

SCC Perineural Invasion Responds to Radiation

BY DOUG BRUNK
San Diego Bureau

SANTA ANA PUEBLO, N.M. — Perineural invasion can occur in 2.5%-15% of patients with squamous cell carcinoma, and 60%-70% of patients are asymptomatic on presentation, Dr. Tri. H. Nguyen said at a meeting of the American Society for Mohs Surgery.

Patients who present with symptomatic perineural involvement most commonly have paresthesia, followed by sharp or achy pain, motor deficits, and formication (sensation of bugs crawling on the skin), said Dr. Nguyen, director of Mohs micrographic and dermatologic surgery at the University of Texas M.D. Anderson Cancer Center, Houston.

Clinical risk factors for perineural invasion include male gender, large tumor size (2 cm or greater), central face location, and recurrent tumor. Histologic risk factors for perineural invasion include moderate to poorly differentiated histology, intravascular or lymphatic invasion, deep invasion, and extensive subcutaneous infiltration.

Imaging studies are valuable in staging and prognosis. For bony invasion, a CT scan is best. To evaluate lymph nodes, a CT scan followed by MRI is preferred. "However, if you have access to an expert radiologist and ultrasound, then [ultrasound] is also an excellent technique to evaluate lymph nodes in the head and neck," Dr. Nguyen said.



Ultrasonography of the head and neck permits fine-needle aspiration of suspicious nodes in real time. If large nerve involvement is suspected, consider an MRI, he said.

"There is greater tissue destruction with perineural squamous cell cancers, which results in a larger defect size, higher rates of recurrences and metastasis—up to 50% in some studies—and definitely a worse prognosis," said Dr. Nguyen, who also directs the procedural dermatology fellowship program at M.D. Anderson.

This is why adjuvant radiation therapy is recommended for these higher-risk squamous cell cancers.

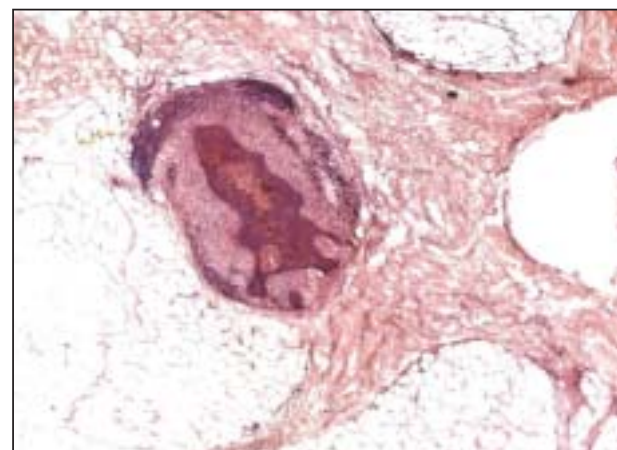
Perineural disease alone, however, is not an absolute indication for radiation. "Only when there are other risk factors should radiation be considered in the adjuvant setting," he said. (See box.)

Radiation therapy "is not a benign process," he said. "There is significant cost ranging from \$1,000 to \$3,000 per treatment dose. There are logistics to work out, with treatments ranging from three to five times per week."

Radiation dermatitis, delayed wound healing, and functional impairment may occur with radiation.

Despite such risks, most adjuvant radiotherapy for cutaneous skin cancer is relatively well tolerated. "When you're talking about radiating oral, pharyngeal, or laryngeal cancer, that's a whole different ball game," he said.

In one early study, when radiation was added to wide



Perineural involvement in a stage IV squamous cell carcinoma can be seen in the above pathology image.

local excision in patients with squamous cell carcinoma of the head and neck and perineural invasion, the 5-year local control rate was 38%, compared with 20% with radiation alone (Head Neck 1989;11:301-8). "I look at radiation as only one tool to treat these higher-risk squamous cell cancers," Dr. Nguyen said.

He divides perineural involvement of squamous cell carcinoma into two groups: incidental disease and clinical disease. Patients with incidental disease are asymptomatic, have isolated perineural involvement of small peripheral nerves in the high dermis, and are imaging negative. "In this group, the local control rate without radiation is 78%-87%," he said.

Patients with clinical disease have perineural tumor of larger nerve trunks, have more extensive perineural involvement, are asymptomatic, and are imaging positive. "These patients have a positive MRI or CT and a worse prognosis," he said. "The local control rate without radiation therapy is 50%-55%."

Tumors that are recurrent worsen the prognosis, especially in the setting of perineural disease. "For example, the local control rate is 50%-75% in a primary squamous cell cancer with perineural disease," he said. "Contrast this to the local control rates of 11%-50% in a recurrent squamous cell cancer with perineural disease." ■

Indications for Adjuvant Radiation Therapy After Surgery

Dr. Nguyen refers patients for postoperative adjuvant radiotherapy if:

- ▶ Recurrence morbidity would be catastrophic.
- ▶ Perineural involvement of large or extensive nerve trunks is confirmed.
- ▶ There is extensive microscopic disease or subcutaneous extension.

- ▶ The size of the tumor is greater than 2 cm and is located on the central face.
- ▶ The tumor is recurrent.
- ▶ The tumor is poorly differentiated or has deep invasion.
- ▶ Disease involves the lymph nodes.
- ▶ The patient is immunosuppressed.

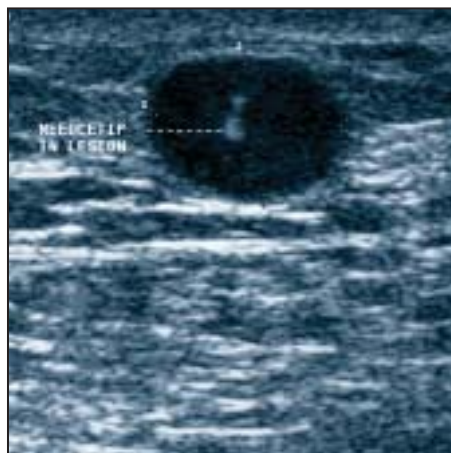
Fine Needle Aspiration May Reduce Need for Sentinel Biopsies

BY JANE SALODOF MACNEIL
Senior Editor

CHICAGO — Screening melanoma patients by ultrasound and fine needle aspiration cytology can avoid sentinel lymph node biopsies in half of node-positive patients, according to the results of a prospective study.

All 503 consecutive patients in a German and Dutch study underwent scintigraphy followed by ultrasound prior to scheduled sentinel lymph node biopsy. If ultrasound revealed a suspicious deposit, the patient went on to fine needle aspiration in an attempt to determine whether the node was positive, Dr. Gregor Schäfer-Hesterberg reported at the annual meeting of the American Society of Clinical Oncology.

Interim data on 400 patients for whom outcomes were available showed that ultrasound identified positive sentinel nodes in 51 of 79 (65%) patients who turned out to be node positive after dissection. Fine needle aspiration confirmed nodal disease in 40 of these patients—a group the investigators concluded could have skipped their scheduled biopsies and gone directly to total lymph node dissection.



Using ultrasound, the needle is guided into a suspicious lymph node.

"If we can verify that there is a metastasis in the sentinel node or another node, we can spare the patient an operation," Dr. Schäfer-Hesterberg said in an interview.

The majority of biopsied patients are node negative, added Dr. Schäfer-Hesterberg, a dermatologist at Charité Universitätsmedizin Berlin. In this study, 321 patients still underwent the surgical procedure without a positive finding.

The investigators, led by Dr. Christiane

Voit of the same institution, previously reported an overall sensitivity of 82% for the combination of ultrasound and fine needle aspiration cytology (Ann. Surg. Oncol. 2006;13:1682-9). In the new data based on outcomes collected at an average of 30 months' follow-up, the group reported the combination became more sensitive in higher-staged tumors. Sensitivity was 65% overall, ranging from 40% in T1 disease to 79% in T4. Overall specificity was 99% with a range of 100% in T1 disease to 97% in T4.

Measurement of histologic nest sizes in 65 of the node-positive patients showed submicroscopic involvement of less than 0.1 mm in 13 patients, only 3 of whom were identified by ultrasound and fine needle aspiration cytology. As tumor load increased, the combination became more sensitive, identifying 11 of 24 tumors (46%) in the 0.1- to 1.0-mm range and 24 of 28 tumors (86%) larger than 1 mm.

"Ultrasound of the sentinel node and

ultrasound guided fine needle aspiration cytology is highly accurate," the authors concluded in their poster.

In a discussion of the study, Dr. Vernon K. Sondak called for "further exploration but with a healthy skepticism."

Preoperative ultrasound has many potential roles in evaluating melanoma, particularly when patients are not eligible for sentinel lymph node biopsy, said Dr. Sondak, chief of cutaneous oncology at the H. Lee Moffitt Cancer Center in Tampa, Fla.

On the basis of the total study population, however, only a small percentage of all patients would be

diverted from sentinel lymph node biopsy. At his own institution, Dr. Sondak said the experience with preoperative ultrasound in 93 patients would have spared no more than 8%.

"The numbers are very much against us when we do this in an unselected fashion," Dr. Sondak said. ■

If a metastasis in the sentinel node or another node is verified, an operation can be avoided.

DR. SCHÄFER-HESTERBERG



COURTESY DR. GREGOR SCHÄFER-HESTERBERG

COURTESY DR. TRI. H. NGUYEN