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Reply to "Correlation of Basal Cell Carcinoma Subtype with Histologically Confirmed Subclinical Extension During Mohs Micrographic Surgery: A Prospective Multi-Center Study.

--Manuscript Draft--

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May 10, 2022

To The Editor:

Attached please find a revised Letter to the Editor, based on reviewers' suggestions in reply to:

Lim GFS, Perez OA, Zitelli JA, Brodland DG, Correlation of Basal Cell Carcinoma Subtype with Histologically Confirmed Subclinical Extension During Mohs Micrographic Surgery: A Prospective Multi-Center Study, *Journal of the American Academy of Dermatology* (2022), doi: https://doi.org/10.1016/j.jaad.2022.02.037.

We agree with the reviewer's suggestion and our reply is shown below. The marked up resubmitted manuscript shows changes highlighted in yellow.

Reviewer #1: No additional comments.

Reviewer #2: Thank you for your revision. It is much more concise and makes your points well.

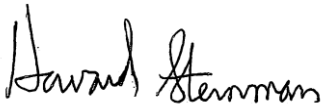
"It is important that cited articles are accurately represented. In lines 27-28 you state, "In addition, MMS for sBCC has been reported to often require higher ASCM and larger, subcutaneous wounds than for aBCC ." The reference cited (Mina MA, Picariello A, Fewkes JL. Superficial basal cell carcinomas of the head and neck. Dermatol Surg. Jul 2013;39(7):1003-8. doi:10.1111/dsu.12178) does not actually make any comparison to aBCC or mention "subcutaneous" wound size. Their conclusion refers only to "significantly larger defect sizes than would be expected clinically". Your description of their findings and conclusions are an overstatement."

Reply:

We agree with the reviewer and have cited a different reference (Orengo IF, et al.) and cite its findings. [Lines 22-26]

Thank you for considering this resubmission.

Sincerely,



Howard K. Steinman, M.D.

Article type: Letter to the Editor

Title: Reply to "Correlation of Basal Cell Carcinoma Subtype with Histologically Confirmed Subclinical Extension During Mohs Micrographic Surgery: A Prospective Multi-Center Study

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We read with interest Lim, et al's[1] study evaluating consecutive basal cell carcinomas (BCC) treated by Mohs micrographic surgery (MMS). The study measured subclinical tumor extension (SCE) by assessing average stages to clear margins (ASCM). It also assessed histologic subtype drift (HSD), defined as a change in BCC subtype (BCCS) from the index biopsy to that present on the final MMS stage.

They found that superficial BCC (sBCC) and aggressive BCC (aBCC) exhibited similar and significantly greater SCE than for other BCCS and that sBCC was commonly the final marginal subtype when HSD was noted.[1]

They contend these results challenge the perception that sBCC is a low-risk BCCS, because its degree of SCE akin to traditionally defined aBCC demonstrates its "…significant potential to be clinically occult". Thus, they assert that sBCC merit complete margin clearance to minimize recurrence, and it is reasonable to consider MMS as potentially beneficial in their treatment.[1]

We disagree with these conclusions because suggesting sBCC to be treated as an aBCC runs counter to sBCC's very indolent clinical behavior, superficial growth pattern, and reported high cure rates with alternative destructive treatments that do not assess surgical margins. sBCC SCE is primarily very superficial whereas aBCC SCE is commonly deeper, destructive, and associated with perineural invasion. Their conclusion significantly deviates from Sexton's BCC classification, MMS criteria and national guidelines.[2]

The presence of sBCC SCE and HSD of all BCCS is well documented. Orango et al in 1997 reported that 54.4% of sBCC were "troublesome" in that they required three or more MMS stages and exhibited "wide extensions beyond their clinical appearance." They further noted

that all BCCS exhibit a high rate of HSD, with only a 42.7 % correlation between the biopsy BCCS and that noted on the final MMS stage.[3]

Optimal treatments for BCCS are determined by their cure rates, morbidity, complication risks, cosmesis, cost, patient health status and other factors. They are not determined by any single histologic clinical characteristic. Cure rates with excision[4] and curettage techniques[5], which may incompletely remove sBCC SCE, have reported cure rates similar to those with for MMS.

There exists legitimate debate about the appropriateness of various treatments for sBCC. To meaningfully compare MMS with other treatments would require prospective randomized controlled trials, ideally evaluating recurrence rates and other factors. Current evidence suggests that complete marginal clearance is not required to cure a substantial number of sBCC. MMS likely has a select place among treatment options. However, for the reasons stated above, we contend sBCC does not merit treatment as an aBCC, and MMS routine use in the treatment of sBCC merits reconsideration.

Abbreviations:

aBCC = aggressive basal cell carcinoma subtypes

ASCM = average stages to clear margins

BCC = basal cell carcinoma

BCCS = basal cell carcinoma subtype

HSD = histologic subtype drift

MMS = Mohs micrographic surgery

sBCC = superficial basal cell carcinoma

SCE = subclinical extension

References

1. Lim GFS, Perez OA, Zitelli JA, Brodland DG. Correlation of Basal Cell Carcinoma Subtype with Histologically Confirmed Subclinical Extension During Mohs Micrographic Surgery: A Prospective Multi-Center Study. *J Am Acad Dermatol*. Feb 26 2022;doi:10.1016/j.jaad.2022.02.037

2. Schmults C, Blitzblau R, Aasi S, et.al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Basal Cell Skin Cancer Version 1.2022. Accessed 3/26/2022, 2022. https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1416

3. Orengo IF, Salasche SJ, Fewkes J, Khan J, Thornby J, Rubin F. Correlation of histologic subtypes of primary basal cell carcinoma and number of Mohs stages required to achieve a tumor-free plane. *J Am Acad Dermatol*. Sep 1997;37(3 Pt 1):395-7.

4. Kiely JR, Patel AJK. A retrospective study of 694 Basal Cell Carcinoma excisions to quantify deep margin documentation and clearance compared to histological type and surgical margin. *J Plast Reconstr Aesthet Surg*. Nov 2019;72(11):1805-1812. doi:10.1016/j.bjps.2019.06.002

5. Barlow JO, Zalla MJ, Kyle A, DiCaudo DJ, Lim KK, Yiannias JA. Treatment of basal cell carcinoma with curettage alone. *J Am Acad Dermatol*. Jun 2006;54(6):1039-45. doi:10.1016/j.jaad.2006.01.041

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