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Mohs Surgery of basal cell carcinoma—a critical review

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SUMMARY. **Mohs surgery for basal cell carcinoma (BCC) of the skin attempts to ensure complete tumour removal by histological examination of the entire excision margin and further excision of involved sites. Advocates recommend its use in recurrent or incompletely excised tumours, poorly defined, histologically aggressive or large primary tumours and BCCs situated at high risk or cosmetically important sites. The claimed advantages over other surgical therapies are that it provides a better chance of cure and since less normal tissue is removed the simpler surgical repair ensures a superior cosmetic result. This review examines the published evidence that supports the enthusiasm for the use of Mohs surgery in the treatment of BCC, contrasting cure rates and cosmetic outcome with results achieved by attempted single complete excision and examines the 2 principles upon which Mohs surgery is based, namely that BCCs spread by contiguous growth and that all tumour cells have to be destroyed to achieve a cure.**

Fred Mohs devised his method of tumour excision in order completely to excise difficult skin tumours.[1] After debulking the visible tumour mass, the entire wound cut surface is excised and histologically examined using horizontal sections so all excised surfaces are inspected. Areas containing residual tumour can be identified and the process repeated until no further tumour is seen. Tissue can be prepared for histological examination using *in situ*,[2] formalin[3] or fresh frozen[4] tissue fixation. Details of the technique are described elsewhere.[5–7] Although first devised in the 1940s by a general surgeon[1] the method was not wholeheartedly embraced until two dermatologists[4] described the frozen tissue technique. It is now extensively employed by dermatologists and head and neck surgeons[8] and variations on the method of complete tissue margin control[9–14] have been described. Mohs and others have advocated the use of this excision technique for a variety of skin tumours; this paper will only discuss the treatment of basal cell carcinoma (BCC). Advocates of the technique recommend its use in recurrent or incompletely excised tumours and poorly defined, histologically aggressive or large primary tumours, or those situated at high risk or cosmetically important sites.[5,7]

The claimed advantage of Mohs, or micrographic, surgery over other surgical therapies[5,6] are that it provides a better chance of cure and since less normal tissue is removed, the simpler surgical repair ensures a superior cosmetic result. A search for published evidence for these assertions has found no randomised prospective studies of cure rates or cosmetic results comparing the Mohs technique to attempted single stage excision. Whilst there are several series describing patients treated by Mohs surgery[2,15] and numerous illustrated accounts of its use to remove difficult and potentially life threatening tumours,[16] all the claims of improved cure rates are made by comparing outcome with previously published material.

Before Mohs surgery can become fully accepted as first line therapy in the management of difficult BCCs[5,7] the published scientific evidence upon which the various assertions are made needs to be examined. If the technique is as good as claimed, it should be a generally available therapy being taught to the next generation of dermatologists and plastic surgeons. This review will examine the evidence that supports the enthusiasm for the use of Mohs surgery in the treatment of BCC and will examine the 2 principles upon which Mohs surgery is based, namely that BCCs spread by contiguous growth and that all tumour cells have to be destroyed to achieve a cure. Since there are no prospective randomised studies comparing Mohs and attempted single complete excision, any comparison of these methods can only be made by contrasting different series. It is important to recognise that because BCC size,[2,17,18] previous treatment,[19] site[20] and histological type[21] influence the possibility of tumour recurrence, any comparison critically depends on the similarity of the tumours treated and the length of follow-up.

What is the evidence for improved cure rates with Mohs Surgery?

All BCCs

Studies that include a large or undefined proportion of other tumours[4] have been ignored, as have attempted single complete excision series performed by dermatologists.

Mohs surgery. The largest series is Mohs' own group of 7574 patients,[2] all of whom were followed up for 5 years. 11% of the previously untreated tumours were > 20 mm diameter and 18.3% of the BCCs were recurrences; the overall recurrence rate was 0.7%. The author disregarded 2142 other patients, without evidence of recurrence, in whom 5 year follow-up was impossible. The second largest series of 6982 BCCs

Table 1 All BCCs: results of Mohs surgery

Author Year of publication	*Number of tumours surgically treated*	*% > 19 mm*	*% recurrent tumours included*	*Duration of follow-up (years)*	*Number recurred (%)*
Mohs[2] 1978	7574	11	18.3	5	52 (0.7)
Robins[15] 1981	6982*	67	49	2960 ⩾ 5	(2.6)**
Phelan[24] 1968	339	ns	61	ns	17 (5)

* including 615 other cutaneous tumours treated by Mohs surgery.
** 97.4% cure rate amongst 2966 BCCs followed for at least 5 years.
ns not stated.

Table 2 All BCCs: results of attempted single complete excision

Author Year of publication	*Number of tumours surgically treated*	*% > 19 mm*	*% recurrent tumours included*	*Duration of follow-up (years)*	*Number recurred (%)*
Emmett[20] 1981	1411	8**	17	84% > 2	(0.7)
Emmett[21] 1990	2277	ns	20	mean 4	(1.5)
Rank[25] 1973	611	ns	7	all > 4	5 (0.8)
Blomqvist[26] 1982	477	ns	none	ns	11 (2)
McCallum[27] 1966	409	16**	none†	1–5	4 (1)
de Cholnoky[28] 1945	310	ns	26	5	12 (3.9)
Monballiu[29] 1968	290*	ns	ns	0–20	14 (5)
Sundell[30] 1966	109	ns	59	1–7 mean 3	10 (9)

* These 290 were selected from 633 BCCs, of which 18% were recurrences and 28% were > 19 mm in diameter.
** this proportion was > 20 mm in diameter.
† 10 recurrent BCCs treated surgically were described separately.
ns not stated.

Table 3 Recurrent tumours: results of Mohs surgery

Author Year of publication	*Number of recurrent BCCs surgically treated and followed up*	*Duration of follow-up*	*Number of recurrences after Mohs excision (%)*	*Initial therapy before recurrence*
Robins[15] 1981	3149	ns*	ns (3.4)*	various
Mohs[2] 1978	1387	All followed for 5 y	44 (3.2)	various
Roenigk[37] 1986	190	ns**	8 (4.2)	various
Sakura[35] 1979	40	All followed for 5 y	5 (12)	various
Smith[36] 1991	27	range 2–55 months (av. 25 months)	2 (7.4)	various

* In this study there were 3149 recurrent tumours, including an unspecified small proportion of non BCCs. 2966 BCCs were followed for 5 years but how many of these were previously treated tumours is not stated. The 5-year cure rate for recurrent BCC is given as 96.6%.
** Patients had been followed up for up to 4 years.
ns not stated.
The Phelan[24] and Tromovitch[4] studies are not included as they do not give separate results for the treatment of recurrent BCCs.

included 49% recurrent tumours and 67% of the tumours were greater than 19 mm in diameter; 2960 tumours followed up for 5 years gave recurrence rates of 1.8% for primary and 3.4% for recurrent tumours.[15] These authors have published updated results of periocular BCCs showing five-year cure rates of 98% in 1414 cases,[22] and 98.1% for primary and 93.6% for recurrent tumours amongst 631 BCCs treated by Mohs surgery.[23] The combined recurrence rate for these and Phelan's series[24] shown in Table 1 is 1.7% (250 recurrences amongst 14895 tumours).

Attempted single complete excision. The best documented and largest series of BCCs is Emmett's[20] series of 1411 patients, 8% of the untreated tumours were > 20 mm in diameter and 17% were recurrences; in these respects the BCCs treated were similar to those described by Mohs.[2] Although the recurrence rate was just 0.7% only 84% were followed for more than 2 years. These surgeons used selective frozen sections for intraoperative excision margin control and took 10 mm margins of normal tissue around recurrent tumours. Furthermore, 10 tumours were re-excised when routine histological sections showed incomplete excision. In a recent report from the same author[21] 2277 BCCs were followed up for an average of 50 months (range 1 week – 19 years) with 35 recurrences (1.5%), including 6 that recurred twice. Other series[25–30] are listed in Table 2. Combining these results and excluding Emmett's 1981 series, as these cases are

Table 4 Recurrent BCCs: results of attempted single complete excision

Author Year of publication	*Number of recurrent BCCs surgically treated and followed up*	*Duration of follow-up (years)*	*Number of recurrences after surgical excision (%)*	*Original therapy before recurrence*
Taylor[38] 1973*	282	55% followed for > 2, 17% for < 6 months	31 (11)	various
Emmett[20] 1981	258	84% followed > 2	5 (2)	various
Hayes[39] 1962	202	< 1–20	49 (24)‡	various
Rank[40] 1958	178†	1–10 56 were followed for ⩾ 5	25 (14)	DXT
de Cholnoky[28] 1945	81	All followed up for 5	10 (12)	various
Cobbett[41] 1965	96	39 followed for 5	16 (16) 8 of 39 (20) followed for 5 yrs	DXT
Ward[31] 1950	56	3–18	10 (18)	various
Collin[42] 1976	50	55% > 3 (0.5–11)	12 (24)	38 DXT, 10 surgery, 2 DXT + surgery
Rank[25] 1973	45	4	2 (4.4)	ns
Sakura[35] 1979	20	All followed up for 5	1 (5)	various

* series taken from a group 55% of whom were followed up for > 2 years.
** 35% of 676 patients, 15% of whom developed recurrent disease.
† 183 cases were reported 5 of whom could not be traced, 14 other cases of basi-squamous carcinoma are not included.
‡ 22 of the 49 recurrences occurred after more than 5 years follow-up.
ns not stated.
DXT-Previous radiotherapy therapy.

likely to be included in the 1990 results, gives an overall recurrence rate of 2% (90 recurrences amongst 4483 tumours), similar to those achieved using Mohs surgery, although in only one study were all patients followed up for at least 5 years.

Recurrent BCCs

Recurrent tumours are notoriously difficult to eradicate.[19,31,32] In Tables 3 and 4 only the results of Mohs and attempted complete surgical excision of recurrent tumours are shown. Studies in which information is incomplete or ambiguous[33] have been ignored and results of other therapies are reviewed elsewhere.[34]

Mohs surgery. The two largest series[2,15] both give recurrence rates of just over 3% (Table 3). In Mohs'[2] series all cases were followed up for 5 years although the length of follow-up was not given in Robins'[15] series. Sakura[35] studied 97 recurrent tumours treated by radiotherapy, plastic surgery or Mohs surgery at one institution and followed up for a minimum of 5 years. The results suggest that with the aid of selective frozen sections plastic surgery is superior, despite treating bigger tumours, with recurrence occurring in 1 of 20 patients compared to 5 out of 40 (12.5% recurrence) Mohs cases and 4 out of 35 radiotherapy treated BCCs. However, relatively few tumours were treated and because patients were not randomly allocated to the 3 treatment groups there were substantial differences in number of previous treatments, tumour size and the number of patients in each group. Moreover the Mohs group was limited to inpatients only, an unusually severely affected group by comparison with an earlier report from the same institution[24] in which there were 17 recurrences amongst 339 patients (5% recurrence) after Mohs surgery; 11 of these recurrences were subsequently successfully treated by further Mohs surgery. Combining these and other results listed[36,37] in Table 3 gives 166 recurrences amongst 4793 recurrent BCCs treated by Mohs surgery, a recurrence rate of 3.5%.

Attempted single complete excision. Ten studies[20,25,28,31,35,38–42] are listed (Table 4) and most are relatively small series with limited follow-up and inadequate tumour details. Combining these results gives 161 recurrences occurring in 1268 (13%) previously treated BCCs, almost 4 times that reported after Mohs surgery, and a possible underestimate because of the restricted follow-up.

Does all basal cell carcinoma have to be removed to achieve cure?

The underlining principle of Mohs surgery is that all tumour has to be removed to ensure adequate treatment. However, some BCCs heal spontaneously[43] and the high success rate of a blindly destructive therapy, such as curettage, suggests that complete tumour eradication is not required for treatment success. Examination of the idea that not all tumour cells have to be removed to cure can be made by studying the results of leaving tumour behind after curettage and excision of BCCs.

Curettage of BCC. Provided small[17,44,45] (< 20 mm in diameter), non-recurrent tumours[32,46–48] on suitable sites are treated by experts,[49,50] the 5-year cure rate after curettage is around 95% (86 of the total 1615 BCCs listed in Table 5 recurred). Thus when used correctly curettage results in very high cure rates although the studies described below demonstrate that tumour is frequently left behind initially. There are 2 studies of the frequency of tumour persistence after an attempt to mimic the effect of curative curettage and

Table 5 Cure rates following curettage and cautery of primary BCCs

Author Year of publication	*Number of tumours*	*Duration of follow-up (years)*	*Number of recurrences (%)*	*Tumour size*
Simpson[47] 1966	495	2–5	35 (7)	ns
Williamson[50] 1962	287	3	22 (7.6)	ns
Knox[45] 1967	282	5	4 (1.4)	< 20 mm
Sweet[18] 1963	268	⩾ 3	19 (7.1)	< 20 mm
Spiller[44] 1984	208	5	3 (1.4)	< 20 mm
Tromovitch[48] 1965	75	⩾ 5	(4)	ns

ns not stated.

Table 6 Result of not re-excising incompletely excised BCCs

Author Year of publication	*Number of incompletely excised BCCs not retreated*	*Duration of follow-up range (mean) years*	*Number of recurrences (%)*	*Interval between surgery and recurrence range (mean) years*
Taylor[38] 1973	78	ns**	19 (24)	ns
Gooding[55] 1965	66	5 minimum	23 (35)	0.1–4
Richmond[53] 1987	60	1–10 (5)	23 (38)	1–8 (2.8)
Dellon[54] 1985	53*	3–6	24 (42)	0.6–5
Hayes[39] 1962	44	1–14	7 (16)	(1.4)
Pascal[56] 1968	42	10 minimum	14 (33)	0.3–21
Doxanas[13] 1981	23	2–12 (6.4)	7 (30)	0.1–1
McGregor[57] 1979	17	ns	3 (17)	2, 4 and 7

* Excludes 4 patients with no evidence of recurrence who died from other causes.
** Over half of this group was followed up for more than 2 years.
ns not stated.

cautery (C & C).[51,52] The tumours selected were small, < 20 mm[52] and < 10 mm,[51] primary nodular or nodular ulcerated BCCs and tumour persistence was demonstrated by examining horizontal Mohs sections taken after curettage. After C & C done 3 times 15 of 50 (30%) tumours on the nose and naso-labial fold, 6 of 50 (12%)[51] BCCs from other head and neck sites and 46 of 127 (36%) of BCCs from all sites[52] showed positive Mohs margins. Thus overall tumour was left behind in 67 of 227 (30%) small BCCs treated by aggressive C & C, a marked contrast to the published 95% 5 year cure rates for the treatment of similar BCCs (Table 5). There are similar examples of the same phenomenon after the incomplete excision of BCC.

Incompletely excised BCC. Incompletely excised BCCs do not invariably recur when not retreated. Whether this is due to tumour cell death or false positive excision margins can be examined by comparing recurrence rates of incompletely excised BCCs with the number showing persistent tumour when immediately re-excised. In the series listed[13,38,39,53–57] (Table 6), between 16–42% of histologically incompletely excised BCCs recurred, an average of 31% (120 recurrences amongst 383 incompletely excised tumours). Some studies may have underestimated recurrence by inadequate follow-up;[38,57] this is particularly important after flap repair or direct closure, when recurrences can appear after 4 years compared to 1–2 years following skin grafting.[53]

Incompletely excised tumours are occasionally re-excised,[20] although more commonly a wait and see policy is adopted[57] judged by the finding that only 87 of the 302 (29%) of the incompletely excised tumours listed in Table 7[13,20,53,55,56,58,59] were re-excised. In the studies listed no reason was given why some tumours were re-excised and others observed. It seems probable that operators chose cases they considered likely to have genuine residual tumour, since there was a slightly lower proportion with residual tumour in the two series[20,58] where all incompletely excised tumours were re-excised. The presence of residual tumour may also have been underestimated by incomplete histological examination of the resected specimen or by persistent tumour cells being obscured by the associated heavy inflammatory infiltrate. Six of the seven studies listed (Table 7) showed that between 40–83% of cases (overall 27 out of 44 specimens, average 61%) still contained residual tumour when re-excised within 2 months of the original procedure. In the remaining study only 3 of 43 (7%) inadequately excised BCCs contained persistent tumour,[59] although the study can be disregarded since the re-excised specimens were incompletely examined histologically. Thus, approximately 60% of specimens contain residual tumour after incomplete excision although only 30% recur despite not being retreated.

Do basal cell carcinomas spread by contiguous growth?

Tracing the unpredictable extensions of a BCC using Mohs horizontal sections depends on the tumour spreading by contiguous growth. Without continuity

Table 7 Result of re-excision of incompletely excised BCCs (i.e. tumour present at deep or lateral margin)

Author Year of publication	*Number of incompletely excised tumours*	*Interval between excision and re-excision (months)*	*Number re-excised*	*Number with residual tumour (%)*
Sarma[59] 1984	73	0.5–1	43	3 (7)**
Richmond[53] 1987	67	1	6	5 (83)
Gooding[55] 1965	66	ns	5	4 (80)
Pascal[56] 1968	42*	ns	6	3 (50)
Doxanas[13] 1981	34	1–2	7	5 (71)
Lawrence[58] 1986	10	0.3	10	4 (40)
Emmett[20] 1981	10	0.3	10	6 (60)

* The 6 cases indicated were not included in the original group.
** There was incomplete examination of the resected issue.
Hauben's study[33] has been excluded as the authors have combined results for tumour recurrence and persistence.

or very close proximity islands of tumour could remain hidden. Previously treated BCCs may have areas of disconnected tumour[60–62] and there is some evidence to suggest that untreated BCCs contain islands of tumour cells. In a careful study Madsen[63] devised semi 3-dimensional models of 19 primary BCCs by making enlarged serial drawings of 20 μ horizontal sections and superimposing these on top of each other. Isolated strands or nests of tumours cells, not connected to the main body of tumour, were found in 4 of 10 superficial BCCs, and 4 of 7 invasive or nodular tumours, but not in 2 small BCCs which showed a contiguous growth pattern. In superficial BCCs a virtually contiguous ring of tumour, surrounding islands of separate tumour, was observed. Madsen suggested that BCCs spread by contiguous growth from a central point and isolated islands of tumour cells were created by the loss of tumour connections as a result of spontaneous tumour cell death. In a similar computer assisted study of 7 typical superficial multicentric BCCs the authors found that tumour strands were connected in each case.[64] In conclusion, although BCCs may be unifocal initially, isolated areas of tumour are present in a proportion of primary BCCs as a result of spontaneous tumour cell death. If the gaps between tumour clumps are wide enough and as frequent as suggested, it seems unlikely that any excision technique that depends on contiguous tumour growth would work.

Do standard excision margins inevitably lead to incomplete excision?

It is claimed that because BCCs spread beyond the visible edge in an unpredictable fashion, the margin of normal tissue needed to be excised to ensure complete removal is greater than standard excision margins. Three studies[65–67] have examined this idea by measuring the subclinical extension of BCCs as the difference between the visible tumour margin diameter and the tumour extent determined by the wound size after Mohs excision. Each study found that the subclinical extension was greater than widely used excision margins. Larger morphoeic BCCs extended on average by 8.6 mm,[65] primary BCCs by 5.5 mm and recurrent BCCs by 8.9 mm[66] beyond the visible border. Wolf[67] concluded that to excise 95% of the well defined primary BCCs, smaller than 20 mm in diameter, a 4 mm margin was required. Each study made the assumption that the tumour size was equivalent to the wound size after Mohs excision. This is incorrect firstly because wounds created by lesion excision are approximately 20% bigger in area than the proposed defect size;[68] Wolf[67] avoided this error by marking serial diameters on the skin before tumour excision. Secondly, there is inevitable excision of uninvolved tissue due to the need to remove a minimum 1–2 mm thick slice of tissue to be able to prepare and section the material properly; moreover it seems unlikely that these negative margins contained concealed tumour as judged by the finding of occult tumour in just 4% of negative Mohs excision margins in other studies.[52] Finally, unlike a standard vertical excision, because the cut edge of the Mohs excision is angled at approximately 45°, the resulting surface defect size is always greater than that of the deeper levels, where tumour may persist. Thus, because tumour size and final defect size are not equivalent this type of comparison is not valid.

What is the evidence that Mohs surgery is tissue sparing and thereby provides a superior cosmetic result?

An often quoted advantage of Mohs surgery is that the technique minimises the removal of uninvolved tissue, thus leaving a smaller defect and consequently a technically easier repair with a better chance of a good cosmetic result. There are no prospective randomised studies of the final cosmetic outcome after Mohs surgery compared to attempted single complete excision, although there are 2 prospective studies comparing theoretical surgical margins to final Mohs determined margins. In 71 auricular tumours,[8] including 40 BCCs and 29 SCCs, 41% of which were recurrences, the conventional surgical excision margins were determined using 8 mm margins for primary BCC < 30 mm diameter, 10 mm for primary SCC < 30 mm diameter, and 15 mm margins for all recurrent tumours and primary lesions greater than 30 mm. The tumours were then excised using Mohs surgery and the resulting and predicted defect size and shape compared. An average 180% excess of normal tissue in the primary lesions and 27% in recurrent tumours would have been unnecessarily excised if conventional

margins had been used. Furthermore, inadequate excisions would have occurred in 9 primary lesions and 8 recurrent tumours.[8] In another study[69] 22 patients with BCCs around the eye, including 9 recurrences, were examined by an oculo-plastic surgeon who predicted the type of repair required to close the expected defect after routine tumour excision. It was anticipated that simple local repair, graft or direct closure was required in 6 patients whereas after Mohs surgery this was possible in 15 patients. Complicated flaps or extensive reconstruction were only required in 7 patients compared with the anticipated 14 cases. Assuming that the cure rates for each technique are equivalent, using Mohs histological sections the extent of surgery was much less extensive than anticipated in 41% of cases. Furthermore, if tumours had been excised with the standard 4 mm margin, it was estimated from the size of the final defect that 64% of the tumours, including small (< 10 mm) primary BCCs, would have been incompletely excised. These studies are possibly the strongest evidence for the use of Mohs surgery in such tumours and if equivalent excision margins are widely used mean that patients with periocular and auricular BCCs are having unnecessarily extensive surgery, with all the consequent implications.

Conclusion

Any new treatment must first be demonstrated to have an effect and then be shown to be superior to current practice in some or all respects if it is to replace an existing therapy. There seems little doubt that in specified cases,[70] for example where there is perineural tumour spread, disease extent would only become apparent after complete tumour margin control and under these circumstances a type of all encompassing margin control would be essential. How far this principle should be extended is not established.

Comparison of the published series shows that both Mohs and attempted single complete excision give similar excellent cure rates in primary BCC although the absence of any large and well documented attempted single complete excision study with 5-year follow-up of all cases is immediately obvious. By contrast the overall recurrence rate after Mohs surgery for recurrent tumours in all the listed studies was 3.5% compared to 13% after attempted single complete excision. These results are striking but cannot be accepted as proof without a more rigorous attempt to ensure that the patient groups are similar. An equivalent follow-up period may demonstrate an even greater benefit of Mohs surgery in recurrent tumours. Randomised prospective studies, although time consuming, are required.

The effect of leaving residual BCC behind following curettage or incomplete excision demonstrates that not all tumour cells have to be removed to ensure cure. However, this fascinating but unpredictable biological phenomenon cannot be used as a method of disease control in the individual patient. Until it is possible to predict which inadequately excised tumours will recur, a policy of attempted complete removal is the only practical solution.

Patient acceptability should be considered. The current widespread use of fresh tissue frozen sections avoids the pain associated with Mohs original *in situ* fixation chemosurgical method.[1] The patient, however, may prefer a single excision under local or general anaesthesia to several sequential procedures done under local anaesthetic.

Financial considerations are important. Mohs surgical excisions are virtually always an outpatient procedure under local anaesthetic.[2] By comparison plastic surgical excision and repair was done under local anaesthesia in 14%,[57] and 84%[20] of cases and in one study 41% were inpatients.[26] If in order to achieve acceptable cure rates plastic surgeons are excising unnecessarily large areas of normal tissue, thus incurring large and difficult repairs, then the potential savings that could be made using Mohs surgery must be examined. If Mohs surgery can remove tumours as effectively and with similar morbidity and cosmetic results as attempted single complete excision, but with the use of fewer resources, these attributes alone should confirm the value of the technique.

Mohs surgery is based upon the commonsense idea that all tumour cells have to be excised in order for the patient to be cured. This attractively simple concept may have led many to accept the claims made for the method without waiting for the scientific proof. The technique may be superior to existing methods and offer all the advantages its exponents claim. However, before it can become generally accepted these advantages will have to be demonstrated by controlled prospective clinical studies.

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Sam Shuster's constant questioning of accepted dogma and earlier unpublished presentations on the missing facts in the case for Mohs surgery have been the springboard for these ideas.

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