Guideline Resource Unit
guru@ahs.ca

Mohs Micrographic Surgery

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Alberta Health Services
CancerControl Alberta

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www.ahs.ca/guru

Background

Nonmelanoma skin cancer (NMSC)

Nonmelanoma skin cancer (NMSC) is the most commonly diagnosed cancer among Canadians.[1] The most prevalent form of NMSC is basal cell carcinoma (BCC), followed by squamous cell carcinoma (SCC). Together they account for approximately 95% of all cases of NMSC in Canada.[2] From 1988 to 2007, there were 66,192 BCCs, 19,959 invasive SCCs, and 12,494 SCCs *in situ* in Alberta.[3] Sunlight exposure is the most significant risk factor in the etiology of NMSC. Fair complexion, lighter hair and eye colour, and a positive personal or family history are also risk factors for developing BCC or SCC.[4,5]

There are many approaches to the treatment of NMSC. Generally, the primary goal of treatment is complete tumour eradication with maximal preservation of function and cosmesis. Current guidelines for the management of BCC and SCC consider surgery (including standard excision, Mohs micrographic surgery, or curettage and electrodessication) as the most effective treatment option for most cases of NMSC.[4-13] Other treatment options include cryotherapy, radiation, photodynamic therapy, and topical therapy. This guideline focuses on the indications for Mohs micrographic surgery (MMS) in NMSC.

Mohs micrographic surgery (MMS)

Mohs micrographic surgery (MMS) is a specialized technique, originally developed by Dr. Frederick E. Mohs, which has been refined to allow the precise microscopically controlled removal of skin tumors. The technique involves excising a skin tumor with a minimum margin, and processing the tissue in a very specific way using a fresh frozen preparation technique to create pathology slides. This ultimately allows the surgeon to examine the entire margin of the excised skin cancer. MMS is suitable for the surgical extraction of tumors that have a contiguous pattern of growth occurring on sensitive body sites such as the face, hands feet and genitals where the sparing of healthy surrounding tissue is considered essential. In certain cases, the skin cancer may be debulked or curetted prior to removing a layer of tissue. This debulking is not considered as taking a layer of skin.

The Mohs procedure begins with the precise marking of clinically tumor free margins immediately adjacent to the skin tumor (and any associated scar) to be removed. Typically utilizing local anesthesia, these margins are incised in a beveled fashion and a precise layer of tissue is removed surgically. This tissue layer is color inked in a manner devised to map its orientation relative to the patient's surgical wound. The beveled margins of the layer are then flattened to facilitate frozen section processing. The resultant tissue sections are subsequently stained so microscopic slides can be produced that demonstrate 100% of the tissue margins for examination.

The performance of Mohs technique includes the capability to provide reliable pathologic analysis of these slides. If tumor is noted to persist at the margin, its location is related back to the original tissue map and another layer is incised while again sparing tissue not involved by tumor. A correlating map of this layer is generated again being sure to include color inked margins to preserve it precise orientation. This process is repeated until all margins are clear of tumor microscopically. This insures that the Mohs technique attains some of the highest success rates in the treatment of non-melanoma skin cancer – up to 99%.

Finally, MMS involves the knowledge and skill to offer management of the resulting surgical wound including complex reconstructive surgical flap repair as necessary. The combination of this expertise allows

reconstruction to be performed on the same day the cancer is removed further optimizing the patient's care, convenience and surgical outcome.

Guideline Questions

(1) What are the indications for MMS?
(2) Are there any cases where the use of MMS is inappropriate?

Search Strategy

A literature search for articles relating to Moh's Surgery for Basal or Squamous Cell Carcinoma published between 1997 and 2019, in English, were identified and reviewed by the guideline working group. Additionally, existing guidelines from other jurisdictions were identified and reviewed by the guideline working group. In depth search criteria, and identified articles/guidelines can be found in Appendix A.

Target Population

The recommendations outlined in this guideline apply to adults over the age of 18 years with basal cell carcinoma or squamous cell carcinoma. Different principles may apply to pediatric patients.

Recommendations

Level of Evidence and Strength of Recommendation Details in Appendix B (pg. 27)

Basal cell carcinoma (BCC)

1. Mohs micrographic surgery (MMS) is recommended for those with histologically confirmed recurrent BCC of the face.[37,41] *(Level of Evidence: I, Strength of Recommendation: A)*

2. MMS may be considered as a first line option for the treatment of BCC considered high-risk for recurrence (see Tables 1 and 2). If any high-risk feature is present, the patient should be considered high-risk for recurrence.[19, 22, 33, 34, 35, 53, 54] *(Level of Evidence: III, Strength of Recommendation: B)*

3. MMS may be considered in tumours <10mm where tissue sparing is of functional or cosmetic significance. [45, 46, 47] *(Level of Evidence: IV, Strength of Recommendation: C)*

4. MMS is a treatment option for incompletely excised high-risk BCC. Patients with complicated BCC or locally advanced BCC should be considered for multidisciplinary assessment by dermatologists, surgical specialists, medical, and radiation oncologists. *(Levels of Evidence: III[35, 37, 41, 53], IV[29, 30, 47, 49, 52], and V, Strength of Recommendation: B)*

5. **Table 1. Risk stratification for BCC**

Parameters		Low risk	High risk
Clinical			
	Location*/Size	Area L <20mm	Area L ≥20mm
		Area M <10mm**	Area M ≥10mm
			Area H (independent of size)
	Borders	Well defined	Poorly defined
	Primary vs recurrent	Primary	Recurrent
	Immunosuppression	No	Yes
	Site of prior radiation therapy	No	Yes
Pathologic			
	Growth pattern	Nodular	Morpheaform/sclerosing
		Superficial	Basosquamous
			Micronodular
			Infiltrative
			Mixed
	Perineural involvement	No	Yes

*Area H: "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M: cheeks, forehead, scalp, neck, and pretibia.
Area L: trunk and extremities (excluding pretibial, hands, feet, nail units, and ankles).
**Location independent of size may constitute high risk.

(Recurrent disease: Level of Evidence: I, Strength of Recommendation: A)
(Other features: Levels of Evidence: III[35, 37, 41, 53], IV[29, 30, 47, 49, 52], and V, Strength of Recommendation: B-C)

Squamous cell carcinoma (SCC)

6. MMS may be considered as a first line option for the treatment of SCC considered high-risk for recurrence (see Table 2). If any high-risk feature is present, the patient should be considered high-risk for recurrence. *(Levels of Evidence: III[63] and IV[61], Strength of Recommendation: B)*

7. MMS may be considered in tumours <10mm where tissue sparing is of functional or cosmetic significance. *(Level of Evidence: IV[61], Strength of Recommendation: B)*

8. MMS is a treatment option where wide local excision has resulted in incomplete excision of high risk NMSC, regardless of the body location, if deemed appropriate by the surgeon. *(Level of Evidence: V, Strength of Recommendation: B)*

9. **Table 2. Risk stratification for SCC**

Parameters	Low risk	High risk
Clinical		
Location*/Size	Area L <20mm	Area L ≥20mm
	Area M <10mm**	Area M ≥10mm
		Area H (independent of size)
Borders	Well defined	Poorly defined
Primary vs recurrent	Primary	Recurrent
Immunosuppression	No	Yes
Site of prior radiation therapy	No	Yes
Rapidly growing tumour	No	Yes
Neurologic symptoms	No	Yes
Etiology	Ultraviolet radiation	Other
Originating from chronic wound or scar	No	Yes
Pathologic		
Degree of differentiation	Well or moderately differentiated	Poorly differentiated
High-risk histologic subtype***	No	Yes
Depth: Thickness or Clark level****	<2mm or I, II, III	≥2mm or IV, V
Perineural, lymphatic or vascular involvement	No	Yes

*Area H: "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M: cheeks, forehead, scalp, neck, and pretibia.
Area L: trunk and extremities (excluding pretibial, hands, feet, nail units, and ankles).
**Location independent of size may constitute high risk.
***High-risk histologic subtypes: acantholytic (adenoid), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes.
**** Clark level defines depth of invasion, with level I being confined to the epidermis as a carcinoma in situ and with all other levels being invasive tumours that extend into the dermis. Clark level V tumours extend all the way through the dermis and have entered the subcutaneous fat layer.

(Recurrent disease: Level of Evidence: III[63] and IV[61], Strength of Recommendation: B-C)

(Other features: Level of Evidence: V; Strength of Recommendation: B)

Appendix A: Detailed Search Strategy

Search for Primary Literature

The MEDLINE, Pubmed, EMBASE, and Cochrane databases were searched (1997 through 2019) for clinical trials, comparative studies, cohort studies, meta-analyses, and systematic reviews. Search terms included ‘mohs surgery’, ‘mohs micrographic surgery’, ‘squamous cell carcinoma’, ‘basal cell carcinoma’, ‘quality of life’, and the following MeSH terms: Mohs surgery; carcinoma, basal cell; carcinoma, squamous cell; neoplasm recurrence, local; treatment outcome; “Quality of Life”; and tumour recurrence. Search results were limited to human studies and English language. A total of 571 records were identified after duplicates were removed. Title and abstracts of records were screened, 79 full-text articles were assessed for eligibility, and 44 studies were included for review. Additionally, 7 articles were identified through a review of the included articles reference section, bringing the total included primary articles to 51.

Medline Detailed Search

1. exp Mohs Surgery/
2. "Mohs surgery".ab,ti.
3. "Mohs micrographic surgery".ab,ti.
4. 1 or 2 or 3
5. "basal cell carcinoma".ab,ti.
6. "squamous cell carcinoma".ab,ti.
7. exp Carcinoma, Basal Cell/
8. exp Carcinoma, Squamous Cell/
9. 5 or 6 or 7 or 8
10. exp Neoplasm Recurrence, Local/
11. exp Treatment Outcome/
12. exp "Quality of Life"/
13. "quality of life".ab,ti.
14. "QOL".ab,ti.
15. 10 or 11 or 12 or 13 or 14
16. 4 and 9 and 15
17. limit 16 to (english language and humans and yr="1997 -Current" and (clinical study or clinical trial, all or comparative study or journal article or meta analysis or randomized controlled trial or multicenter study))

Pubmed Detailed Search

((((("mohs surgery"[MeSH Terms] OR ("mohs"[All Fields] AND "surgery"[All Fields]) OR "mohs surgery"[All Fields]) OR "Mohs surgery"[TIAB]) OR "Mohs Micrographic surgery"[TIAB]) AND ((((("carcinoma, squamous cell"[MeSH Terms] OR ("carcinoma"[All Fields] AND "squamous"[All Fields] AND "cell"[All Fields]) OR "squamous cell carcinoma"[All Fields] OR ("squamous"[All Fields] AND "cell"[All Fields] AND "carcinoma"[All Fields])) OR ("carcinoma, basal cell"[MeSH Terms] OR ("carcinoma"[All Fields] AND "basal"[All Fields] AND "cell"[All Fields]) OR "basal cell carcinoma"[All Fields] OR ("basal"[All Fields] AND "cell"[All Fields] AND "carcinoma"[All Fields]))) OR "basal cell carcinoma"[TIAB]) OR "squamous cell carcinoma"[TIAB])) AND (((((("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields] OR ("health"[All Fields] AND "related"[All Fields] AND "quality"[All Fields] AND "life"[All Fields]) OR "health

related quality of life"[All Fields]) OR ("treatment outcome"[MeSH Terms] OR ("treatment"[All Fields] AND "outcome"[All Fields]) OR "treatment outcome"[All Fields])) OR ("neoplasm recurrence, local"[MeSH Terms] OR ("neoplasm"[All Fields] AND "recurrence"[All Fields] AND "local"[All Fields]) OR "local neoplasm recurrence"[All Fields] OR ("local"[All Fields] AND "neoplasm"[All Fields] AND "recurrence"[All Fields]))) OR "quality of life"[TIAB]) OR "QOL"[TIAB]) AND ((Clinical Study[ptyp] OR Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Journal Article[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp]) AND ("1997/01/01"[PDAT] : "2018/12/31"[PDAT]) AND "humans"[MeSH Terms] AND English[lang])
[Results: 392]

Embase Detailed Search

1. exp basal cell carcinoma/
2. exp squamous cell carcinoma/
3. "basal cell carcinoma".ab,ti.
4. "squamous cell carcinoma".ab,ti.
5. 1 or 2 or 3 or 4
6. "mohs micrographic surgery".ab,ti.
7. "mohs surgery".ab,ti.
8. 6 or 7
9. exp treatment outcome/
10. exp tumor recurrence/ or exp cancer recurrence/
11. exp "quality of life"/
12. 9 or 10 or 11
13. 5 and 8 and 12
14. limit 13 to (human and english language and yr="1997 -Current")
15. limit 14 to (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study)

Results: 325

Cochrane Systematic Review Search

1. "basal cell carcinoma".mp. [mp=title, short title, abstract, full text, keywords, caption text]
2. "squamous cell carcinoma".mp. [mp=title, short title, abstract, full text, keywords, caption text]
3. 1 or 2
4. "mohs micrographic surgery".ti,ab.
5. "mohs surgery".ti,ab.
6. "mohs".ti,ab.
7. 4 or 5 or 6
8. 3 and 7

Results: 2

Inclusion Criteria:

Randomized controlled trials, controlled clinical trials, or multicenter studies conducted on humans that were published between 1997 and 2018 in English. Study topic had to be on basal cell or squamous cell carcinoma where treatment included Moh's micrographic surgery. Studies needed to report on at least one of the

following: treatment outcomes, tumour reoccurrence rates, or quality of life. Reference sections from all included articles were screened for additional literature.

Exclusion Criteria:

Reasons for excluding abstracts (571 articles reviewed)

- Single centre experience, no treatment outcomes published
- Indications other than BCC and SCC
- Surgical techniques
    - Novel techniques
    - Wound closure
    - Tumour mapping
    - Dermoscopy
    - Reconstructive surgical techniques following Moh's surgery
    - Diagnostic biopsies
    - Surgical defects
- Case report, case series n<20
- Cost analyses, wait time studies, assessment of consultation practices
- Educational gap analysis of oncologists
- Other treatment options with no comparison to Mohs (chemotherapy, RT, surgical excision) **this was explored in other lit search*
- Secondary pathology review, surgeon error
- Reasons for aborted MMS
- Consensus statements
- Reviews without meta-analysis
- Letters to editor, commentaries on research
- Article no longer accessible

Reasons for excluding full text

- Full article not available, full article not in English
- Retrospective review predicting surgical complexity of MMS surgery
- Algorithm for surgical treatment (not mohs), Surgical techniques other than mohs
- Descriptive study of pts undergoing Mohs (no outcome data)
- Factors predicting PIN
- Mohs AUC criteria retrospectively applied to NMSC (single center)
- Single centre retrospective review with surgical outcomes only (ie. Factors predictive of more surgical stages)
- Assessment of surgical rates
- Access to care studies/cost analysis/ looking at differences between centres to assess access to care
- Proposed deficit vs mohs deficit
- Surgical outcomes slow mohs
- Earlier version of article
- Incidence epidemiological studies

Predictors of satisfaction with Mohs (no comparisons to other treatments)

Search for Existing Guidelines:

The National Guidelines Clearinghouse and individual guideline organizations were searched for practice guidelines relevant to this topic. A total of fifteen clinical practice guidelines with at least one recommendation directly related to MMS were identified from the following organizations or groups: American Academy of Dermatology, National Comprehensive Cancer Network, UptoDate, and American Society for Dermatologic Surgery, British Association of Dermatologists, London Cancer Alliance, Scottish Intercollegiate Guidelines Network, Cancer Council Australia, and the UK National Multidisciplinary Guidelines committee.

Literature Search Outcomes:

In total 1098 primary articles were identified from the Medline/ Pubmed/ Embase/ Cochrane literature searches of which 571 articles were unique. 492 articles were excluded based on an abstract screen, and a further 35 were excluded after a full-text screen, leaving 44 articles. 7 articles were added after a review of the reference sections from the included articles.

In total, 51 primary articles were identified and included in the literature search (below). 22 articles were focused on both BCC and SCC (Appendix A Table 1), 18 focused exclusively on BCC (Appendix A Table 2), and 11 focused exclusively on SCC (Appendix A Table 3).

Additionally, 13 relevant guidelines were identified and reviewed by the guideline working group (Appendix A Table 4).

Appendix A Table 1. BCC and SCC

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Comparison of treatments								
Patel, 2017 (15)	1 and 2	Matched pair cohort study (multicentre)	369 (416 lesions)	226 BCC (113 MMS, 113 EBT) 190 SCC (95 MMS, 95 EBT) Most lesions >1cm and ≤2cm, located on head	188 pts EBT (208 lesions): mean age 80.7 181 pts MMS (208 lesions): mean age 76.8 *EBT patients matched with MMS patients based on age, lesion size, type, location, tx date	EBT (mean f/u 3.3 y) MMS (mean f/u 3.5 y)	Cosmesis rated as 'good' or 'excellent' by pts in 90% of EBT group and 95% of MMS group 85.1% of MMS lesions required 1 level for clear margins	1/208 recurrence EBT group (BCC), 0/208 recurrences MMS group (p=1.00) Most common toxicity was hypopigmentation (59.6% of EBT and 52.4% of MMS)
Stuart, 2017 (16)	1 and 2	Retrospective cohort (single centre)	1483	All tumours judged appropriate for MMS using AUC Treated with MMS: 42.3% BCC aggressive 37.4% BCC superficial/nod 13.7% SCC invasive 6.7% SCC in situ Treated with other: 26% BCC aggressive	Mean age MMS 66.4 y Mean age other 68.4 y (p=0.03)	MMS: 672 Excision: 523 Destruction: 139 Other: 149	None reported	5 yr recurrence rates: MMS: 2.9% (1.4-4.3) Excision: 5.5% (3.1-7.9) Destruction: 4% (0.6-7.2) Other: 5.9% (1.5-10.2) HR of tumour recurrence after MMS compared to excision was 0.6 (95%CI 0.3-1.0, p=0.06).

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
				43% BCC superficial/nod 14.8% SCC invasive 16.2% SCC in situ				
O'Neill, 2014 (17)	1 and 2	Prospective study	2418 (Site 1: 1230, Site 2: 1188)	353 SE tumours 1525 MMS tumours Type unspecified	Site 1 mean age 70.4 Site 2 mean age 66.7	SE <2cm Site 1 7%, Site 2 16.2% (P<0.001) SE>/=2 cm Site 1 3.7%, Site 2 16.2% (P<0.08) MMS <2cm Site 1 44.9%, Site 2 62.0% (P<0.001) MMS >/=2cm Site 1 8.7%, Site 2 10.8% (P=0.1)	Most common AE were infection 2.1% at site 1 vs 0.5% at site 2 (p<0.001). Mohs surgery, Site 1, older age, and anatomic location of surgery associated with higher risk of infection (multivariate logistic regression).	
Alam, 2013 (18)	1 and 2	Prospective cohort (multicentre)	20,821	13,111 BCC (63%) 7,215 SCC (34.7%) 495 Other (2.4%)	Data collected from 23 centres across US	MMS	149 adverse events reported (0.72% of all procedures): infection (61.1%), dehiscence and partial/full necrosis (20.1%), bleeding and hematoma (15.4%) 4 serious adverse events (0.02% of all procedures)	None reported
Chren, 2013 (19)	1 and 2	Prospective cohort (two sites)	1,174 (1,488 lesions)	BCC SCC All tumours primary	Med age differed by site and tumour location	556 MMS (37.4%) 361 Destruction (24.3%) 571 Excision (38.3%) Med f/u 7.4 yrs (all groups)	n/a	Overall 5 yr recurrence rate 3.3% (95% CI 2.3-4.4) No difference between unadjusted recurrence rates between treatments: 4.9% (2.3-7.4%) ED&C, 3.5% (1.8-5.2%) excision, 2.1% (0.6-3.5%) MMS; p=0.26
Kropp, 2012 (20)	1 and 2	Retrospective cohort (single centre)	36 (MMS group)	BCC and SCC to head and neck with incidental PNI MMS group 89% SCC, 11% BCC	MMS med age 67.5 y, M:F 6:1 SE med age	MMS + RT (n=36); med f/u 4.2 y Med RT dose after MMS: 63 Gy (15-77.2 Gy) SE + RT (n=82) *another publication from same centre	5 yr OS 53% MMS + RT vs 56% non-MMS group (p=0.809) 5 yr cause-specific survival 84% MMS vs 68% non-MMS (p=0.0329) 5 yr local control MMS 86% vs 76% non MMS (p=0.0606) *Note MMS group compared with results from earlier study (non-MMS excision and RT for NMSC w PNI)*	

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Bordea, 2011 (21)	1 and 2	Prospective study	1911	Nose (21%), cheek (16%), forehead (15%), and back (8%) Type unspecified	731 (38%) pts on one anticoagulant or antiplatelet med, 136 (7%) were on 2, 16 (0.84%) were on 3, and on pt was on 4.	MMS: 1369 (72%) SE: 542 (28%)	Complex repair (OR 5.80), flap repair (OR=11.93), and partial repair (43.13) were more likely to result in bleeding than intermediate repair. Pts on both clopidrogrel and warfarin were 40X more likely to have bleeding than all others (P=0.03). Risk of incection was 1.3%, but was greater than 3% on genitalia, scalp, back, and leg. Partial flap necrosis occurred in 1.7% of flaps and partial graft necrosis occurred in 8.6% of grafts. Partial graft necrosis occurred in 20% of grafts on the scalp and 10% of grafts on the nose. Rate of complications low even with use of multiple oral anticoagulants and antiplatelet medications and when prophylactic antibiotics not used.	
Chren, 2011 (22)	1 and 2	Prospective cohort (single centre)	495 (616 lesions)	ED&C: 87% BCC, 13% SCC SE: 66% BCC, 34% SCC MMS: 75% BCC, 25% SCC	Mean age 71 y 97% men	127 ED&C (20.9%) 309 SE (50.8%) 172 MMS (28.3%) Med f/u overall 6.6 y (ED&C 6.7y, SE 6.2y, MMS 7y, p=0.6)	Overall recurrence 21/608 (3.5%, 95% CI 2.2-5.2%) ED&C: 1.6% (95% CI 0.2-5.6%) SE: 4.2% (95% CI 2.2-7.1%) MMS: 3.5% (95% CI 1.3 – 7.4%) Estimated 5 yr recurrence: ED&C: 1.8% (95% CI 0.4-6.9%) SE: 4% (95% CI 2.2-7.4%) MMS: 2.6 (95% CI 0.8-7.7%)	
Van de Eerden, 2010 (23)	1 and 2	Retrospective cohort (single centre)	1,504	628 Non-aggressive pBCC (41.8%) 114 non-aggressive rBCC (7.6%) 383 aggressive pBCC (25.5%) 173 aggressive rBCC (11.5%) 183 pSCC (12.2%) 23 rSCC (1.5%) *non-aggressive = nodular and superficial BCC **aggressive = sclerosing, infiltrating, micronodular BCCs	Med age 73 y 291 M, 713 F	MMS (n=795) med f/u 24 months SE (n=709) med f/u 16 months	72% of MMS and 92% of SE cases controlled after one excision cycle 22% MMS cases required 2 Defects smaller after MMS (p=0.038) for recurrent tumours of nose	MMS 6/795 (0.75%) recurred SE 7/709 (0.98%) recurred; p=0.78 Analysis of the resection defects with general linear models adjusted for localization and primary or recurrent disease showed significantly smaller defects after MMS (p = .008)
Asgari, 2009 (24)	1 and 2	Prospective cohort	834	BCC (76.6%) SCC (23.4%) 68% of lesions located on head or neck	Mean age 65.8 y	ED&C (n=162) SE (n=332) MMS (n=340)	Across domains, no sig difference between groups in short-term satisfaction (1 week after tx, PSQ-18) Higher long term satisfaction (1 yr post tx) independently associated with young age, better pretreatment mental health and skin-related QOL, and treatment with MMS (p<0.05).	

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Chren, 2007 (25)	1 and 2	Prospective cohort	508	ED&C: BCC 82% , SCC 18% SE: BCC 69%, SCC 31% MMS: BCC 83%, SCC 17%	Mean age ED&C 65y Mean age SE 68y Mean age MMS 65y	ED&C (n=136) SE (n=251) MMS (n=246)	Pts treated with surgery or MMS experienced improvements in all 3 QOL domains (Symptoms, Emotions, Function) (p<0.05). Pts treated with ED&C experienced no change in tumour-related QOL. Pts treated with surgery or MMS had significantly better scores in all 3 QOL domains in comparison to pts treated with ED&C (p<0.05). No difference between excision and MMS.	
Mohs only								
O'Hallorran, 2017 (26)		Retrospective cohort (single centre)	690	Periocular tumours 589 BCC (85.4%) 60 SCC (8.7%) 29 SCC *in situ* (4.2%) 12 Other (1.7%) 58% lower eyelid, 26% medial canthus, 10% lateral canthus, 6% upper eyelid	Mean age 65 y 212 pts (31%) repaired by Mohs surgeon 478 (69%) patients repaired by oculoplastic surgeon	MMS *(f/u not reported)*	Mean preop lesion size 0.5cm^2 Mean postop size 1.5cm^2 Mohs surgeons vs 1.9cm^2 oculoplastic surgeons (p<0.002) Mean # stages 1.5 mohs surgeons vs 1.9 oculoplastic (p<0.0001)	Recurrence rate 1.1% (5) for cases repaired by oculoplastic surgeons, no recurrence for Mohs surgeons
Santos-Arroyo, 2016 (27) **conference abstract only*		Retrospective cohort (single centre)	219	179 BCC: 73.3% nodular, 2.4% superficial, 12.7% micronodular, 7.9% morpheaform, 1.8% basosquamous, 1.8% infundibulocystic 54 SCC: 16.7% SCC in situ, 83.3% SCC invasive	Not available	MMS	Mean # stages 2.03 for aggressive BCC (micronodular/morpheaphorm) vs 1.56 for least aggressive BCC (nodular/superficial) p = 0.034 No sig diff bw mean # stages for SCC in situ and invasive SCC (1.56 vs 1.67, p=.701) Mean # stages for recurrent tumours 2.22 vs 1.61 primary (p=0.006)	N/A
Vajdi, 2016 (28) **conference abstract only*		Retrospective cohort (single centre)	1110	724 BCC 357 SCC 29 Other subtypes NMSC	Not available	MMS, pts followed up for a minimum 5 yrs	Not available	Overall recurrence 5/1110 (0.45%) 3/724 BCC (0.41%) 2/357 SCC (0.56%) All recurrences on cheeks, ears, or nose Mean time to recurrence 23.6 months (range 11-38)
Treacy, 2015 (29)		Retrospective cohort (single centre)	127	107 pBCC: 68 nodular, 26 infiltrating, 8 nodulocystic, 5 adenoid, 3 multifocal, 2 superficial	Mean age 68 y 63 W, 64 M	MMS; ; mean f/u 2 y	61% cleared stage 1 32% cleared stage 2 5% cleared stage 3 2% cleared stage 4 11 postop complications (8.7%)	No recurrences to date

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
				5 rBCC: 3 nodular, 2 sclerosing 6 SCC *9 pts had non-malignant lesions removed				
Zabielinski, 2015 (30)		Retrospective cohort (single-centre) QI project examining locally recurrent NMSC undergoing 2nd MMS procedure	3,169 (22 recurrences studied)	Inclusion: local recurrence ≤5 yr from original MMS, photo confirmation of original tumour site, and clinical recurrence at previous site 22 recurrences: 17 SCC, 4 BCC, 1 sebaceous carcinoma, 1 atypical fibroxanthoma	Not reported	2nd MMS; time to recurrence not reported	Laboratory errors possibly leading to recurrence identified in 18/22 cases (82%): Dense inflammation (6) Residual tumour on slide (5) At least 15% epidermis or dermis missing (5)	0.7% (22/3169 MMS cases) recurred within 5 years of original surgery
Merrit, 2012 (31)		Prospective cohort (multicentre)	1,150 (1,792 lesions)	BCC (61%) SCC (31%) Melanoma (6%) Other (2%) Most procedures head and neck	Mean age 69 y	MMS *(f/u within 4 weeks of surgery for 95.3% of pts)*	Mean preop size 1.14cm Mean defect size 1.89 cm Mean # stages 1.6 (1-8) No deaths or major complications in postop period 44.1709 (2.6%) had primary minor complications (active bleeding, hematoma, infection, necrosis)	N/A
Macfarlane, 2012 (32)		Retrospective cohort (multicentre)	798	BCC (93%) SCC (4.3%) BSC (0.8%) DFSP (0.5%) Other (1.7%) Most procedures on head or neck	Mean age 69 y (22-92)	MMS *(f/u recorded at 3 months, 2 years, and 5 years)*	Outcome data only available for 28% of pts in 2yr f/u group and 38% in 5yr f/u group	5/798 tumours recurred (all BCC) KM overall recurrence 0.5% at 2 years and 2.7% at 5 years for BCC KM overall recurrence 0.3% at 2 and 5 years for pBCC only
Leibovitch, 2006 (33)		Prospective cohort (Australia-wide, Skin and Cancer Foundation)	316	Scalp tumours: 183 BCC (57.9%) 113 SCC (35.8%) 13 BD (4.1%) 5 AFX (1.6%) Recurrent tumours comprised 36% of cases	Mean age 65±15 y 100 W, 216 M	MMS	Mean # MMS stages: 1.53 BCC 1.57 SCC	70 BCC completed followup; recurrence rate 5.7% 31 SCC completed followup; recurrence rate 3.2% No recurrence in pts w BD or AFX

1st Author	Included for Guideline Question:	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Leibovitch, 2005 (34)		Prospective cohort (Australia-wide, Skin and Cancer Foundation)	581	Cutaneous lip tumours: BCC 82.3% SCC 16.5% BD 0.5% MAC 0.5% Primary tumour in 64.9% of cases, recurrent in 35.1%	Mean age 58±15 y 66.1% W	MMS	BCC more common on upper lip and in women SCC more common in lower lip and men	5 yr recurrence 4/133 BCC (3%) No cases of recurrence for SCC, BD, MAC
Leibovitch, 2005 (35)		Prospective cohort (Australia-wide, Skin and Cancer Foundation)	178	Basosquamous carcinoma (95.6% in the head and neck area) 60.9% recurring tumours	Mean age 63 ±11y Diagnosed initially as BBC in 87.4% and SCC in 12% of pts 115 M, 63 F	MMS	Mean # stages 1.7±0.7	4/98 completing 5 yr follow up had recurrence (4.1%)
Batra, 2002 (36)		Retrospective analysis	1131	BCC or SCC Size and location on nose, ear, eyelid, temple, and neck has significantly higher odds of subclinical spread Morphenaform BCCs 2.3X (P<0.001), recurrent BCCs were 3.2X (P<0.001), and recurrent SCCs 4.2X (P=0.01) as likely to exhibit subclinical spread compared to nodular BCCs.	Mean age 64.1 +/- 15.3 yrs vs 65.8+/- 14.5 yrs among pts with extensive subclinical spread (P=0.13)	244 (21.6%) required 3 or more MMS (considered indicator of subclinical spread)	Pre-op size significant indicator of extensive subclinical spread. Increasing ORs from 1.8-3.7 were directly correlated with increasing size >10mm. ID lesions significantly associated with subclinical spread to help guide management to ensure complete tumour eradication.	

Appendix A Table 2. BCC Only

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Comparison of treatments							
Van Loo, 2014 (37)	RCT	612	408 pBCC: ≥1cm in diameter, located in either H-zone face or aggressive histologic l subtype 204 rBCC: at least 1 facial BCC recurring for the first or second time	pBCC: mean age 67.4 y (MMS) and 68.7 y (SE) rBCC: mean age 69.2 y (MMS) and 67.1 y (SE)	Pts randomly assigned to MMS or SE (1:1) Med f/u pBCC group: 79.2 months (0-150.3) Med f/u rBCC group: 85.0 months (0-149.3)	None reported	pBCC: 10 yr recurrence rates 4.4% MMS vs 12.2% SE (Log-rank test $\chi 2$ 2.704, p = 0.100); 56% of recurrences occurred >5 yrs post-tx rBCC: 10 yr recurrence rates 3.9% MMS

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
							vs 13.5% SE (Log-rank test χ^2 5.166, p = 0.023); 14% of recurrences occurred >5 yrs post-tx
Narayanan, 2014 (38)	Cochrane Systematic Review	N/A	Periocular BCC	N/A	SE MMS	No RCTs identified comparing SE with MMS in periocular BCC; no reliable conclusions could be reached regarding whether SE or MMS = lower recurrence or complication rate for periocular BCC	
Jebodhsingh, 2012 (39)	Retrospective chart review	385	BCC- 385	Average age of pts with recurrence were 67.7+/-15 Average of pts without recurrence were 75.4+/-13.6 (P=0.025)	MSS frozen w – margins (recurrence free rate (RFR) 92%) Permanent sections with – margins (RFR 87%) Permanent sections with + margins (RFR 80%) Difference P<0.05 170 mo F/U	3 yr follow up recommended for pts with BCC Average time to recurrence was 40 mo SD 39 mo Only predictor of recurrence was younger age (HR=0.97 95% CI 0.94, 0.99; P=0.021)	
Muller, 2009 (40)	RCT	30	BCC (nodular, <1cm, at least 1cm away from eyelids and nose) Exclusion criteria: immunosuppression, superficial, recurrent, morpheic, infiltrative	MMS mean age 66 y SE mean age 72 y Almost all tumours on head and neck (12/15 MMS, 14/15 SE)	MMS (n=15); excised with 2mm margins SE (n=15); excised with 4mm margins	Blind observer calculated defect size. Median area of surgical defects MMS group 116.6cm^2 vs 187.7cm^2 in standard surgery group (95% CI for difference 61-126, p<.001)	N/A
Mosterd, 2008 (41)	Prospective RCT	612 (393 at 60mo f/u) rBCCs: 204 (134 at 60mo f/u)	pBCCs: 408 (259 at 60mo f/u)	Mean age 67.7y (SD 12.7; range 23-92)	pBCC: MMS (n=198) SE (199) rBCC: MMS (n=102) SE (n=102)	Recurrences in pts with pBCC: 7 (4.1%) in SE and 4 (2.5%) in MMS. In rBCC 2 in 2 (2.4%) pts with MMS recurred vs 10 in 10 (12.1%) with SE (p=0.015). Difference in recurrence not significant for pBCC but significantly favored MMS in rBCC. Cox-regression showed no effect from risk factor in pBCC but in RBCC aggressive histological subtype was significant. pBCC treatment cost: 1248 euro for MMS, 990 euro for SE rBCC treatment cost: 1284 euro for MME, 1043 euro for SE incremental cost effectiveness ratio of 23454 euro for pBCC and 3171 for rBCC.	
Essers, 2007 (42)	Survey parallel to RCT	222	pBCC: 133 rBCC: 89	Mean age: pBCC 65.61 (SD 12.51), rBCC 64.69 (SD 12.20)	pBCC: MMS (n=77) SE (n=56) rBCC: MMS (n=41) SE (n=48)	No statistically significant difference on facial asthetics btw the pBCC or rBCC groups or those treated with MMS or SE. Evaluation of postsurgical facial aesthetics can be predicted by both visibility of	

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
						tumour and preoperative perceptions. Administer pre-op questionnaire about perceptions of facial aesthetics.	
Chren, 2004 (43)	Prospective cohort study	1375	1777 pBCCs (Private clinic n=1111 BCC 76.8%, SCC 23.2%) (Veterans Affairs (VA) n=666 BCC 72.7%, SCC 27.3%) Tumour present in H zone of Face Private 30.4%, VA=45.7% (P<0.001)	Private Clinic mean age 62.7 (SD 16.2) VA mean age 72.0 (SD 11.6)	Electrodissection (Private 23.0%, VA 18.9%) Excision (Private 24.6%, VA=48.2%) MMS (Private 36.7%, VA 25.4%) All P<0.001 Chi square	Mohs more likely to be performed at the private site. Controlling for clinical features that may have affected treatment choice tumours at private clinic more likely to be treated with Mohs than at the VA (OR=2.39, 955 CI 1.54-3.70)	
Mohs only							
Hoorens, 2016 (44)	Prospective cohort (single centre)	1062	BCC (head and neck) 744 pBCC (70%) 311 rBCC (29.3%) 561 morphoeaform (56.4%) 279 solid (28%) 37 micronodular (3.7%) 20 superficial (2%) 7 basosquamous (0.7%) 91 mixed (9.1%)	Mean age 63.8 y M 50.6%	MMS 25.1% 1 round 55.6% 2 rounds 13% 3 rounds 3.8% 4 rounds 1.9% 5 rounds	Mean # stages 2.01 ±0.84 Sig variables for >1 round MMS: Age >80y (OR 1.9, 95% CI 1-3.5) Tumour surface >1cm2 (OR 1.8, 95%CI 1.2-2.6) Mophoeaform (OR 2.5, 95% CI 1.8-3.4) Micronodular (OR 3.6, 95% CI 1.3-8.9) Mixed histology (OR 3.1, 95% CI 1.7-6.0) *authors assume that 1 round of MMS (2mm) would have been cleared with SE	
Sin, 2016 (45)	Retrospective cohort (single centre)	390	Periocular BCC (80.2% pBCC, 19.7% rBCC) High risk areas (upper/lower lids and medial/lateral canthal regions)	Mean age 67 y 170 M, 220 F	MMS; mean f/u 30 months (1-120)	N/A	6/390 recurred (1.5%) 1 pBCC and 5 rBCC
Gniadecki, 2015 (46)	Retrospective cohort (single centre)	231 (236 lesions)	54% pBCC 46% rBCC Localizations: forehead (31.3%), nose (31%), cheek (14.7%)	Mean age 66.1 y 111 M, 120 W rBCC most freq previously treated with curettage (36.9%), RT (18.9%), and photodynamic therapy (11.7%)	MMS	BCC removed: 36.5% 1 stage 45.2% 2 stage 12.5% 3 stage 5.8% 4+ stage MMS leads to 40% smaller skin defects than SE with 4 or 6 margins	No recurrences reported *only 44.8% of tumours followed for one year or more after surgery
Catala, 2014 (47)	Retrospective cohort (single centre)	534	256 pBCC (47.9%) 278 residual or rBCC (52.1%) 38.4% nose, 24.3% periocular region, 37.3% other **MMS criteria:** 1+ features associated w high risk of recurrence: anatomic areas high	M: 241, F: 248 Age: 69 (med); 24-92	MMS; mean f/u 30.5 months (1-145 months)	MMS completed w 1 stage in 55.8% of cases	32/534 recurred (6%) 1.2% recurrence rate pBCC 10.4% recurrence rate rBCC Prior tx, multiple prior tx, and healing by 2nd intention predicted recurrence after

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
			potential recurrence, require max preservation healthy tissue for functional or cosmetic outcomes, tumours w poorly defined clinical margins, tumours w aggressive histopathological patterns, on previously irradiated area, recurrent or persistent BCC and tumours in immunosuppressed pts				MMS (p = 0.018, 0.013, 0.041, respectively) KM 5 yr recurrence 3.2% (95% CI 0-7.1%) pBCC and 32.3% (95% CI 20.2-44.5%) for rBCC
Allen, 2014 (48)	Retrospective cohort (single centre)	160	32 BSC (basosquamous carcinoma) 128 MBCC (metatypical BCC) 94% of tumours occurred on head, most commonly nose (29%)	M: 117, W: 42 Med age 73.8; 35-93 range	MMS; med f/u 39 months	Med # MMS stages: 1	KM 1 yr recurrence 100% BSC and MBCC, 5 yr recurrence 100% BSC and 93.8% MBCC (p=0.19)
Flohil, 2013 (49)	Retrospective cohort (single centre)	1464	BCC Indication criteria: head and neck area AND one or more of: indistinct clinical margins, aggressive histo subtype, >20mm, H-zone, incompletely excised, PNI, recurrent	M: 49.2% Mean age 66.3 y (18-96)	MMS	2+ stages significantly associated with: H-zone location OR 1.51 (95%CI 1.16-1.96) Aggressive subtype OR 1.25 (95% CI 1.01-1.56) ≥11mm OR 1.53 (95% CI 1.20-1.96) Extensive subclinical spread (3+ stages) associated with: Recurrent tumour OR 2.26 (95% CI 1.61-3.17) ≥21mm OR 1.69 (95% CI 1.13-2.51) H-zone location OR 1.68 (95% CI 1.15-2.46)	
Litwin, 2013 (50)	Retrospective cohort (single centre)	104	Periocular BCC (62% pBCC, 25% rBCC)	M: 57, F:47 Mean age 66 y (35-98)	MMS; mean f/u 28 months (1-85)	None reported	Overall recurrence 5.9% pBCC 1/63 (1.6%) rBCC 5/25 (20%)
Veronese, 2012 (51)	Retrospective cohort (single centre)	350	BCC of head region: 51.4% of tumours located on nose, 13.1% periocular, 9.1% paranasal 169 pBCC (48%) 156 rBCC (45%) 25 incomplete excision (7%) Histological subtype: Aggressive 221 (63%) Non-aggressive 87 (25%) Undetermined 42 (12%)	M: 176, F: 174 Age: 66y (med); 30-91	MMS; med f/u 7 yrs (11 months – 14 yrs) 180 direct MMS (51.4%), 170 delayed MMS (48.6%)	None reported	29/350 recurred (12 pBCC and 17 rBCC/incompletely excised BCC) 3.4% recurrence rate pBCC 4.9% recurrence rate rBCC

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Paoli, 2011 (52)	Retrospective cohort (single centre)	587	328 pBCC: 223 morphoeic, 20 infiltrative, 33 nodular or superficial, 52 NOS 258 rBCC: 121 morphoeic, 20 infiltrative, 33 nodular or superficial, 78 NOS 42.6% of tumours located on nose	M: 240, F: 315 Age: 69y (med); 26-89	MMS; med f/u 5 years (range 0.5-11.5)	Mean # MMS stages: 2.39 (95% CI 2.32-2.47) Pre-MMS defect: 1.98cm^2 (med) Post-MMS defect: 3.9 cm^2 (med)	16/486 recurred (6 pBCC, 10 rBCC) 5 yr recurrence: pBCC 2.1% (95% CI 0.4-3.8%) rBCC 5.2% (95% CI 1.6-8.7%) Overall 3.3% (95% CI 1.6-5.0%)
Leibovitch, 2005 (53)	Prospective cohort (Australia-wide, Skin and Cancer Foundation)	3370	1886 pBCC (56%) 1484 rBCC (44%) 98.4% located on head and neck; 38.4% nose, 17.1% cheek and maxilla, 10.9% auricular region, 10.9% periocular	M: 1776, F: 1594 Mean age 61 ± 14 y	MMS (f/u 5 years)	N/A	5 yr recurrence pBCC 1.4% 5 yr recurrence rBCC 4% Predictors for recurrence @ 5 yrs: previous recurrence (p<0.001), longer tumour duration before MMS (p=0.015), and more levels of tumour (p<0.001)
Leibovitch, 2005 (54)	Prospective cohort (Australia-wide, Skin and Cancer Foundation)	283	BCC with PNI Nose (24.7%) Cheek and maxilla (23.7%) Forehead (18%)	M: 173, F:110 Mean age 65 ± 12 y	MMS	Mean # MMS stages 2.5 (vs 1.72 in rest of cohort, p<.0001)	6/78 pts who completed 5 yr f/u recurred (7.7%)
Smeets, 2004 (55)	Retrospective cohort (single-centre)	620 (720 BCC)	pBCC: 365 rBCC: 226 219 nose (30%) 167 forehead/temporal area (23%)	M: 345, F: 275	MMS; med f/u 3.6 y (0-9.6) 292 had 5+ years f/u	25% cleared in stage 1 46% cleared in stage 2	Overall 5 yr recurrence 4.5% 5 yr recurrence pBCC 3.2% 5 yr recurrence rBCC 6.7% (p=0.023) Prognostic factors for recurrence: aggressive subtype (p=0.015), 4+ MMS stages (p=0.0013), large defect size (p=0.0027)

Appendix A Table 3. SCC Only

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
Comparison of treatments							
Bergeron, 2016 (56)	Retrospective cohort (multicentre)	117	Oral cavity SCC	Mean age 60.7y MMS vs 60.3y conventional (p=0.86)	60 MMS; med f/u 1093 days 57 Conventional; med f/u 2162 days	Complication rate 42.2% MMS vs 50.9% conventional (p=0.488)	1 yr recurrence rate was lower for MMS (10% vs 21.1%, p=0.019)

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
						Margins >2mm 91.7% MMS vs 83.6% conventional (p=0.188)	2 yr recurrence rate lower for MMS in Tis-T4N0M0 pts (10.5% vs 25.7%, z-score 1.849, p = 0.032)
Lansbury, 2013 (57)	Systematic review	N/A	Primary, non-metastatic, invasive SCC 118 publications included	N/A	WLE, MMS, RT, Cryotherapy, C&E	None reported	Pooled estimates of recurrence: WLE: 5.4% (95% CI 2.5-9.1%) MMS: 3% (95% CI 22.-3.9%) RT: 6.4% (95% CI 3-11%) Cryo: 0.8% (95% CI 0.1-2%) C&E: 1.2% (95% CI 0.5-3.4%)
Askari, 2013 (58)	Retrospective cohort (single-centre)	86	SCC of the hand	Mean age 69 y (39-89)	37 WE (43%) 2 amputation(2%) 23 MMS (27%) 24 shave excisions + curettage and cryotherapy (28%) Mean f/u 6.4 y (1-15)	N/A	No benefit noted with treatment modality (OS, RFS, SCC occurrence in ipsilateral upper extremity)
Mohs only							
Machan, 2016 (59)	Retrospective cohort (single-centre)	44	Penile SCC: 23 pSCC in situ, 3 rSCC in sutu, 14 pSCC, 8 rSCC Location: 17 glans penis, 18 shaft, 6 base, 2 prepuce	Mean age 64.4 y (29-92)	MMS	Mean # stages 2 (1-7) Mean margin for clearance 0.83cm	pSCC and rSCC in situ: 2/20 reucrrences (mean f/u 94.9 months) pSCC: 0/10 recurrences (mean f/u 161 months) rSCC: 2/6 recurrences (mean f/u 84.2 months)
Dika, 2015 (60)	Retrospective cohort (single-centre)	57	SCC of the nail: microinvasive SCC (5), in situ SCC (7), invasive (45) Locations: first fingernail (27), other digits of hand (22), big toe (5), other digits of foot (3)	Mean age 63 yrs 39 M, 18 F	MMS (43 pts) (f/u every 6 months for 5 yrs)	N/A	2/43 pts treated with MMS recurred (3.5%)
Pugliono-Mauro, 2010 (61)	Retrospective cohort (single-centre)	260	High risk SCC (231 primrary, 29 recurrent) (invasive tumours of ear and lip, tumours of temple in elderly men, >2cm diameter, rapid growth >1cm, perineural involvement,	Mean age 70.6y 77% male, 23% female 20% pts immunosuppressed	MMS Mean f/u 3.9 yrs	Mean preop diameter 1.5 +- 0.7cm Mean postop wound 2.6 +- 1.2cm	1.2% of cases (3) locally recurred 2.3% of tumours metastasized (1 fatality) 75% of patients developed another SCC

1st Author	Study Type	N	Tumour characteristics	Patients	Treatment and F/U	Surgical outcomes	Disease outcomes
			immunosuppressed pts)				
Shindel, 2007 (62)	Retrospective cohort (single-centre)	33 (25 with f/u)	Penile cancers: 17 SCC 27 SCC in situ 4 verrucous carcinoma 1 BCC 1 epidermoid carcinoma	Not available	MMS Mean f/u 58 ± 63 months (data available for 25 pts)	Mean # stages 2.6±1.4 5 procedures terminated w positive margins	8/25 pts recurred (32%); managed by MMS in 7 and penectomy in 1
Leibovitch, 2005 (63)	Prospective cohort (Australia wide – Skin and Cancer Foundation)	1263	61.1% pSCC 38.9% rSCC 96.5% on head and neck	Mean age 66 ±13 y 25.7% F, 74.3% M	MMS	rSCC larger than pSCC, had a larger postexcision defect, required more levels of excision, and had more cases of subclinical extension (p <.001, <.001, <.001, =.002, respectively)	15/381 (3.9%) pts who completed 5 y f/u recurred after MMS Recurrence rate 2.6% pSCC and 5.9% in rSCC (p<.001)
Leibovitch, 2005 (64)	Prospective cohort (Australia wide – Skin and Cancer Foundation)	70	SCC with PNI (36 pSCC, 34 rSCC) PNI most common in auricular area (25.7%), cheek and maxilla (21.4%), forehead (18.6%) 55.7% of PNI tumours were >2cm compared to 17.6% of cases in cohort without PNI	Mean age 64 ±15 y 54 M, 16 W	MMS (+ RT in 52.9% of patients)	Mean # MMS levels 2.64±1.0 versus 1.70±0.8 in non-PNI cases in cohort (p<.0001)	2/25 (8%) pts who completed 5 y f/u recurred (95% CI 5.2-13.5%)
Leibovitch, 2005 (65)	Prospective cohort (Australia wide – Skin and Cancer Foundation)	270	Bowens disease (SCC in situ) 50.7% recurrent tumours 93.4% head and neck	Mean age 63 ±13 y 191 M, 79 W	MMS	Mean # MMS levels 2 ±0.9	6/95 pts who completed 5 yr f/u recurred (6.3%; 95% CI 2.4-13.4%)
Silapunt, 2005 (66)	Retrospective cohort (single-centre)	114	SCC of the ear Helix most common site (50.7%)	Mean age 71 y (34-90) M:F ratio 22:1	MMS Of those followed for 2+ years, mean f/u 41.8 months	Free margins after 1 stage in 49.3%, 2nd stage 31.9%, 3rd stage 9.7%	5/122 available for followup recurred 2 year local recurrence rate 5.7% (5/87 tumours)
Murphy 2008 (67)	Retrospective cohort (single-centre)	N=1347 (path sections)	Fellow in training reviewed Mohs histopathology and compared to Mohs program directors review	NA	NA	It took 6 months of Mohs surgery fellowship before the fellow reduced their error rate to less than 1 critical error per 100 cases (defined as the minimum acceptable level)	NA

Appendix Table 4. Relevant Guidelines

Guideline Developer	Recommendations
NCCN, 2017(67,68)	**Local, low-risk SCC or BCC**: 1) curettage & electrodessication, OR 2) standard excision → Mohs micrographic surgery or resection if positive margins, OR 3) radiotherapy if not surgical candidate **Local, high-risk SCC or BCC:** 1) Mohs micrographic surgery or resection with complete margin assessment, OR 2) standard excision → Mohs micrographic surgery or resection if positive margins, OR 3) radiotherapy ± systemic therapy if not surgical candidate
UptoDate, 2017(69)	**General indications:** locally aggressive tumours at high risk for recurrence - *Tumour characteristics:* large (≥2cm), poorly defined clinical borders, recurrent tumour, incompletely excised (positive margins), aggressive histological features (morpheaform, micronodular, infiltrative BCC; basoswuamous features; poorly differentiated and deeply infiltrative SCC; perineural invasion), or chronic scar (Marjolin's ulcer) - *Patient characteristics*: immunosuppressed, irradiated skin, or genetic syndrome (eg xeroderma pigmentosum, Gorlin or nevoid BCC) - *Anatomic location:* areas where tissue preservation is essential, embryonic fusion lines, or 'mask areas' of face **BCC:** high-risk pBCC and rBCC are most common tumours treated w MMS. - Tumours ≥6 mm located in high-risk areas (central face, nose, lips, eyelids, eyebrows, periorbital skin, chin, mandible, ears, preauricular and postauricular areas, temles, hands, feet); OR - Tumours ≥10 mm in other areas of face (cheeks, forehead, scalp, and neck); OR - Tumour ≥ 20 mm on trunk or limbs; OR - Tumours with aggressive pathologic features **SCC:** high risk SCC (eg, tumours ≥20mm, involving high-risk area of face such as ears and lips, or tumour showing perineural invasion or poor histologic differentiation)
UK National Multidisciplinary Guidelines, 2016 (70)	**BCC:** Where there is a high risk of recurrence, delayed reconstruction of MMS should be sued **SCC:** MMS has a role in some high-risk cSCC cases following MDT discussion
Canadian Non-melanoma Skin Cancer Guidelines Committee, 2015 (8,12,)	**BCC:** Mohs micrographic surgery may be considered as a first-line option for high-risk primary BCC, incompletely excised high-risk BCC, and most recurrent BCCs amenable to surgery. **High-risk primary or recurrent SCC:** Mohs micrographic surgery should always be considered for lesions with poorly defined borders, particularly if such lesions occur on cosmetically sensitive areas, such as face, hands, and feet. For reasons of cosmesis and function, SCCs on certain sites (eyebrows, eyelids, nose, hands, and feet) should also be treated as high risk, with preferential use of Mohs micrographic surgery to spare as much as possible of the surrounding healthy tissue.
American Society for Dermatologic Surgery, 2015 (5)	**BCC:** Mohs surgery is the treatment of choice for high-risk BCCs and recurrent BCCs because of its high cure rate and tissue-sparing benefit. Because the most effective treatment for any BCC is Mohs surgery, it also remains the best treatment option for tumors at high risk of recurrence after other treatment modalities.
British Association of Dermatologists, 2014 (71)	**SCC:** Mohs micrographic surgery may be indicated for digital SCC *in situ* (around the nail in particular) and for some cases of genital (especially penile) SCC *in situ* for its tissue-sparing benefits. There may also be a role for Mohs in recurrent or incompletely excised lesions.
London Cancer Alliance, 2014 (72)	**BCC:** poorly defined borders, high-risk site (i.e. H-zone), aggressive histology such as morphoeic or infiltrative or micronodular, perineural invasion, lymphovascular invasion, recurrent tumors (or incompletely excised), large tumors (>2cm), immune-compromised patient **SCC:** poorly defined borders, high-risk site (i.e. H-zone), perineural invasion, lymphovascular invasion, recurrent tumors (or incompletely excised), large tumors (>2cm), immune-compromised patient, persistent Bowen's disease at awkward site (i.e. genitals, eyelid, scalp, nails)
Scottish Intercollegiate Guidelines Network (SIGN), 2014 (73)	Mohs micrographic surgery should be considered at the MDT meeting, for selected patients with high-risk tumours where tissue preservation or margin control is challenging, and on an individual case basis for patients with any tumour at a critical anatomical site.
AAD/ACMS/ASDSA/ASMS Appropriate Use Criteria, 2012 (74)	**Area H** (mask areas of face, genitalia, hands, feet, nails, ankles, nipples/areola): - **BCC**: appropriate for primary or recurrent aggressive, nodular, or superficial - **SCC:** appropriate for primary or recurrent aggressive, nonaggressive, verrucous, KA-type, *or in situ*/Bowen - Lentigo and *in situ* melanoma: appropriate for primary or recurrent disease **Area M** (cheeks, forehead, scalp, neck, jawline, pretibial surface): - **BCC**: appropriate for recurrent or primary aggressive, nodular, or superficial (IC) and primary superficial ≥0.6cm - **SCC**: appropriate for primary or recurrent aggressive, nonaggressive, KA-type and *in situ*/Bowen - Lentigo and *in situ* melanoma: appropriate for primary or recurrent disease

Guideline Developer	Recommendations
	Area L (trunk and extremities): - **BCC:** appropriate for recurrent aggressive or nodular, primary aggressive ≥0.6cm, primary nodular > 2cm, or nodular (IC) ≥1.1cm - **SCC:** appropriate for primary or recurrent aggressive, recurrent KA-type or nonaggressive, primary >2m nonaggressive or *in situ*/Bowen, primary ≥1.1cm nonaggressive (IC), KA-type, or *in situ*/Bowen, and KA-type (IC) ≥0.6cm - Lentigo and *in situ* melanoma: appropriate for recurrent disease
Cancer Council Australia, 2008 (75)	Mohs surgery may be considered in the following situations: 1. tumours with poorly defined borders, in particular those with poor tumour biology and located in anatomically sensitive areas 2. tumours that have been recurrent (or residual) following previous treatment 3. extensive disease
British Association of Dermatologists Guidelines, 2008 (76)	MMS is a good treatment for high-risk primary BCC and high-risk recurrent BCC Indications for MOHs • Tumour site (especially central face, around the eyes, nose, lips, and ears) • Tumour size (any size, but esp >2cm) • Histological subtype (morphoeic, infiltrative, micronodular, and basosquamous subtypes) • Poor clinical definition of tumour margins • Recurrent lesions • Perineural or perivascular involvement
Canadian Agency for Drugs and Technologies in Health (CADTH) Rapid Response Report: Summary with Critical Appraisal "Mohs Surgery for the Treatment of Skin Cancer: A Review of Guidelines", 2019 (77)	Key Findings: 1) MMS is recommended as a first-line option for high-risk primary or recurrent basal cell carcinoma or squamous cell carcinoma 2) MMS may be considered as one of the options for squamous cell carcinoma, especially where tissue preservation or margin controls are challenging, or when the tumor is at a critical anatomical site 3) In squamous cell carcinoma in situ (Bowden's disease), MMS may be indicated for digital and penile tumour, or in recurrent or incompletely excised lesions. 4) MMS may be considered for melanoma in situ (lentigo maligna) and Merkel cell carcinoma, especially when the tumor is in a sensitive area and there are concerns of functional impairment from an excision that is too radical. 5) Although the size of the lesion should be analyzed together with its location and histological pattern, MMS could be a better treatment option for tumors larger than 2 cm which present higher chance of incomplete removal with conventional surgery. 6) MMS leads to a smaller recurrence rate than conventional surgery for dermatofibrosarcoma protuberans. 7) The majority of the recommendations on the use of MMS for skin cancers were based on evidence of limited quality and need to be interpreted with caution. More high-quality trials are required to elucidate the role of MMS on skin cancers.
Cancer Care Ontario: Patient Indications for Mohs Micrographic Surgery, 2018 (13)	Recommendations: 1. Surgery (with postoperative or intraoperative marginal assessment), or radiation for those who are ineligible for surgery, should remain the standard of care for patients with skin cancer given the lack of high-quality, comparative evidence. 2. MMS is recommended for those with histologically confirmed recurrent basal cell carcinoma (BCC) of the face, and is appropriate for primary BCCs of the face that are >1 cm, have aggressive histology, or are located on the H zone of the face (Figure 1-1). 3. MMS should be performed by physicians who have completed a degree in medicine or equivalent, including a Royal College of Physicians and Surgeons of Canada Specialist Certificate or equivalent, and have received advanced training in MMS. 4. Surgery (with postoperative or intraoperative marginal assessment), or radiation for those who are ineligible for surgery, should remain the standard of care for patients with skin cancer given the lack of high-quality, comparative evidence. 5. MMS is recommended for those with histologically confirmed recurrent basal cell carcinoma (BCC) of the face, and is appropriate for primary BCCs of the face that are >1 cm, have aggressive histology, or are located on the H zone of the face (Figure 2-1). 6. MMS should be performed by physicians who have completed a degree in medicine or equivalent, including a Royal College of Physicians and Surgeons of Canada (RCPSC) Specialist Certificate or equivalent, and have received advanced training in MMS.
Guidelines of care for the management of cutaneous squamous cell carcinoma JAAD, 2018 (7)	Recommendations: 1. Stratification of localized SCCs using the NCCN guideline framework is recommended for clinical practice. Clinicians should refer to the BWH tumor classification system to obtain the most accurate prognostication of patients with localized cSCC. 2. The recommended biopsy techniques for cSCC are punch biopsy, shave biopsy, and excisional biopsy. The biopsy technique used will depend on the characteristics of the suspected malignancy (morphology, location, etc) and the judgment of the physician. The biopsy size and depth should be adequate to provide the recommended clinical information and pathology report elements to permit accurate diagnosis and guide therapy.

Guideline Developer	Recommendations
	3. A treatment plan that considers recurrence rate, preservation of function, patient expectations, and potential adverse effects is recommended. C&E may be considered for low-risk, primary cSCC in none terminal hairebearing locations. For low-risk primary cSCC, standard excision with a 4- to 6-mm margin to a depth of the mid-subcutaneous adipose tissue with histologic margin assessment is recommended. Standard excision may be considered for select high-risk tumors. However, strong caution is advised when selecting a treatment modality for high-risk tumors without a complete margin assessment. MMS is recommended for high-risk cSCC.t biopsy may be considered if the initial biopsy specimen is inadequate for accurate diagnosis. 4. If surgical therapy is not feasible or preferred, radiation therapy (eg, superficial radiation therapy, brachytherapy, external electron beam therapy, and other traditional radiotherapy forms) can be considered when tumors are low risk, with the understanding that the cure rate may be lower. Cryosurgery may be considered for low-risk cSCC when more effective therapies are contraindicated or impractical. Topical therapies (imiquimod or 5-FU) and PDT are not recommended for the treatment of cSCC on the basis of available data. There is insufficient evidence available to make a recommendation on the use laser therapies or electronic surface brachytherapy in the treatment of cSCC. 5. Surgical resection, with or without adjuvant radiation therapy and possible systemic therapy are recommended for regional lymph node metastases. Combination chemoradiation therapy should be considered for inoperable disease. Epidermal growth factor inhibitors and cisplatin, as a single agent or in combination therapy, may be considered, as they have demonstrated efficacy for metastatic disease, albeit on the basis of limited data. Multidisciplinary consultation and management, particularly in immunosuppressed individuals, is recommended for patients with locoregional or distant metastases. In some cases, such consultation may be appropriate for patients with locally advanced disease without known metastases. Patients with advanced disease should be provided with or referred for best supportive and palliative care to optimize symptom management and maximize quality of life. 6. After diagnosis of a first SCC, screening for new keratinocyte cancers (BCC or cSCC) and for melanoma should be performed on at least an annual basis. Patients with a history of cSCC should be counseled on skin self-examination and sun protection. Topical and oral retinoids (eg, tretinoin, retinol, acitretin, and isotretinoin) should not be prescribed to reduce the incidence of keratinocyte cancers in those with a history of cSCC, unless they are SOTRs. In the situation of SOTRs, only acitretin may be beneficial. Dietary supplementation of selenium and b-carotene is not recommended to reduce the incidence of future keratinocyte cancers in those with a history of cSCC. There is insufficient evidence to make a recommendation on the use of oral nicotinamide, DFMO, or celecoxib in the chemoprevention of cSCC.
Guidelines of care for the management of basal cell carcinoma JAAD, 2018 (6)	Recommendations: 1. Stratification of localized BCC using the NCCN guideline framework is recommended for clinical practice. 2. The recommended biopsy techniques for BCC are punch biopsy, shave biopsy, and excisional biopsy. The biopsy technique used will depend on the characteristics of the suspected malignancy (morphology, location, etc) and the judgment of the physician. The biopsy size and depth should be adequate to provide the recommended clinical information and pathology report elements to permit accurate diagnosis and guide therapy. Repeat biopsy may be considered if initial biopsy specimen is inadequate for accurate diagnosis. 3. A treatment plan that considers recurrence rate, preservation of function, patient expectations, and potential adverse effects is recommended. C&E may be considered for low-risk tumors in none terminal hairebearing locations. For low-risk primary BCC, surgical excision with 4-mm clinical margins and histologic margin assessment is recommended. Standard excision may be considered for select high-risk tumors. However, strong caution is advised when selecting a treatment modality without complete margin assessment for high-risk tumors. Mohs micrographic surgery is recommended for high-risk BCC. 4. Cryosurgery may be considered for low-risk BCC when more effective therapies are contraindicated or impractical. If surgical therapy is not feasible or preferred, topical therapy (eg, imiquimod or 5-FU), MAL- or ALA-PDT, and radiation therapy (eg, superficial radiation therapy, brachytherapy, external electron beam, and other traditional radiotherapy forms for BCC) can be considered when tumors are low risk, with the understanding that the cure rate may be lower. Adjustment of topical therapy dosing regimen on the basis of side effect tolerance is recommended. There is insufficient evidence to recommend the routine use of laser or electronic surface brachytherapy in the treatment of BCC. 5. Multidisciplinary consultation and smoothened inhibitors are recommended for patients with metastatic BCC. If treatment of metastatic BCC with smoothened inhibitors is not feasible, platinum-based chemotherapy or best supportive care is recommended. If surgery and radiation therapy are contraindicated or inappropriate for the treatment of locally advanced BCC, or if residual tumor persists following surgery and/or radiation therapy and further surgery and radiation therapy are contraindicated or inappropriate, systemic therapy with a smoothened inhibitor should be considered. Patients with advanced disease should be provided with or referred for best supportive and palliative care, to optimize symptom management and maximize quality of life.

Appendix B: Level of Evidence and Grade of Recommendation

Level of evidence

I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity.
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, experts opinion

Grade of recommendation

A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

References

1. Guenther LC, Barber K, Searles GE, Lynde CW, Janiszewski P, Ashkenas J. Non-melanoma Skin Cancer in Canada Chapter 1: Introduction to the Guidelines. J Cutan Med Surg 2015 May-Jun;19(3):205-215 .
2. Demers AA, Nugent Z, Mihalcioiu C, Wiseman MC, Kliewer EV. Trends of nonmelanoma skin cancer from 1960 through 2000 in a Canadian population. J Am Acad Dermatol 2005 Aug;53(2):320-328.
3. Jung GW, Metelitsa AI, Dover DC, Salopek TG. Trends in incidence of nonmelanoma skin cancers in Alberta, Canada, 1988-2007. Br J Dermatol 2010 Jul;163(1):146-154 .
4. Kauvar ANB, Cronin TJ, Roenigk R, Hruza G, Bennett R, American Society for Dermatologic Surgery. Consensus for nonmelanoma skin cancer treatment: basal cell carcinoma, including a cost analysis of treatment methods. Dermatologic Surgery 2015 May;41(5):550-571.
5. Kauvar ANB, Arpey CJ, Hruza G, Olbricht SM, Bennett R, Mahmoud BH. Consensus for Nonmelanoma Skin Cancer Treatment, Part II: Squamous Cell Carcinoma, Including a Cost Analysis of Treatment Methods. Dermatologic Surgery 2015 Nov;41(11):1214-1240 .
6. Bichakjian C, Armstrong A, Baum C, Bordeaux JS, Brown M, Busam KJ, et al. Guidelines of care for the management of basal cell carcinoma. J Am Acad Dermatol 2018 79(5): e99-e100.
7. Alam M, Armstrong A, Baum C, et al. Guidelines of care for the management of cutaneous squamous cell carcininoma. J Am Acad Dermatol 2018 78(3): 560-578
8. Zloty D, Guenther LC, Sapijaszko M, Barber K, Claveau J, Adamek T, et al. Non-melanoma Skin Cancer in Canada Chapter 4: Management of Basal Cell Carcinoma. Journal of Cutaneous Medicine & Surgery 2015;19(3):239-248 .
9. Newlands C, Currie R, Memon A, Whitaker S, Woolford T. Non-melanoma skin cancer: United Kingdom National Multidisciplinary Guidelines. Journal of Laryngology & Otology 2016 May;130(S2):S132.
10. National Comprehensive Cancer Network. Squamous Cell Skin Cancer. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed September 12, 2017.
11. National Comprehensive Cancer Network. Basal Cell Skin Cancer. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed September 12, 2017.
12. Sapijaszko M, Zloty D, Bourcier M, Poulin Y, Janiszewski P, Ashkenas J, et al. Non-melanoma Skin Cancer in Canada Chapter 5: Management of Squamous Cell Carcinoma. Journal of Cutaneous Medicine & Surgery 2015;19(3):249-259 .
13. Murray C, Sivajohanathan D, Hanna T, et al. Patient Indications for Mohs Micrographic Surgery (Report date: January 9, 2018) Cancer Care Ontario; Program in Evidence-Based Care Guideline No.:8-11
14. Murray C, Sivajohanathan D, Hanna TP, et al. Patient indications for Mohs micrographic surgery: a clinical practice guideline. Current Oncology 26(1): e94-e99
15. Patel R., Strimling R., Doggett S., Willoughby M., Miller K., Dardick L., et al. Comparison of electronic brachytherapy and Mohs micrographic surgery for the treatment of early-stage non-melanoma skin cancer: a matched pair cohort study. J Contemp Brachytherapy 2017;9(4):338-344.
16. Stuart SE, Schoen P, Jin C, Parvataneni R, Arron S, Linos E, et al. Tumor recurrence of keratinocyte carcinomas judged appropriate for Mohs micrographic surgery using Appropriate Use Criteria. J Am Acad Dermatol 2017;76(6):1131-1138.e1.
17. O'Niell J.l., Shutty B., Sun Lee Y., Solomon J.A., Patel N, Davis S.A., et al. Comparing demographic characteristics and adverse event rates at two dermatologic surgery practices. J Cut Med Surg 2014;18(5):337-40.
18. Alam M, Ibrahim O, Nodzenski M, Strasswimmer JM, Jiang SI, Cohen JL, et al. Adverse events associated with mohs micrographic surgery: multicenter prospective cohort study of 20,821 cases at 23 centers. JAMA dermatology JID - 101589530 2013.
19. Chren M.-M., Linos E., Torres J.S., Stuart S.E., Parvataneni R., Boscardin W.J. Tumor recurrence 5 years after treatment of cutaneous basal cell carcinoma and squamous cell carcinoma. J Invest Dermatol 2013;133(5):1188-1196.
20. Kropp L, Balamucki CJ, Morris CG, Kirwan J, Cognetta AB, Stoer CB, et al. Mohs resection and postoperative radiotherapy for head and neck cancers with incidental perineural invasion. Am J Otolaryngol 2013;34(5):373-7.
21. Bordeaux J.S., Martires K.J., Goldberg D., Pattee S.F., Fu P., Maloney M.E. Prospective evaluation of dermatologic surgery complicaitons incldluign patients on multiple antiplatelet and anticoagulant medications. J Am Acad Dermatol 2011;65(3):576-83.
22. Chren M, Torres JS, Stuart SE, Bertenthal D, Labrador RJ, Boscardin WJ. Recurrence after treatment of nonmelanoma skin cancer: a prospective cohort study. Arch Dermatol 2011;147(5):540-6.

23. van der Eerden PA, FAU PM, FAU LP, FAU BF, Vuyk HD. Eighteen years of experience in Mohs micrographic surgery and conventional excision for nonmelanoma skin cancer treated by a single facial plastic surgeon and pathologist. The Laryngoscope JID - 8607378 2010(0023-852).
24. Asgari M.M., Bertenthal D., Sen S., Sahay A., Chren M.-M. Patient satisfaction after treatment of nonmelanoma skin cancer. Dermatol Surg 2009;35(7):1041-1049.
25. Chren M.-M., Sahay A.P., Bertenthal D.S., Sen S., Landefeld C.S. Quality-of-life outcomes of treatments for cutaneous basal cell carcinoma and squamous cell carcinoma. J Invest Dermatol 2007;127(6):1351-1357.
26. O'Halloran L., Smith H., Vinciullo C. Periocular Mohs micrographic surgery in Western Australia 2009-2012: A single centre retrospective review and proposal for practice benchmarks. Australas J Dermatol 2017;58(2):106-110
27. Santos-Arroyo A., Carrasquillo-Gonzalez O., Cardona R., Sanchez J., Valentin-Nogueras S. Nonmelanoma skin cancer histologic subtype as a predictor for subclinical spread and number of Mohs stages required to achieve tumor-free margins. J Am Acad Dermatol 2016;74(5):AB202.
28. Vajdi T., Eilers R., Jiang B. Clinical characteristics of nonmelanoma skin cancers recurring within 5 years after Mohs micrographic surgery. J Am Acad Dermatol 2016;74(5):AB194.
29. Treacy MP, Wynne NC, Gale JL, Duignan E, Moran B, Flynn AM, et al. Mohs micrographic surgery for periocular skin tumours in Ireland. Ir J Med Sci 2016;185(4):779-783.
30. Zabielinski M., Leithauser L., Godsey T., Gloster H.M. Laboratory Errors Leading to Nonmelanoma Skin Cancer Recurrence after Mohs Micrographic Surgery. Dermatol Surg 2015;41(8):913-916.
31. Merritt BG, FAU LN, FAU BD, FAU ZJ, Cook J. The safety of Mohs surgery: a prospective multicenter cohort study. Journal of the American Academy of Dermatology JID - 7907132 2012.
32. Macfarlane L, Waters A, Evans A, Affleck A, Fleming C. Seven years' experience of Mohs micrographic surgery in a UK centre, and development of a UK minimum dataset and audit standards. Clin Exp Dermatol 2013 Apr;38(3):262-269.
33. Leibovitch I., Huilgol S.C., Richards S., Paver R., Selva D. Scalp tumors treated with Mohs micrographic surgery: Clinical features and surgical outcome. Dermatol Surg 2006;32(11):1369-1374.
34. Leibovitch I., Huilgol S.C., Selva D., Paver R., Richards S. Cutaneous lip tumours treated with Mohs micrographic surgery: Clinical features and surgical outcome. Br J Dermatol 2005;153(6):1147-1152.
35. Leibovitch I., Huilgol S.C., Selva D., Richards S., Paver R. Basosquamous carcinoma: Treatment with Mohs micrographic surgery. Cancer 2005;104(1):170-175.
36. Batra R.S., Kelley L.C. Predictors of extensive subclinical spread in nonmelanoma skin cancer treated with Mohs micrographic surgery. Arch dermatol 2002;138:1043-51.
37. Van LE, Mosterd K., Krekels G.A.M., Roozeboom M.H., Ostertag J.U., Dirksen C.D., et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: A randomised clinical trial with 10 year follow-up. Eur J Cancer 2014;50(17):3011-3020.
38. Narayanan K, Hadid OH, Barnes EA. Mohs micrographic surgery versus surgical excision for periocular basal cell carcinoma. Cochrane Database of Systematic Reviews 2014;12.
39. Jebodhsingh K.N., Calafati J., Farrokhyar F., Harvey J.T. Recurrence rates of basal cell carcinoma of the periocular skin: What to do with patients who have positive margins after resection. Can J Opthalmol 2012;47(2):181-84.
40. Muller F.M., Dawe R.S., Moseley H., Fleming C.J. Randomized comparison of mohs micrographic surgery and surgical excision for small nodular basal cell carcinoma: Tissue-sparing outcome. Dermatol Surg 2009;35(9):1349-1354.
41. Mosterd K., Krekels G.A.M., Nieman F.H.M., Ostertag J.U., Essers B.A.B., Dirksen C.D. Surgical excision versus Mohs' micrographic surgery for primary and recurrent basal-cell carcinoma of the face: A prospective randomized controlled trial with 5-years' follow-up. Lancet oncol 2008;9:1149-56.
42. Essers B., Nieman F., Prins M., Smeets N., Neumann H. Perceptions of facial aesthetics in surgical patients with basal cell carcinoma. JEADV 2007;21:1209-14.
43. Chren M., Sahay A.P., Sands L.P., Maddock L., Lindquist K., Bertenthal D., et al. Variation in care for nonmelanoma skin cancer in a private practice and a veteran's affairs clinic. Med Care 2004;42(10):1019-26.
44. Hoorens I., Batteauw A., Van MG, Lapiere K., Boone B., Ongenae K. Mohs micrographic surgery for basal cell carcinoma: Evaluation of the indication criteria and predictive factors for extensive subclinical spread. Br J Dermatol 2016;174(4):847-852.
45. Sin CW, Barua A, Cook A. Recurrence rates of periocular basal cell carcinoma following Mohs micrographic surgery: a retrospective study. Int J Dermatol 2016;55(9):1044-7.
46. Gniadecki R., Glud M., Mortensen K., Bang B., Biskup E., Omland S.H. Favourable results of Mohs micrographic surgery for basal cell carcinoma. Dan Med J 2015;62(12):A5171.

47. Catala A., Garces J.R., Alegre M., Gich I.J., Puig L. Mohs micrographic surgery for basal cell carcinomas: Results of a Spanish retrospective study and Kaplan-Meier survival analysis of tumour recurrence. J Eur Acad Dermatol Venereol 2014;28(10):1363-1369.
48. Allen K.J., Cappel M.A., Killian J.M., Brewer J.D. Basosquamous carcinoma and metatypical basal cell carcinoma: A review of treatment with Mohs micrographic surgery. Int J Dermatol 2014;53(11):1395-1403.
49. Flohil S.C., Van DA, Nijsten T., Martino NH, Munte K. Mohs micrographic surgery for basal cell carcinomas: Appropriateness of 'Rotterdam' criteria and predictive factors for three or more stages. J Eur Acad Dermatol Venereol 2013;27(10):1228-1235.
50. Litwin A.S., Rytina E., Ha T., Rene C., Woodruff S.A. Management of periocular basal cell carcinoma by Mohs micrographic surgery. J Dermatol Treat 2013;24(3):232-234.
51. Veronese F., Farinelli P., Zavattaro E., Zuccoli R., Bonvini D., Leigheb G., et al. Basal cell carcinoma of the head region: Therapeutical results of 350 lesions treated with Mohs micrographic surgery. J Eur Acad Dermatol Venereol 2012;26(7):838-843.
52. Paoli J, Daryoni S, Wennberg A, Molne L, Gillstedt M, Miocic M, et al. 5-year recurrence rates of Mohs micrographic surgery for aggressive and recurrent facial basal cell carcinoma. Acta Derm Venereol 2011;91(6):689-93.
53. Leibovitch I, Huilgol SC, Selva D, Richards S, Paver R. Basal cell carcinoma treated with Mohs surgery in Australia II. Outcome at 5-year follow-up. J Am Acad Dermatol 2005;53(3):452-7.
54. Leibovitch I, Huilgol SC, Selva D, Richards S, Paver R. Basal cell carcinoma treated with Mohs surgery in Australia III. Perineural invasion. J Am Acad Dermatol 2005;53(3):458-63.
55. Smeets N.W.J., Kuijpers D.I.M., Nelemans P., Ostertag J.U., Verhaegh M.E.J.M., Krekels G.A.M., et al. Mohs' micrographic surgery for treatment of basal cell carcinoma of the face - Results of a retrospective study and review of the literature. Br J Dermatol 2004;151(1):141-147.
56. Bergeron M, Gauthier P, Audet N. Decreasing loco-regional recurrence for oral cavity cancer with total Mohs margins technique. J Otolaryngol Head Neck Surg 2016 Dec 1;45(1):63.
57. Lansbury L., Bath-Hextall F., Perkins W., Stanton W., Leonardi-Bee J. Interventions for non-metastatic squamous cell carcinoma of the skin: Systematic review and pooled analysis of observational studies. BMJ (Online) 2013;347:f6153.
58. Askari M, Kakar S, Moran SL. Squamous cell carcinoma of the hand: a 20-year review. J Hand Surg Am] 2013;38(11):2124-33.
59. Machan M., Brodland D., Zitelli J. Penile squamous cell carcinoma: Penis-preserving treatment with Mohs micrographic surgery. Dermatol Surg 2016;42(8):936-944.
60. Dika E., Fanti P.A., Patrizi A., Misciali C., Vaccari S., Piraccini B.M. Mohs surgery for squamous cell carcinoma of the nail unit: 10 years of experience. Dermatol Surg 2015;41(9):1015-1019.
61. Pugliano-Mauro M., Goldman G. Mohs surgery is effective for high-risk cutaneous squamous cell carcinoma. Dermatol Surg 2010;36(10):1544-1553.
62. Shindel AW, FAU MM, FAU LR, Sengelmann RF, Petersen J FAU - Hruza, George,J., FAU HG, et al. Mohs micrographic surgery for penile cancer: management and long-term followup. The Journal of urology JID - 0376374 1106.Leibovitch I., Huilgol S.C., Selva D., Hill D., Richards S., Paver R. Cutaneous squamous cell carcinoma treated with Mohs micrographic surgery in Australia I. Experience over 10 years. J Am Acad Dermatol 2005;53(2):253-260.
63. Leibovitch I., Huilgol S.C., Selva D., Hill D., Richards S., Paver R. Cutaneous squamous cell carcinoma treated with Mohs micrographic surgery in Australia II. Perineural invasion. J Am Acad Dermatol 2005;53(2):261-266.
64. Leibovitch I., Huilgol S.C., Selva D., Richards S., Paver R. Cutaneous squamous carcinoma in situ (Bowen's disease): Treatment with Mohs micrographic surgery. J Am Acad Dermatol 2005;52(6):997-1002.
65. Silapunt S., Peterson S.R., Goldberg L.H. Squamous cell carcinoma of the auricle and Mohs micrographic surgery. Dermatol Surg 2005;31(11):1423-1427.
66. Murphy M.E., Brodland D.G., Zitelli J.A. Errors in the interpretation of Mohs histopathology sections over a 1-year fellowship. Dermatol Surg 2008; 34(12): 1637-41
67. National Comprehensive Cancer Network. Basal Cell Skin Cancer. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed September 12, 2017.
68. National Comprehensive Cancer Network. Squamous Cell Skin Cancer. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/squamous.pdf. Accessed September 12, 2017.
69. Nehal K, Lee E. Mohs Surgery. 2017; Available at: https://www.uptodate.com/contents/mohs-surgery?source=search_result&search=mohs%20surgery%20%3D&selectedTitle=1~150#H1574000248. Accessed September 12, 2017.
70. Newlands C, Currie R, Memon A, Whitaker S, Woolford T. Non-melanoma skin cancer: United Kingdom National Multidisciplinary Guidelines. Journal of Laryngology & Otology 2016 May;130(S2):S132

71. Morton CA, Birnie AJ, Eedy DJ. British Association of Dermatologists' guidelines for the management of squamous cell carcinoma in situ (Bowen's disease) 2014. Br J Dermatol 2014 Feb;170(2):245-260
72. London Cancer Alliance. LCA Skin Cancer Clinical Guidelines. 2014 July
73. SIGN 140: Management of primary cutaneous squamous cell carcinoma
74. Ad Hoc Task Force, Connolly SM, Baker DR, Coldiron BM, Fazio MJ, Storrs PA, et al. AAD/ACMS/ASDSA/ASMS 2012 appropriate use criteria for Mohs micrographic surgery: a report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association, and the American Society for Mohs Surgery. J Am Acad Dermatol 2012 Oct;67(4):531-550
75. Cancer Council Australia. Basal cell carcinoma, squamous cell carcinoma (and related lesions) - a guide to clinical management in Australia. 2008 November
76. Telfer NR, Colver GB, Morton CA. Guidelines for the management of basal cell carcinoma. Br J Dermatol 2008 Jul;159(1):35-48
77. Ho C, Argaez C. Mohs surgery for the treatment of skin cancer: a review of guidelines. Ottawa: CADTH; 2019 Mar. (CADTH rapid response report: summary with critical appraisal). ISSN: 1922-8147 (online)

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Cutaneous Tumour Team. Members of the Alberta Cutaneous Tumour Team include surgical oncologists, radiation oncologists, medical oncologists, dermatologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Cutaneous Tumour Team, external participants identified by the Working Group Lead, and a Knowledge Management Specialist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in August 2019.

Maintenance

A formal review of the guideline will be conducted in 2020. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AFX, atypical fibroxanthoma; AUC, appropriate use criteria; BCC, basal cell carcinoma; BSC, Basosquamous carcinoma; BD, Bowen's disease; C&E (or ED&C), cutterage and electrodessication; DFSP, dermatofibrosarcoma protuberans; EBT, electronic brachytherapy; f/u, follow-up; HR, hazard ratio; MAC, microcystic adnexal carcinoma; MBCC, Metatypical BCC; MDT, multidisciplinary team; MIS, melanoma in situ; MMS, Mohs micrographic surgery; NMSC, non-melanoma skin cancer; NRT, non-randomized trials; PFS, progression free survival; PNI, Perineural invasion; QOL, quality of life; RCT, randomized control trial; RT, radiation therapy; SCC, squamous cell carcinoma; SE, surgical excision; WLE, wide local excision

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Cutaneous Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

Dr. **Thomas Salopek** has nothing to disclose.

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