (1.4%), a glabellar flap (1.4%), and a double rotation flap, also called an "'8 to Z' yin and yang" flap (2.9%). Reconstruction using skin grafting was used in only 5 patients (7%) (Table 3).

Regarding surgical complications in our study, 2 (2.9%) patients developed wound infections and one patient developed hematoma (1.4%). From all patients who underwent MMS, only 3 recurrences were recorded (4.3%) (Table 3); 2 of those were BCC over the nose and scalp, while the third was SCC over the nose. One of these 3 patients was suffering from Gorlin syndrome.

Table 2 - Types, localization, and status of tumors.

Variables	n	%
Type of tumors		
BCC	47	67
SCC	13	18.6
Sebaceous carcinoma	4	5.7
DFSP	3	4.3
Primary mucinous carcinoma	1	1.4
Basosquamous carcinoma	1	1.4
Localization of tumors		
Nose	28	40
Scalp	10	14.3
Cheek	6	8.6
Forehead	4	5.7
Eyelid	6	8.6
Leg	3	4.3
Ear	2	2.9
Chest	2	2.9
Abdomen	2	2.9
Jaw	1	1.4
Shoulder	1	1.4
Arm	1	1.4
Hand	1	1.4
Finger	1	1.4
Back	1	1.4
Genital	1	1.4
Status of tumors		
Primary	63	90
Recurrence	7	10
High risk	53	75.7
Low risk	17	24.3

BCC: basal-cell carcinomas, SCC: squamous cell carcinomas, DFSP: dermatofibrosarcoma protuberans

Table 3 - The number of Mohs micrographic surgery (MMS) stages, types of reconstructions, Short-term complications, and recurrence for the 70 patients.

Variables	n	%
Number of MMS stages		
1	37	52.9
2	20	28.6
3	7	10
4	5	7.1
5	1	1.4
Types of reconstructions		
Primary closure	37	53
Secondary intention healing	14	20
Flap	14	20
Advancement flap	7	10
Rhombic transposition flap	2	2.9
Double rotation flap "'8 to Z' yin and yang"	2	2.9
Unilateral rotation flap	1	1.4
O to Z flap	1	1.4
Glabellar flap	1	1.4
Graft	5	7
Short-term complications		
Wound infections	2	2.9
Hematoma	1	1.4
Recurrence		
Yes	3	4.3
No	67	95.7

Discussion. Our study demonstrates that patients who undergo MMS in Saudi Arabia are usually males aged above 60 years. Basal-cell carcinoma is the most treated malignancy using MMS and the nose is the most common location to be treated. The most common type of surgical defect reconstruction is primary closure followed by secondary intention healing. Surgical complications are very rare; only one patient developed hematoma and 2 patients had wound infections. The overall recurrence rate of skin cancer post-MMS in our study was low (4.3%).

In the literature, BCC and SCC are the tumors most frequently treated with MMS. Also in our study, we found that BCC is the most common tumor treated by MMS (67%). The second most common was SCC (18.6%). From these, tumors with aggressive histopathological subtypes such as tumors with perineural invasion, tumors larger than 1 cm in diameter on the face or neck and 2 cm on the torso or limbs, tumors in patients with immunosuppression, and tumors localized in the H-zone of the face, the genital area, the hands, the feet, or the areolar region

are all classified as high-risk.[6] In our study, the majority of the treated tumors (75%) were considered high-risk tumors as they were localized in high-risk areas, such as the H-zone of the face (51.4%); or recurrent tumors; or tumors with aggressive histopathological subtypes, for example invasive, morpheaform, or micronodular types; or tumors over a scar; or tumors in immunosuppressed patients.

Beyond NMSC, several other malignant skin tumors have all been successfully treated with MMS, including melanoma in situ, sebaceous carcinoma, extramammary Paget's disease, atypical fibroxanthoma, microcystic adnexal carcinomas, Merkel cell carcinomas, and DFSP.[9] In our study, we used MMS for the treatment of rare or uncommon aggressive tumors such as DFSP, primary mucinous carcinoma, sebaceous carcinoma, and basosquamous carcinoma. Of particular interest is DFSP, which is considered to be a locally aggressive dermal tumor that is notoriously difficult to completely excise. It has been reported that even a 10 cm oncologic margin around the tumor in some cases would not lead to complete excision. The usual recurrence rate of this tumor is somewhere between 7% and 20% when wide surgical excision is used with an oncologic safety margin of 3-5 cm, as opposed to 1.7% recurrence rate when MMS is used.[9,11] In our study, we used MMS to treat 3 patients with DFSP (4.3% of total tumors). One of these patients needed 4 stages and a slow MMS technique.

Several studies have evaluated the recurrence rate of BCC following MMS. According to one study, the recurrence rate for primary tumors was 1% for MMS and 10.1% for the standard wide excision, while the recurrence rate for recurrent tumors was 5.6% for MMS and 17.4% for the standard wide surgical excision.[7,8] Stanciu et al[9] reported only 4 (0.29%) recurrences – 3 recurrent infiltrative BCC and one poorly differentiated SCC – in a retrospective cohort spanning more than 10 years and including 1300 patients who underwent MMS. In our study, we reported only 3 recurrence tumors post-MMS; one of them was a known case of Gorlin syndrome.

A major advantage of MMS is normal tissue preservation, especially in certain locations where tissue conservation is paramount such as eyelids, lips, ears, nose, and genitalia. When treating nodular or superficial BCC, the tumor is removed by MMS with a margin of 1-2 mm, compared to a 4-5 mm safe margin in the case of standard wide excision. It has been found that this approach results in reduction of the post-surgical defect size by 50%.[10] In our study, we used MMS for tissue preservation in high-risk sites including the nose, eyelids, ears, hands, and genitals.

Most defect reconstructions are carried out by the primary MMS surgeon. In special situations, when the cutaneous defects are complex or involve a large surface area, especially in very critical locations such as the eyelids or lips, referral to other surgical specialties is organized. This was also the technique used in our study. The majority of the reconstructions were carried out by the Mohs surgeons (91.4%), and the rest were carried out by plastic surgeons.

Several studies have examined the rate of postoperative complications following MMS, with all of them reaching the same conclusion, namely that MMS is an undeniably safe procedure and carries a low risk of postoperative surgical complications. A review examined the postoperative complications of 546 patients who underwent MMS, stratifying the postoperative complications into mild, moderate, and severe. They concluded that MMS carries about a 4.58% risk of moderate to severe complication. A larger prospective study involving 1052 patients performed in an outpatient setting reported that surgical complications occurred in only 22 of the 1343 MMS procedures done, which translates into a complication rate of 1.64%. The majority of the complications that were reported involved postoperative hemorrhage.[2] Another study examined prospectively the frequency of hemorrhage in MMS patients who were using anticoagulants or NSAID. It showed that out of the 322 patients they studied, only eight developed bleeding as a complication, which translates into a 2.5% risk of hemorrhage after MMS.[12] Fortunately, in our study, we did not report any case of postoperative hemorrhage. We reported only one case of postoperative hematoma in a patient who was taking aspirin, which was resolved with conservative management.

A modest amount of scientific literature has discussed the nature of infection in a dermatologic surgery setting. A retrospective study evaluated the infection rate among 1047 dermatologic surgeries, which included 530 MMS. They found only 13 infections (2.5%) after MMS.[12] It has been demonstrated that the high sterility of an operating room environment is not necessary for the safe use of MMS and the subsequent reconstructive treatments in terms of the low occurrences of wound infection reported in several studies.[2] In our study, MMS was performed in a clean environment with the surgeons, nurses, and assistants wearing surgical gowns, masks, and sterile gloves. Surgical sites were cleaned with antiseptic povidone solution and prepared with sterile paper drapes, and sterile instruments were used

to carried out the procedure. Our rate of surgical site infection was similar to the previous studies (2.9%); both patients who developed surgical site infection had multiple comorbidities.

Regarding reconstruction-specific surgical complications such as tissue necrosis, the majority of previously published studies were designed to examine the effect of independent risk factors such as smoking on the survival of cutaneous flaps and grafts. A study assessed the effect of cigarette smoking on the viability of tissue reconstruction after MMS. It concluded that about 4.8% of MMS defects that were repaired with tissue reconstruction using flaps or full-thickness grafts showed some form of tissue necrosis that could be attributed to smoking.[13] We did not report any case of skin graft or skin flap necrosis in our study.

Study limitations. Our study suffered from many limitations. First, the number of patient records that were evaluated in this study was small. Second, the retrospective nature of the study carried its own inherited limitations, which include recall bias and misclassification bias. Third, our study focused only on the central region and the capital city in particular, where medical resources are available and well organized to provide better advanced medical care. Therefore, it is not representative of the clinical settings and health resources in other regions, especially agricultural regions, where there is significant sunlight exposure and therefore a possibly high rate of skin cancer.

In conclusion, the use of MMS in Saudi Arabia has been increasing over the last decade. The most common skin cancer to have been treated was BCC, followed by SCC. The most commonly treated site was the nose. It is a one-day ambulatory procedure that is carried out in an outpatient setting under local anesthesia and it has demonstrated a high cure rate with a low risk of recurrence. There were minimal to no surgical complications in the majority of patients. Therefore, we recommend more adoption and spread of MMS as a treatment for various skin cancers, especially NMSC, across Saudi Arabia through providing the necessary resources and training to improve its reach to skin cancer patients, especially in rural areas.

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