Mohs Micrographic Surgery vs Traditional Surgical Excision

A Cost Comparison Analysis

Tracy L. Bialy, MD, MPH; James Whalen, MD; Emir Veledar, PhD; Denis Lafreniere, MD; Jeffrey Spiro, MD; Timothy Chartier, MD; Suephy C. Chen, MD, MS

Objective: To compare the cost and margin adequacy of Mohs micrographic surgery (Mohs) and traditional surgical excision (TSE) for the treatment of facial and auricular nonmelanoma skin cancer (NMSC).

Design: Prospective cost analysis with each patient serving as his or her own control.

Setting: Study was performed from 1999 to 2001 at the University of Connecticut dermatology clinic, a tertiary care referral center.

Patients: A total of 98 consecutive patients with a primary diagnosis of NMSC on the face and ears.

Main Outcome Measures: The average cost of Mohs and TSE per patient for the treatment and repair of NMSC; adequacy of TSE margins after the initial procedure (because this outcome affects overall cost).

Results: Mohs was cost comparable to TSE when the subsequent procedure for inadequate TSE margins after permanent section was Mohs ($937 vs $1029; \( P = .16 \)) or a subsequent TSE ($937 vs $944; \( P = .53 \)). When facility-based frozen sections were requested for TSE, Mohs was significantly less costly ($956 vs $1399; \( P < .001 \)). The cost difference between Mohs and TSE was sensitive to the type of repair chosen.

Conclusions: If the end point is clear margins, Mohs is cost comparable to TSE performed by otolaryngologic surgeons. Some caution is needed when evaluating the cost of facial and auricular NMSC treatment because the choice of repair can significantly affect the cost conclusions.

Arch Dermatol. 2004;140:736-742

S

kin cancer in the United States is a large and growing public health concern. Nonmelanoma skin cancers (NMSCs), including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the most common cancers in the United States, accounting for more than 1 million new cases per year.\(^1,2\) Fortunately, NMSCs rarely metastasize and are usually curable if treated early. Although the overall metastatic rate for NMSC is small (0.003%-0.55% for BCC\(^3,4\) and approximately 5% for SCC),\(^5\) NMSCs may cause significant local tissue destruction and potential disfigurement and dysfunction in involved sites. Furthermore, certain higher-risk NMSCs (eg, recurrent SCC or SCC with lip involvement or perineural invasion) carry significantly higher risks of local recurrence and metastasis.\(^6,10\) Once NMSC metastasizes, the overall 5-year survival for both metastatic BCC and SCC is less than 33%.\(^11\)

Nonmelanoma skin cancer most commonly affects chronically sun-exposed sites, including the head, neck, trunk, and upper extremities. The head and neck are affected in 80% to 90% of the cases. More than 65% of all BCCs and SCCs affect facial sites\(^8\) and create cosmetic and functional sequelae. Therefore, a major goal of NMSC treatment is to remove the cancer while preserving maximal function and cosmesis. Many treatment modalities for NMSC have been developed, each with a different efficacy and cost. Currently accepted treatments for NMSC include traditional surgical excision (TSE), radiotherapy, cryosurgery, electrodesiccation and curettage, photodynamic therapy, topical chemotherapy agents, and Mohs micro-
graphic surgery (Mohs). Traditional surgical excision has a 5-year recurrence rate of 10.1% for primary BCC \(^1\) and from 10.9% (lip) to 18.7% (ear) for SCC. \(^6\) An alternative, Mohs, has a 5-year recurrence rate of 1% for primary BCC\(^1\) and from 3.1% (lip) to 5.3% (ear) for SCC.\(^6\)

Because the cost of these procedures is substantial, direct comparison of both cost and efficacy of each treatment modality is essential for health care policy design. Given the constantly changing health care landscape, the presence of managed care, and the uncertainty of Medicare reimbursements, the dermatologic community has made several published requests for definitive cost analysis studies for the use of Mohs in cases of NMSC that meet established criteria warranting such surgery.\(^13\)\(^,\)\(^14\) However, there is a paucity of research determining the least costly technique to effectively treat facial NMSC.

Two retrospective studies have compared the cost of Mohs with TSE for the treatment of NMSC.\(^5\)\(^,\)\(^16\) Cook and Zitelli\(^15\) compared total procedure costs of Mohs with those of TSE for many types of tumors, including primary and recurrent NMSC, melanoma, and extramammary Paget disease in multiple anatomic locations (including torso and extremities). They found Mohs to be marginally more expensive than TSE when performed in the office with permanent sections (PS) and less expensive than ambulatory surgery–based TSE with frozen sections (FS). Our study focuses on facial and auricular NMSC and is limited to the published indications for Mohs.\(^13\)

Bentkover et al\(^16\) compared the cost of Mohs with that of TSE using rapid cross-sectional FS for treatment of BCC on the head and neck and found a cost savings for TSE over Mohs for their capitated practice setting. As their practice setting did not include a Mohs surgeon, all Mohs was outsourced as fee-for-service procedures and so resulted in cost outcomes specific to this capitated setting.

The purpose of our study was to compare the cost of Mohs and TSE performed by otolaryngologic (ENT) surgeons for the treatment of facial and auricular NMSC. We chose ENT surgeons for comparison because they are among several nondermatologic physician specialists to perform TSE procedures for NMSC.\(^17\) A secondary goal was to examine the frequency of positive margins after TSE and to determine the additional costs incurred to establish clear margins. Additionally, as a point of interest, we determined the total area of tissue removed by each method to report if either surgical procedure offered a tissue-sparing technique. Area as opposed to volume was measured because, as a result of our study design, the depth of our TSE procedures could not be determined. We hypothesized that the treatment of facial and auricular NMSC with Mohs would be comparable in terms of cost to TSE because Mohs is typically performed in the office setting, while nondermatologists typically utilize ambulatory surgery centers and formal operating rooms for TSE.

### METHODS

#### DESIGN

Consecutive patients referred for Mohs surgery with biopsy-proven primary NMSC involving the face and ears were enrolled in this study. The subjects included men and women 18 years and older.

The cost comparison analysis was performed using the American Medical Association 2002 Current Procedural Terminology (CPT) codes.\(^18\) We converted the CPT codes into dollar amounts using the Connecticut Medicare reimbursement rates for 2002.\(^19\) The actual dollar amounts (Connecticut Medicare reimbursements) corresponding to the CPT codes cited below are listed in Table 1.

This study was conducted prospectively, and each patient served as his or her own control. The data were collected at the University of Connecticut, Departments of Dermatology and Otolaryngology, and analyzed at Emory University, Department of Dermatology.

Initially, the Mohs surgeon (J.W.) independently examined and photographed the lesion. The planned Mohs margins were marked on the photograph to minimize the bias that may have been created by the surgical markings of the ENT surgeon. Next, an ENT surgeon (D.L. or J.S.) independently examined the patient, measured the tumor, and documented its size. He then drew his surgical margins on the patient with a surgical marker. The tumor size plus the planned surgical margins represented the “theoretical” size of the defect if a TSE were to be performed. The ENT surgeon then documented his choice of margin analysis: PS or FS. He also documented his preferred surgical setting: office, ambulatory surgical center, or formal operating room. Finally, the ENT surgeon recorded a proposed reconstruction based on the theoretical surgical defect.

After these data were recorded, Mohs surgery and subsequent repair were performed by the Mohs surgeon (J.W.) on each patient. After complete tumor extirpation, the real size of the surgical defect was documented to represent the actual defect size resulting from Mohs. As a result of this approach, a documented theoretical size of the TSE defect as determined by the ENT surgeons and an actual size of the Mohs defect created by the Mohs surgeon was available for all patients.

#### Table 1. Actual Dollar Amounts (Connecticut Medicare Reimbursements) Corresponding to an Office/Outpatient Setting vs a Facility Setting for Each CPT Code Used

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Outpatient/Office Reimbursement</th>
<th>Reduced MD Fee (When in Facility)</th>
<th>Facility Fee</th>
</tr>
</thead>
<tbody>
<tr>
<td>11640</td>
<td>166.69</td>
<td>115.63</td>
<td>214.81</td>
</tr>
<tr>
<td>11641</td>
<td>221.02</td>
<td>172.47</td>
<td>214.81</td>
</tr>
<tr>
<td>11642</td>
<td>258.68</td>
<td>202.81</td>
<td>214.81</td>
</tr>
<tr>
<td>11643</td>
<td>x</td>
<td>238.51</td>
<td>429.63</td>
</tr>
<tr>
<td>11644</td>
<td>x</td>
<td>307.93</td>
<td>x</td>
</tr>
<tr>
<td>88305</td>
<td>104.74</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>88331</td>
<td>84.08</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>88332</td>
<td>43.49</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>99212</td>
<td>39.98</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>12051</td>
<td>229.62</td>
<td>161.83</td>
<td>116.06</td>
</tr>
<tr>
<td>12052</td>
<td>236.77</td>
<td>172.74</td>
<td>116.06</td>
</tr>
<tr>
<td>12053</td>
<td>259.49</td>
<td>193.79</td>
<td>116.06</td>
</tr>
<tr>
<td>14040</td>
<td>660.39</td>
<td>580.04</td>
<td>642.41</td>
</tr>
<tr>
<td>14060</td>
<td>705.26</td>
<td>642.07</td>
<td>642.41</td>
</tr>
<tr>
<td>15240</td>
<td>747.56</td>
<td>674.75</td>
<td>642.41</td>
</tr>
<tr>
<td>15260</td>
<td>781.44</td>
<td>728.29</td>
<td>642.41</td>
</tr>
<tr>
<td>15576</td>
<td>x</td>
<td>629.57</td>
<td>642.41</td>
</tr>
<tr>
<td>15630</td>
<td>x</td>
<td>294.35</td>
<td>642.41</td>
</tr>
<tr>
<td>17304</td>
<td>624.44</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>17305</td>
<td>263.17</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>17306</td>
<td>264.84</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>17397</td>
<td>264.01</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Abbreviations: CPT, Current Procedural Terminology; x, treatment event did not occur in this study.
Costs for TSE were calculated for each patient based on the theoretical plan by the ENT surgeon. The cost of the excision (1164X) was charged with intermediate closures and grafts (1205X, 152XX) but not with adjacent tissue transfer (140XX), since the excision is bundled with the flap. Additionally, TSE costs included the charges for pathologic analysis, PS or FS (88305, 88331, 88332); reconstruction (1205X, 140XX, and 152XX series); and the facility fee when indicated (Table 1).

In 2003, the method of determining lesion or excision size changed. We used the existing method of measuring the lesion and not the excision size because this corresponded to the current technique for correct coding. Starting in August 2000, the facility fees included preoperative laboratory tests and radiographs. The excision and reconstruction costs were appropriately reduced when a facility fee was charged, and the excision or reconstruction costs were reduced according to the multiple surgery reduction policy. For each FS examination (88331, 88332), a PS examination and report (88305) are also generated; this is the standard of care. We assumed that these PS reports would confirm the clear margins. When the ENT surgeon chose healing by granulation, only 1 follow-up visit (99212) was charged because the TSE had a 10-day global period. A separate intravenous sedation fee was added as an additional cost in 4 cases as anticipated by the ENT surgeon.

For the TSE cases where a positive FS margin would require the ENT surgeon to excise more tissue before repair, a single subsequent FS was billed (88331 + 88305). We assumed that the negative margins would be confirmed after this subsequent FS. We did not alter the reconstructive plan of the ENT surgeon for those cases with positive FS margins (Figure 1).

For TSE cases where PS margins were determined to be inadequate, we assumed that those cases would require an additional procedure (Figure 1). We calculated the cost of 2 possible retreatment pathway outcomes: scenario 1 entailed retreatment with Mohs for the cases with inadequate margins and repair chosen by the Mohs surgeon. The additional Mohs and repair costs were determined by using the actual Mohs data from the same case less 1 Mohs stage. Scenario 2 consisted of a second excision via TSE with PS margin analysis and repair chosen by the ENT surgeons. We assumed subsequent clear margins with this additional TSE and estimated the cost by duplicating the original TSE costs.

We also performed a sensitivity analysis on our results. A sensitivity analysis explores variables that may influence the results of the original cost analysis, also called the baseline case. Our baseline case comparison for scenario 1 was Mohs with Mohs repair vs TSE with repairs chosen by the ENT surgeon (ENT-chosen repair) plus Mohs and Mohs repair for positive-margin cases. For scenario 2, the baseline case was Mohs with Mohs repair vs TSE with ENT-chosen repair plus a second TSE for positive-margin cases and a subsequent ENT-chosen repair for these cases only. We varied the values assigned to variables in the baseline cases that we felt would most likely alter the baseline results.

Analysis of the data was conducted using S-Plus 6 for Windows Statistical Package (Insightful Corp, Seattle, Wash; version 6.2). The distribution of our data for both cost and area of tissue removed was not normally distributed. Since each of the patients served as both the case and control, each datum was considered paired, and the Wilcoxon signed-rank test was used.

**RESULTS**

**PATIENTS, MARGINS, AND COST**

We enrolled 98 consecutive patients (mean age, 67.8 years), 56 men (57%) and 42 women (43%). The BCC/
SCC ratio was 77:21. The average number of Mohs stages per case was 1.5 (range, 1-5 stages). The location of the facial NMSC, setting of TSE procedures, and the distribution of repairs for both procedures are illustrated in Table 2.

Of the 98 patients in the study, the ENT surgeon recommended 67 for PS and 31 for FS pathologic analysis. Of the 67 patients with PS, 22 (32%) had inadequate margins. Of the 31 patients recommended for FS, 12 (39%) had inadequate margins and so required further extirpation (Figure 1).

The mean Mohs cost per patient for removal of facial and auricular NMSC was $937 (95% confidence interval, $889.50-$984.50) compared with the mean TSE cost per patient of $831 (95% confidence interval, $724.90-$937.10) (P=.04), not accounting for the additional cost of a second procedure required for positive margins (inadequate TSE) when PS was used. To account for the cost of complete tumor extirpation after inadequate PS TSE, we calculated the cost of the 2 possible treatment pathway outcomes. In scenario 1, the inadequate TSE cases were treated with Mohs and Mohs repair, and the mean cost per patient became $1029. Compared with Mohs alone ($937 per patient), the cost of TSE plus Mohs for the TSE positive-margin cases ($1029 per patient) was more expensive by a difference of $92 (P=.16). In scenario 2, the PS TSE inadequate cases were re-treated with a second TSE. We found that the mean cost per patient for TSE+TSE and ENT repair was comparable to Mohs alone, $944 vs $937, respectively (P=.53).

SUBGROUP AND SENSITIVITY ANALYSES

We performed a subgroup analysis, examining the difference between TSE cases sent for FS margin analysis vs Mohs. When comparing the cost in the subgroup of patients where FS were requested (n=31), we found that the average Mohs cost for this subgroup was $956, while the average cost of TSE with FS was $1399 (a difference of $443; P<.001).

We conducted several sensitivity analyses to address potential biases in our study design. The variable with the most potential to alter the baseline cases was the cost of the repair chosen by both the Mohs and ENT surgeons. In the Mohs group, there was a greater proportion of defects that were allowed to heal by second intention compared with the repair choices of the ENT surgeons (Table 2).

To explore potential reconstruction biases, the data were reevaluated after substituting ENT-chosen repair and Mohs repair in various combinations. We then determined whether these substitutions altered the results of the original cost analysis, also called the baseline case (Mohs with Mohs repair vs TSE with ENT-chosen repair plus Mohs and Mohs repair for positive-margin cases). We performed these sensitivity analyses for scenarios 1 and 2. In scenario 1, all positive margins after the initial TSE were treated with Mohs, while in scenario 2, inadequate TSE cases were treated with a second TSE (Figure 1).

When we substituted the cost of Mohs repairs with that of ENT repairs we found that the results of our original cost analysis or baseline case were sensitive to the choice of repairs for scenario 1. For example, as demonstrated in Figure 2, when we substituted Mohs repair with ENT repair (Mohs procedure with ENT repair, hereinafter “modified Mohs”) and compared this with baseline TSE (TSE with ENT repair plus Mohs and Mohs repair for positive-margin cases) we found that the modified Mohs was significantly more expensive than baseline TSE ($1110 vs $1029; P=.02).
We compared the cost of Mohs and TSE for the treatment of facial and auricular NMSC. Our study design was based on the current clinical practice for TSE in which the setting of the surgery and the type of margin analysis, PS or FS, are chosen by individual physicians. Traditional surgical excision when conducted in an office setting with PS would be the least expensive treatment pathway if the margins were always clear. In our study, 32% of TSE cases were found to have inadequate margins. To fully compare the Mohs alone with the TSE approach, we needed to account for positive margins by TSE and subsequent procedural costs to remove the remaining tumor. We found Mohs alone to be comparable to the TSE strategy both when the subsequent procedure was Mohs ($937 vs $1029, respectively) and when the subsequent procedure was another TSE ($937 vs $944). However, we must also consider a certain failure rate with this second TSE, which would necessitate additional costs and additional time incurred by the patient for another surgery and repair. Additionally, we made an assumption that all deep margins were clear with the TSE, which if not true, would lead the TSE arm to require even more subsequent procedures and possibly more complicated repairs.

We hypothesized that treatment of NMSC with Mohs was cost comparable to TSE because Mohs is typically performed in the office setting rather than in ambulatory surgery centers and formal operating rooms. In our subgroup analysis, we found that some of the most significant differences in cost were seen when Mohs was compared with facility-based TSE with FS. Mohs offered a cost savings of $443 compared with facility-based TSE with FS. The difference would have been even greater had we not assumed clear margins on all second FS and subsequent PS confirmations. A large part of the ENT surgical expense when FS margin control was required was that the ENT surgeon’s outpatient facility could not offer FS, and so the cost of an ambulatory surgery center was incurred. The result was a significant cost-savings advantage for non–facility-based Mohs procedures.

Our findings differed from those of Bentkover et al., who compared the cost of Mohs with the cost of TSE with cross-sectional FS technique for BCC. They found a $150 to $454 cost-savings benefit to TSE over Mohs per tumor. However, their study was conducted in a capitlated health maintenance organization setting in which a contracted out-of-plan Mohs surgeon operated on a fee-for-service basis. For TSE, all facility and excision fees were covered under global capitation, which left only the pathology fees to compare with the outsourced cost of Mohs. This is probably the reason for our discordant findings.

In our study, the proportion of positive margins in the TSE cases was relatively high (32% of patients with PS and 39% of the patients with FS) compared with other studies. These differing rates may partially result from the amount of margin actually analyzed. Traditional vertical sectioning techniques with PS examine only a small sample (usually <1%) of the excised margin while Mohs evaluates nearly 100% of the excised margin. Other possible reasons for the rate of positive margins are explored below.

As a point of interest, we determined the total area of tissue removed by each method to determine whether one surgical procedure was more efficient than the other at tissue conservation. We found no significant difference in area of tissue taken between the 2 procedures. The area of tissue taken and the frequency of positive margins may be interrelated. As the surgeon takes wider margins of normal-appearing tissue in TSE and sacrifices tissue conservation, the likelihood of clear margins increases. The attempt at TSE with conservative margins for facial NMSC may have resulted in the 32% and 39% positive-margin rates in the PS and FS cases, respectively.

The limitations of this study must be addressed. We recognize that a randomized trial with the 2 surgical strategies would be a superior methodologic design. How-

![Figure 3. Sensitivity analysis of repairs (scenario 2) of inadequate traditional surgical excision (TSE) cases treated with an additional excision (N=98). Baseline Mohs micrographic surgery (Mohs) (mean cost of Mohs+Mohs repair, $937) and modified Mohs (mean cost of Mohs+repair by otolaryngologic surgeon [ENT], $1110) compared with modified TSE (mean cost of TSE+ENT-chosen repairs+TSE for positive margin cases+ENT-chosen repairs, $944). The light-shaded area represents the lower quartile of data containing 25% to 50% of the cost data; dark-shaded area, the upper quartile containing 50% to 75% of the cost data; and the error bars, data range beyond the quartiles.](REPRINTED) ©2004 American Medical Association. All rights reserved.
ever, owing to patient recruitment and time constraints, a prospective design was chosen with 98 consecutive patients enrolled, each patient serving as his or her own control. Consistent with this design, several assumptions were made, including the decision that all deep margins in TSE cases were considered to be clear. Additionally, assumptions based on choices made in current clinical practice were made involving the type of subsequent surgical procedure used to remove remaining tumor in the event of positive margins. Of note, other pathways for subsequent surgical procedures exist in practice, such as having ENT reconstruction after Mohs procedure for incomplete tumor removal. We did not address the other potential pathways in our model; they may be pursued in future research.

Another limitation to our study is the potential biases of the ENT and Mohs surgeons. It is possible that because the ENT surgeons performing the TSE were aware that the total area of tissue removed was a measured outcome, they might have systematically underestimated the total amount of tissue required to remove all of the cancer. This potential bias may explain the high rate of inadequate excision. However, the high rate of underestimation of necessary tissue to remove is consistent with reports in the literature. Studies have shown that most incompletely excised BCCs are on the head and neck, including a large case series that found that 16% of BCCs (58/353) extended to the margin of surgical excision and 74% of these (43/58) were on the head and neck. Additionally, in a retrospective study of 143 excisions of primary BCCs on the face, 30% (42/143) were inadequately excised. It is possible that physicians, in an attempt to minimize cosmetic morbidity in facial sites, may excise NMSC with more conservative margins than in other surgical locations. Additionally, studies have shown that physician specialty might affect the frequency of positive margins in the surgical management of BCC. While the patient’s sex, age, and tumor size or physician experience were not significantly related to the presence of tumor in the surgical margin, when compared with dermatologists and general surgeons, otolaryngologists and plastic surgeons were significantly more likely to incompletely excise tumors.

Another potential bias may have been with the Mohs surgeon (J.W.). Since he was aware that costs were the primary outcome of the study, he may have been predisposed toward second-intention healing. As seen in our sensitivity analysis (Figures 2 and 3), significant cost differences are evident when the repair choices of the ENT surgeons are switched with the repair choices of the Mohs surgeon. The Mohs surgeon might have also taken wider margins to reduce the number of stages. However, the 1.5-stage average was consistent with yearly averages of the Mohs surgeon.

Despite these limitations, we have shown that Mohs is cost comparable to 2 sequential TSEs with Ps in the office and much less costly than facility-based TSE with Fs for the treatment of facial and auricular NMSC. Mohs alone offers a marginal ($92) cost savings over TSE plus Mohs when a second procedure is needed to ensure complete tumor removal. Our study had similar findings to those of Cook and Zitelli in terms of the total procedure costs of Mohs vs TSE; however, our focus was specifically limited to NMSC and published criteria for Mohs surgery.

It should be noted, however, that our cost data were sensitive to the type of repair chosen. In other words, when we varied the cost of repair within plausible ranges, the difference between Mohs with Mohs repair and the TSE pathways changed significantly. Thus, our findings must be interpreted with caution. Future work is necessary in determining the choice of repairs by Mohs surgeons across the country to generalize our study findings.

This study provides an evidence-based approach to the least costly way to provide treatment for facial and auricular NMSC. However, efficacy and outcomes (survival and quality-of-life impact) must also be taken into account when comparing the 2 procedures. A cost-effectiveness analysis incorporates efficacy and outcomes of the 2 therapies being compared and would be a preferable to a pure cost analysis because it can quantify the value rather than just the costs of these 2 procedures. Once the ratio of costs to effectiveness is determined, therapeutic guidelines may be created and a recommended treatment algorithm provided whereby the most cost-effective treatments can be offered.

Accepted for publication March 4, 2004.

This project was supported in part by an American Skin Association (ASA) Health Services Research Grant and Emory Skin Disease Research Center Pilot and Feasibility grant P30AR42687 from the National Institute on Arthritis and Musculoskeletal and Skin Disease (NIAMS), National Institutes of Health (NIH).
Dr Bialy is supported by National Research Service Award Training Grant T32 AR07587 from the NIH. Dr Chen is supported in part by Mentored Patient-Oriented Career Development Award K23AR02185-01A1 from NIAMS, NIH, as well as an ASA David Martin Carter Research Scholar Award.

Corresponding author and reprints: James Whalen, MD, Department of Dermatology, University of Connecticut School of Medicine, 263 Farmington Ave MC-6231, Farmington, CT 06030-6231 (e-mail: jwhalen@nso1.uchc.edu).

REFERENCES