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van Kester, Marloes S.; Goeman, Jelle J.; Genders, Roel E.

Published in:
Journal of the American Academy of Dermatology

DOI:
10.1016/j.jaad.2019.01.057

Publication date:
2019

Tissue-sparing properties of Mohs micrographic surgery for infiltrative basal cell carcinoma

Marloes S. van Kester, MD, PhD,[a,b] Jelle J. Goeman, PhD,[c] and Roel E. Genders, MD[a,d]
Leiden and Groningen, The Netherlands

Background: Mohs micrographic surgery (MMS) should lead to tissue sparing of healthy skin compared with standard surgical excision because smaller surgical margins are used.

Objective: To quantify the tissue-sparing properties of MMS in primary basal cell carcinoma (BCC) with an infiltrative growth pattern.

Methods: A prospective study including 256 primary BCCs with an infiltrative growth pattern was performed. Tumor sizes were measured in 2 perpendicular directions. Surface defect areas after MMS were measured. The suspected defect surface area with standard excision using a 5-mm margin was calculated. The primary outcome of this study was the size of the defect surface area spared with MMS compared with the calculated defect surface area with a standard excision.

Results: The median tumor size was 71 mm^2, and the median defect size after MMS was 154 mm^2. The median defect size calculated for standard surgical excision was 298 mm^2. We have shown that MMS of BCC with an infiltrative growth pattern had a 46.4% tissue-sparing effect when compared with standard surgical excision (95% confidence interval, 43.4%-49.1%; P value $< .001$).

Limitations: Single-center study design. Lack of a randomized control group for ethical reasons.

Conclusion: A rate of tissue sparing of 46% can be reached by using MMS for primary BCC with an infiltrative growth pattern. (J Am Acad Dermatol 2019;80:1700-3.)

Key words: Mohs micrographic surgery; basal cell carcinoma; tissue sparing.

Mohs micrographic surgery (MMS) is widely used for primary high-risk basal cell carcinomas (BCCs) and recurrent or residual BCC. On the basis of histologic assessment of all excision margins, 100% tumor control is achieved, resulting in a lower percentage of recurrences.[1] Additionally, a smaller margin is used for MMS, and this should lead to sparing of healthy skin tissue. Muller et al have demonstrated in a randomized controlled trial that MMS is tissue sparing for nodular BCC.[2] However, a large proportion of the BCCs with an indication for Mohs surgery have an infiltrative growth pattern. The aim of this study was to quantify the tissue-sparing properties of MMS in primary facial BCC with an infiltrative growth pattern.

MATERIAL AND METHODS

Study participants

A prospective observational study in patients treated with MMS was performed at Leiden University Medical Center in 2017-2018. Patients were mostly referred by dermatologists. For all patients, the standard procedures were followed for MMS of basal cell carcinoma. The following patients were excluded: patients with recurrent or residual tumors, patients with tumors with solely a

From the Department of Dermatology[a] and Department of Biomedical Data Sciences, Leiden University Medical Center[c]; Department of Dermatology, University Medical Center Groningen[b]; and Department of Dermatology, Roosevelt Clinic, Leiden.[d]

Funding sources: None.
Conflicts of interest: None disclosed.
Accepted for publication January 25, 2019.

Reprint requests: Roel E. Genders, MD, Department of Dermatology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands. E-mail: R.E.Genders@lumc.nl.

Published online January 31, 2019.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2019.01.057

nodular or superficial growth pattern, and patients with tumors other than BCC.

Procedures

Before surgery, the tumor was measured under a theater operating light in 2 perpendicular directions, referred to as diameters t1 and t2, and digital photographs were taken. The tumor was subsequently excised under an angle of 45 to 50 degrees with a 2-mm margin taken from the surface of the skin, and the defect was measured in 2 perpendicular directions starting with the largest diameter, resulting in the diameters d1 and d2. Fresh frozen sections were stained with hematoxylin-eosin stain and then examined microscopically. If tumor was present at the margin, further staging was undertaken until the tumor was completely removed. The final defect was similarly measured in 2 directions and digitally photographed, resulting in the diameters r1 and r2. All measurements were performed by the same Mohs micrographic surgeon. All histologic slides were also reviewed by a pathologist. The defect size in square millimeters was calculated by using the following formula for the surface of an ellipse: $\pi \times r1/2 \times r2/2$, with the radius being half of the diameter, measured in mm. The putative surface defect size with standard excision was calculated as $\pi \times (t1/2 + 5\ mm) \times (t2/2 + 5\ mm)$ according to the Dutch guidelines, in which a 5-mm margin is recommended for standard excision of BCC with an infiltrative growth pattern.[3]

CAPSULE SUMMARY

- Mohs micrographic surgery is the treatment of choice for facial basal cell carcinoma, especially for infiltrative subtypes.
- Besides the advantage of 100% margin control and lowest recurrence rates, this study proves a tissue-sparing effect of Mohs micrographic surgery compared with standard surgical excision. This is beneficial for reconstruction techniques.

Table I

Gender, n	Female 141, Male 115
Age in years; median / mean / range	70 / 68 / 35-94
Tumor size in mm^2; median / mean / range	71 / 122 / 7-1649
Tumor length maximum axis in mm; median / mean / range	11 / 13 / 3-70
Defect size MMS in mm^2; median / mean / range	154 / 262 / 24-3129
Defect size calculated for standard surgical excision in mm^2; median / mean / range	298 / 376 / 132-2513

The relative defect surface area spared with MMS was calculated by using the log ratio of both calculated defect sizes.

Objectives and outcomes

To show tissue-sparing properties, we tested the null hypothesis that MMS is no more tissue sparing than standard surgery. The primary outcome of this study was the size of the defect surface area spared with MMS compared with the calculated defect surface area with a standard excision. Depth of the tumor was not taken into account in this study.

Statistical analysis

SPSS software (version 23, IBM, Armonk, NY) was used for all analyses. A 1-sample *t* test on a log scale was used to compare the log ratio of defect sizes with 0, corresponding to a ratio of 1.

RESULTS

A total of 256 tumors were removed by MMS. For patient demographics, see Table I. The median age was 70 years (range, 35-94). The average maximum tumor length was 13 mm, and the median of calculated tumor surface area was 71 mm^2. The median defect size was 154 mm^2. The median defect size calculated for standard surgical excision was 298 mm^2. All tumors were located in the facial (n = 244) or scalp (n = 12) region (see Table II for locations). The majority of the tumors were located on the nose (n = 125).

We found a statistically significant difference between the Mohs defect size and the calculated defect size. The mean rate of tissue sparing was 46.4% (95% confidence interval, 43.4%-49.1%). For 22 of the 256

Table II. Locations

Region	n
Frontal	16
Temporal	20
Nose	125
Periocular	31
Cheek	28
Perioral	16
Ear	8
Scalp	12

Abbreviations used:

BCC: basal cell carcinoma
MMS: Mohs micrographic surgery

tumors (8.6%), the log ratio was greater than 0, meaning that the calculated defect size was smaller than the Mohs defect size. In these cases, standard excision would have led to inadequate tumor removal. Subgroup analysis for tumors on the nose showed 55.9% tissue sparing (95% confidence interval, 53.0%-58.6%). In 3 of the 125 tumors (2.4%), the calculated defect size was smaller than the Mohs defect size, resulting in inadequate tumor removal. Subgroup analyses of the periocular region showed similar results (see Table III). However, subgroup analyses of the cheek and frontotemporal region showed significant tissue-sparing effects of only 28.0% and 20.6%, respectively (see Table III). The percentage of cases in which standard excision would have led to inadequate tumor was significantly different between different regions (Fisher's exact test P value $< .001$).

DISCUSSION

Overall, we have shown that for removal of infiltrative growing BCCs, MMS has a tissue-sparing effect of 43% to 49% compared with standard excision. In 8.6% of the tumors, standard excision with a 5-mm margin would have led to inadequate tumor removal. The tissue-sparing effect is higher for tumors on the nose and reasonably lower for tumors on the cheek and frontotemporal region (28.0% and 20.6%, respectively). The percentage of tumors in which standard excision would have led to inadequate tumor excision was remarkably higher in the cheek and frontotemporal region, demonstrating an appropriate indication for MMS.

Muller et al showed a slightly smaller tissue-sparing effect for nodular basal cell carcinoma. The median defect size in their MMS group was 116.6 mm^2 versus 187.7 mm^2 in the standard surgery group, showing 38% tissue sparing in terms of median defect size.[2] A margin of 4 mm was taken for standard excision. This is less than the 5 mm that we took into account, which explains the lower tissue-spring effect found. Another difference is that nodular BCC borders are often more easy to define than are the borders of an infiltrative growing BCC. Other possible explanatory factors might be the nodular growth pattern combined with the smaller tumor size (their median tumor area was 58.1 mm^2 versus 71 mm^2 in our group) or variability due to small sample size.

Similarly, Gniadecki et al showed that when compared with standard excision of a primary BCC with 4-mm margins and standard excision of a high-risk, recurrent tumor with use of 6-mm margins, MMS leads to 43% and 45% smaller skin defects, respectively.[4]

Previously, Smeets et al showed zero difference in mean defect size as a secondary outcome in their randomized controlled trial studying recurrences and comparing MMS with standard surgery.[5] For comparability, they used 3-mm margins in both groups. However, since the beginning of their study in 1998, more literature showing that larger margins are appropriate for high-risk tumors, such as recurrent tumors, has become available.[3,6] Furthermore, a 1- to 2-mm and not a 3-mm margin is standard practice for MMS in BCC, and also for recurrent BCC. However, we excluded recurrent tumors, so comparison of results is difficult.

Muche and et al state that in all cases, the defect size is smaller with MMS[7]; however, they did not quantify the tissue-sparing effect, and hence, detailed comparison is also difficult here.

We worked with an arbitrary 5-mm margin in calculation of the surface area for the standard excisions. This 5-mm margin is the recommended margin for infiltrative BCC in the Dutch guideline for treatment of BCC.[3] According to the European guideline, a margin ranging from 4 to 13 mm should be taken, depending on tumor characteristics such as size, histologic growth pattern, and whether the tumor is a primary or a recurrence.[6]

Table III. Statistical analyses

Region	n	Median tumor size, mm^2	Median defect size, mm^2	Mean Mohs stages, n	Defect size > calculated size defect size, % of tumors	Tissue sparing	95% confidence interval	*P* value
Full group	256	71	154	1.77	8.6	46.4%	43.4%-49.1%	<.001
Nose	125	50	112	1.76	2.4	55.9%	53.0%-58.6%	<.001
Periocular	31	71	151	1.74	6.5	50.2%	42.6%-56.8%	<.001
Cheek	28	138	374	1.86	21.4	28.0%	16.3%-38.1%	<.001
Frontotemporal	36	210	421	1.67	25	20.6%	9.7%-30.2%	.001

We realize that our study is limited to a single tertiary referral center and our patient population is biased because of this, with patients referred for MMS. Our study population is limited to tumors with an indication for MMS only. According to our findings, we believe that for infiltrative BCC, a tissue-sparing effect up to 50% can be reached, taking into account that we did not correct for stretch of the surgical defect. This further supports the notion that in functional and cosmetically sensitive regions, using MMS is recommended for infiltrative BCC to avoid larger reconstructions.

The authors would like to thank Dr C.C.P. Haenen and Dr N. Marsidi (Department of Dermatology, Leiden University Medical Center) for their contribution to the study.

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