Conjunctival melanoma is a rare tumor of the ocular surface, with an annual incidence of fewer than 5 cases per million residents of the United States and a 10-year mortality rate of about 30%. The standard management of conjunctival melanoma consists of local excision, with application of cryotherapy to the resection margins. There is currently no reliable method of predicting which patients will develop regional lymph node metastasis, although tumor thickness is associated with poorer prognosis and higher likelihood of metastatic disease. After resection of conjunctival tumors, patients are commonly observed clinically until overt clinical signs of metastasis develop. Once clinically detectable metastatic disease develops, the prognosis is poor.

The regional lymph nodes are thought to be the first site of metastasis for most patients with conjunctival melanoma. The reported frequency of regional lymph node metastasis secondary to conjunctival melanoma varies from 26% to 40%. The histologic status of the sentinel lymph nodes (SLNs) has been shown to be the most significant prognostic factor with respect to recurrence and survival in patients with cutaneous melanoma. Furthermore, the long-term regional control of disease is better achieved when the nodal burden is microscopic compared with when disease is clinically apparent. Because conjunctival melanomas have a pattern of metastasis similar to that of cutaneous melanomas, it is important to investigate the role of SLN biopsy in the management of conjunctival melanoma. We have previously reported a technique of SLN mapping and biopsy for conjunctival melanomas that is safe and may permit early detection of microscopic regional nodal disease. Other investigators have also described SLN biopsy techniques for ocular adnexal tumors. We herein describe a patient with melanoma of the conjunctiva who underwent SLN biopsy using this technique and was found to have an SLN microscopically positive for metastatic melanoma. To our knowledge, this is the first reported case of a positive SLN in association with conjunctival melanoma.

**Report of a Case.** A 58-year-old man with a malignant melanoma of the right bulbar conjunctiva (Figure 1) underwent wide local excision of the lesion and cryotherapy by his local oculoplastic surgeon 4 weeks prior to his initial visit at M. D. Anderson Cancer Center (Houston, Tex). The histopathologic diagnosis was invasive melanoma, 3.1 mm in thickness (Figure 2). The patient was referred to us to be considered for SLN biopsy and possible adjuvant therapy. The patient underwent magnetic resonance imaging of the head and neck, chest roentgenography, computed to-

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mography of the lung, abdomen, and pelvis, analysis of liver enzymes, and a hematologic survey. The results of all of these examinations were within the normal limits. The negative magnetic resonance image at the level of the parotid lymph nodes is shown in Figure 3.

Examination of the right eye revealed a visual acuity of 20/30. Slit-lamp examination did not show any residual pigment, and there was a wide area of recent resection, extending greater than 6 clock hours in the paralimbal conjunctiva. Findings from the rest of the slitlamp examination were within the normal limits except for a mild residual anterior chamber reaction due to the recent cryotherapy. The rest of the examination of the right eye, including a dilated fundus examination, revealed no abnormalities. Findings from the examination of the left eye were normal. The regional lymph nodes were not palpable.

After a discussion of the risks and potential benefits, the patient elected to enroll in an institutional review board–approved protocol for SLN biopsy for conjunctival melanomas. Preoperative lymphoscintigraphy was performed 6 days before the planned surgery date, using radionuclide imaging as described previously. Briefly, after topical application of proparacaine, 0.3 mCi (11.1 MBq) (0.2 mL) of technetium Tc 99m sulfur colloid was injected by an ophthalmologist (B.E.) in the subconjunctival space in 4 spots around the site of the previous excision of the melanoma on the surface of the globe. Using a gamma-camera with a low-energy, high-resolution collimator, dynamic images of the head and neck region were obtained 15 minutes after injection and every 30 minutes thereafter until the SLNs were visualized. The first SLN was visible on lymphoscintigraphy 20 minutes after sulfur colloid injection; 10 minutes later, 3 separate SLNs draining the conjunctival lesion were visible. By 90 minutes after sulfur colloid injection, radiotracer uptake in the SLNs was easily visualized (Figure 4). The SLNs were identified in the right parotid area and the right mid-jugular (level II) and inferior jugular (level III) lymph node basins.

On the day of surgery, general anesthesia was induced, and then 0.3 mCi (11.1 MBq) of technetium Tc 99m sulfur colloid in 0.2 mL was injected at 4 spots around the lesion. In addition, 0.2 mL of isosulfan blue dye was injected in the subconjunctival space around the lesion.

Next, a handheld gamma probe was used to localize SLNs transcutaneously in the parotid and cervical areas, with the images from preoperative lymphoscintigraphy used as a guide. A collimator was used to decrease the background radioactivity, and the areas of increased focal radiotracer uptake were identified and marked on the skin. A curvilinear skin incision was made directly over each SLN, and each SLN was carefully dissected and submitted for histologic processing as described in the next paragraph. Sentinel lymph nodes were defined as lymph nodes that contained radioactivity at least twice that of the background. Sentinel lymph nodes...
node harvest was considered to be complete when radioactivity in the draining nodal basins was less than 10% of the SLN counts. The neck was checked again with the gamma probe after removal of the SLNs to confirm the absence of areas of increased radioactivity and thus confirm that no other SLNs were present.

Three SLNs, corresponding to the 3 SLNs identified during preoperative lymphoscintigraphy, were successfully identified. The SLNs were not blue when they were dissected from their associated lymphatic basins (approximately 90 minutes after injection of the blue dye around the primary tumor).

The SLNs were analyzed following methods described previously.13,14 Briefly, the nodes were serially sectioned at 2-mm intervals and examined by routine hematoxylin-eosin staining. Histologic analysis of the first-order SLN in the right parotid chain revealed melanoma (Figure 5). The other 2 SLNs (second-order) were histologically negative. Findings on immunohistochemical staining of these SLNs with a cocktail containing HMB45, anti-MART 1, and antityrosinase were also negative (not shown). The isosulfan blue dye injected subconjunctivally had completely dissipated by 24 hours after injection (Figure 6). The facial nerve was fully functional, and there were no postoperative complications from this procedure.

Comment. We successfully identified the SLNs for a bulbar conjunctival melanoma, using a combination of blue dye and radiolabeled sulfur colloid. One of the 3 SLNs was histologically positive for metastatic melanoma. To our knowledge, this is the first reported case of a microscopically positive SLN in a patient with conjunctival melanoma, validating the concept that SLN biopsy can provide important staging information—that cannot be obtained by physical examination or radiographic evaluation—in patients with melanoma of the conjunctiva.

The rate of SLN positivity for skin melanomas of intermediate thickness is approximately 15% to 20%.7,15-19 The rate of SLN positivity for conjunctival melanomas is unknown. Previous reports of the natural history of conjunctival melanoma suggest that regional nodal metastasis occurs in 30% to 40% of patients within 10 years after diagnosis.5,6 The current report of a histologically positive SLN suggests the need for further application of SLN biopsy in additional patients to identify the rate of SLN positivity in conjunctival melanomas. We have so far performed SLN biopsy in 3 patients with known tumor thickness (>1 mm). Of these 3 patients, we have identified 1 histologically positive SLN (the patient described in the current report). While tumor thickness has been shown to be the best predictor of SLN involvement in cutaneous melanoma, the relationship between tumor thickness and the status of SLNs has not previously been studied for conjunctival melanoma.

Figure 4. Appearance of sentinel lymph nodes (SLNs) on preoperative lymphoscintigraphy. A, Ninety minutes after sulfur colloid injection. B, Ninety minutes after sulfur colloid injection with radioactive markers placed at different anatomic landmarks.

Figure 5. Histologic analysis of the sentinel lymph node from the right parotid basin demonstrates malignant melanoma (asterisks) metastatic to the lymph node parenchyma (hematoxylin-eosin, original magnification ×10).
though much has been written about the histologic features of conjunctival melanomas, and some studies have found tumor thickness to be an independent prognostic factor for survival,2 no definitive studies have looked at tumor thickness as an independent prognostic factor for regional nodal metastasis. The other problems are lack of proper handling of biopsy specimens and tangential cutting of specimens, which often preclude accurate determination of tumor thickness. The conjunctival tissue, like most mucous membranes, is friable, and proper orientation of the specimen before sectioning is crucial. In the setting of an institutional review board–approved protocol for SLN biopsy, it may be worthwhile to include patients with conjunctival melanoma of unknown thickness, since they may have had tumors thicker than 1 mm. We have performed SLN biopsy in 2 patients in whom the thickness of the conjunctival tumor could not be determined, owing to the poor handling of the conjunctival specimen.

Several technical issues surrounding SLN biopsy in the periorcular region warrant discussion. The injection of 0.3 mCi (11.1 MBq) of technetium Tc 99m sulfur colloid in 0.2 mL around the conjunctival lesion seems to be an effective way to obtain high-quality images during preoperative lymphoscintigraphy. This is a much smaller volume than the standard 1 mL used for lymphatic mapping in other locations.

Given the relatively small size of conjunctival melanomas and the close proximity of these lesions to intraocular structures, we recommend injection of the colloid by an ophthalmic surgeon. The injection can be carried out in the nuclear medicine department, or the patient can be transferred to the nuclear medicine department immediately after injection of the colloid by the ophthalmologist in another outpatient setting. We prefer to do the preoperative lymphoscintigraphy before the planned surgery date so that the pattern of lymphatic drainage is confirmed prior to the surgery. A dose of 0.3 mCi (11.1 MBq) of technetium-labeled sulfur colloid emits an estimated dose of 0.2 rad (0.002 Gy) to the lens during a 6-hour period, if we assume that there is no drainage from the subconjunctival space (Ebrahim Delpassand, MD, e-mail communication, 2000). With successful drainage of the sulfur colloid, the radiation dose to the lens would be a fraction of 0.2 rads (0.002 Gy). This dose is much less than the dose associated with cataract formation or radiation retinopathy.20 Thus, injecting the sulfur colloid on 2 separate occasions separated by at least 6 hours should not place the intraocular structures at any significant radiation risk.

Sentinel node biopsy in the head and neck should be carried out by surgeons who are not only familiar with the anatomy of the parotid region but also have considerable experience with identifying and dissecting SLNs. One of the perils of SLN biopsy in the parotid region is the risk of damage to the facial nerve, which should be minimized with careful dissection and adequate experience of the surgeon.

Another theoretical complication of SLN biopsy in the periorcular region is blue staining of ocular tissues secondary to the blue dye.21 While the conjunctival surface was blue for the first few hours after injection of the blue dye, the color dissipated during the first 24 hours after injection. Our experience so far suggests that there is relatively rapid transport of the blue dye from the conjunctival surface.

Presently, the most common approach to the regional nodal basins in patients with conjunctival melanoma is observation followed by a therapeutic dissection when clinical disease becomes apparent. The use of such an approach for cutaneous head and neck melanoma leads to in-basin failure rates of up to 50%.22,23 Long-term nodal control appears to be significantly better when the formal dissection is performed at the microscopic stage of nodal disease—reported failure rates in this situation are less than 10%.18 Furthermore, overall survival may also be improved by performing regional lymph node dissection early, when nodal disease is microscopic. The American Joint Committee on Cancer staging criteria for cutaneous melanoma clearly demonstrate that survival is better in the stage III group when the burden of disease is microscopic and

Figure 6. Effect of blue dye injection on appearance of the globe. A, Appearance of the right globe immediately after injection of isosulfan blue dye. B, Twenty-four hours after injection, the blue dye had dissipated from the surface of the globe.
the number of involved nodes is small, a situation more common in patients with positive SLNs than in those who develop clinically apparent disease. It is not unreasonable to assume that this pattern is also true for conjunctival melanomas. Therefore, the potential for improved regional control and survival offers a rationale for studying SLN biopsy in patients with conjunctival melanoma.

At present, the role of adjuvant systemic therapy for conjunctival melanomas is unclear. Since nodal disease is a powerful prognostic factor for distant failure, SLN biopsy may allow for early detection of high-risk patients. If this is the case, then patients with nodal disease can be offered protocols for systemic adjuvant therapy in addition to complete surgical dissection of the involved basins. Adjuvant therapy may consist of systemic administration of interferon or chemotherapy, or a combination of these approaches.25-28 Despite the additional surgery time required for SLN biopsy and the potential risk of facial nerve damage if the nodes are in the parotid area, the likely improvement in nodal staging and the possible survival benefit offered by this technique warrant its further study in patients with conjunctival melanoma and possibly other ocular adnexal tumors with a propensity for metastasis to the regional nodes. A larger-scale study needs to be undertaken to evaluate the rate of positivity of SLNs in patients with conjunctival melanoma. Our experience with SLN biopsy for conjunctival melanomas suggests that this technique can be done safely and should be considered for lesions that are thicker than 1 mm; it should be performed, however, in the confines of an institutional review board–approved protocol so that observations about the rate of positivity of SLNs can be reliably reported in the future. It is important to point out that while our observations in this single patient validate the concept that SLN biopsy should be considered for patients with high-risk melanomas of the conjunctiva, they should not be interpreted as recommendations for routine SLN biopsy in every patient with conjunctival melanoma.

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Metastasis of Acinic Cell Carcinoma of the Parotid Gland to the Contralateral Orbit

Acinic cell carcinoma is an uncommon low-grade malignant tumor of the salivary glands, in which some cells resemble normal acinic cells.1 Most of these tumors occur in the parotid gland.1,2 Women are affected more often than men, and the age at occurrence is earlier than in other salivary gland cancers.2 Most cases are unilateral, and bilateral involvement has rarely been reported. Conversely, an unusual case of synchronous acinic cell carcinomas of the left parotid and right submandibular glands has previously been described.3