Hayes Martin, MD, was born on June 24, 1892, in Dayton, Iowa. He graduated from The University of Iowa School of Medicine in 1917 (Figure 1). He served in World War I as a flight surgeon in France. On his return to New York City, he wanted to be a general surgeon but was not accepted into the much sought-after surgical program at Bellevue Hospital. He was told by Dr John Hartwell, the chief of surgery at Bellevue, that since it would be 2 years before an opening would occur, he should prepare himself for that position. In pursuit of this goal, Dr Martin served as an intern and resident at Memorial Hospital in New York, where he was exposed to cancer surgery.

He then was accepted as a resident on Dr Hartwell’s service at Bellevue. A patient was admitted to his service who previously had a tumor of the scrotum and had then developed a mass in the lung. Dr Martin, when questioned, indicated that he thought that this was a new primary tumor because it was single rather than multiple. The rest of the staff believed it was metastasis. When the patient died and Dr Martin was asked to pronounce him dead, he secretly took a needle aspiration biopsy specimen of the mass in the lung, analysis of which demonstrated that this was indeed a new primary cancer. Although this incident got him into a lot of trouble with the chief of pathology and with Dr Hartwell, this is apparently the first evidence of the use of needle aspiration biopsy for diagnosis and is one of Dr Martin’s major contributions to head and neck surgery.1

Dr Martin was appointed chief of the head and neck service at Memorial Hospital in 1934. Dr Martin’s book Surgery of Head and Neck Tumors2 was published in 1957 and became the standard textbook for those interested in head and neck surgery. He also published more than 160 articles. The most famous of his many articles include “Cancer of the Head and Neck,” published in the Journal of the American Medical Association in 1948;3 “Neck Dissection,” published in Cancer in 1951;4 and “Radical Neck Dissection,” published in Clinical Symposia in 1961.5 These articles were so extensively requested by physicians and others at the time that the American Cancer Society made reprints by the thousands to be available to those who requested them as long as 20 years after publication.

Dr Martin was a member of the American Board of Surgery, the American Board of Plastic Surgery, and the American Board of Radiology. He was a founding member of the Society of Head and Neck Surgeons and its first president. He was also a founding member of the James Ewing Society, now known as the Society of Surgical Oncology.

Prior to Dr Martin’s time, radium and radon seed implants were commonly used to treat the neck because external beam radiation therapy was in a very primitive state and not used very often. Radical neck surgery was also not frequently used because it was quite dangerous. After World War II, improved anesthesia techniques,
availability of antibiotics, and blood banking permitted advances in head and neck surgery, and by 1950, 190 neck dissections had been performed at Memorial Hospital.

Dr Martin’s philosophy, as stated in the article “The Diagnostic Significance of a ‘Lump in the Neck,’” was that “asymmetric enlargement of one or more cervical lymph nodes in the adult is almost always cancerous and is usually due to metastasis from a primary lesion in the mouth or pharynx.” He also pointed out the perils of the injudicious removal of an enlarged lymph node for diagnosis. In a patient with cervical metastatic cancer, this invariably lessens the chance for a cure.

Dr Martin retired from active practice in 1957 at the age of 65 years after a small stroke caused by hypertensive arteriosclerotic heart disease. He performed his last operation, assisted by Dr Elliot Strong, in October 1959. He died in Memorial Hospital on Christmas day, 1977.

THE ERA OF THE RADICAL NECK DISSECTION

Although there had been sporadic reports of the use of radical neck dissection (RND), the first systematic approach to the treatment of cancer in the neck was described by Dr George Crile, from The Cleveland Clinic, in the Journal of the American Medical Association in 1906. Crile’s primary goal was excision of the cervical lymph nodes, but to maximize the comprehensiveness of the procedure, he routinely removed the internal jugular vein, the sternocleidomastoid muscle, and the spinal accessory nerve (Figure 2). After Crile’s work, there is little to be found in the literature about the systematic use of RND until Hayes Martin’s classic article was published in Cancer in 1951. As chief of the head and neck service at Memorial Hospital, Dr Martin was in the position to perform or supervise many RNDs and to form some very long-lasting opinions about the treatment of the neck. Dr Martin trained many people from the United States and abroad, and they carried home with them the concept of the RND as the standard of care for patients with cervical lymph node metastasis.

In Dr Martin’s article “The Case for Prophylactic Neck Dissection,” he states that in the head and neck service at Memorial Hospital at that time, there had persisted over the last 30 years a conservative policy that metastatic cervical cancer be treated aggressively (by surgery or radiation therapy or both) only if clinically present. He believed that a rigid routine of prophylactic RND was not practical in cancer of the tongue and lip and doubted that anyone could actually carry out prophylactic neck dissection to a degree sufficient to effect significant improvement in cure rates. Dr Martin’s conclusion was that the “routine prophylactic neck dissection is considered illogical and unacceptable” for cancer of the oral cavity. His arguments against elective neck dissection (END) were purely of oncologic safety and not about functional consequences.

Ultimately, Dr Martin realized that the RND was too “radical” a technique for elective use, at least for cancer of the oral cavity. It is interesting to note that Dr Martin was quoted as saying, “If you are in the neck for any reason, a neck dissection should be seriously considered.” The morbidity associated with RND has been a strong argument in the armamentarium of the proponents of the END. While few have challenged the effectiveness of the RND in the treatment of obvious cervical lymph node metastasis, the driving force away from RND has been the obvious functional and cosmetic deformities that the patient sustains as a result of this operation (Figure 3).

Conley in New York City. Dr Conley was an otolaryngologist by training who had spent 5 years in the Army Medical Corps doing plastic and reconstructive surgery. When he was discharged from the Army at the end of World War II, he became associated in practice with Dr George Pack of Memorial Hospital. Dr Pack was a highly skilled head and neck surgeon who taught Dr Conley about extirpative surgery of the head and neck. When Dr Myers became chairman of the Department of Otolaryngology at the University of Pittsburgh School of Medicine, Pittsburgh, Pa, in late 1972, he carried along with him the Conley–Memorial Hospital concept of the RND as the treatment of choice for metastasis of the cervical lymph nodes, and it remained the standard of care through the 1970s.

Until 1967, when Bocca and Pignataro10 published their work on a more conservative method of neck dissection, the END was the RND. Thus, those who opted to perform neck dissections only on the N-positive neck were using the concept of “watchful waiting” or “observation” for the N0 neck and salvage surgery in those patients who later developed a mass in the neck. At the University of Pittsburgh in the 1970s, this was the approach for most patients with squamous cell carcinoma of the head and neck (SCCHN).11 The University of Pittsburgh surgeons soon learned, however, as others did, that the morbidity associated with the RND could not be underestimated.12 We also all learned that some of the patients in the watchful waiting group presented later with inoperable cancer in the neck.

Another reason that RND continued to be the treatment of choice was concern over the poor prognosis associated with extracapsular spread of cancer (ECS) in cervical lymph nodes. In 1979, Dr Gordon Snow presented the findings of his group13 in Amsterdam, the Netherlands, that ECS in cervical lymph node metastasis carried a very poor prognosis based on regional recurrence and distant metastasis. Until that time, the surgeons at the University of Pittsburgh had recognized soft tissue invasion associated with lymph node metastasis, but usually only in patients who had massive fixed lymph nodes with invasion of soft tissue. However, Snow et al14 indicated that ECS could be found in lymph nodes smaller than 1 cm.14 This information was very important and in large part validated the work of Cachin15 at the Institut Gustav-Roussy, Villejuif, France.

In 1979, the senior author, in cooperation with head and neck pathologist Dr Leon Barnes, instituted a policy at the University of Pittsburgh that all pathology reports note the presence or absence of ECS, since Dr Snow and his colleagues13 had reported that those patients treated with radiation therapy did better as a group than those without ECS. To validate these observations, Johnson et al16 carried out a study, published in 1981, called “The Extracapsular Spread of Tumors in Cervical Lymph Node Metastasis.” In the specimens from 177 RNDs reviewed retrospectively, those researchers found no substantial difference in survivorship between patients who had no metastasis in the cervical lymph nodes and a second group of patients who had metastasis confined to the lymph nodes. However, the 2-year survivorship in patients with ECS was considerably lower than both of these groups. This article16 was the first in the United States to call attention to the poor prognosis associated with ECS in cervical lymph nodes.

A subsequent study on ECS published in 1985 defined the incidence and prognostic significance of ECS in cervical lymph nodes.17 In this series, 371 RNDs from 349 patients were evaluated, and again it was demonstrated that patients with ECS had a marked reduction in survival when compared with a cohort of patients with similarly staged disease when metastasis was confined to the lymph nodes. The patients with cancer confined to the lymph nodes had survival rates similar to patients without cervical metastasis. The data indicated that the mean disease-free interval between surgical therapy and the development of recurrent disease was less than 18 months in patients with ECS. This indicated that patients with ECS had a higher incidence of recurrence and a reduced disease-free survival. The original observation that ECS was an indicator of poor prognosis17 was thus supported.18 These findings made our surgeons reluctant to do less than an RND because of the high rate of regional recurrence.

Further evidence about ECS came from Dr Yves Cachin and his colleagues.19 In 601 cases of carcinoma of the upper aerodigestive tract, there was a 3-year survivorship in 65% of patients who had no evidence of metastasis to the lymph nodes. In contrast, patients with carcinoma limited to the lymph nodes had a 33% survivorship, while patients with ECS experienced a 15% survivorship. Extracapsular spread was found in 65% of patients with cervical metastasis who had been judged N0 clinically and 75% of patients with nodes larger than 3 cm in diameter who had ECS.19 On the basis of their study, Cachin et al19 suggested that a more aggressive approach to the clinically negative neck might be warranted.

More recent work by Vaidya et al20 summarized the current thinking and pointed out these salient findings:

- The rate of disease recurrence increases when the initial pathology findings show ECS in the lymph nodes of the neck.
- The presence of ECS also suggests that a recurrence of the cancer is more likely to involve distant metastatic sites.
• Pathologic staging of neck disease does not seem to significantly alter the rate of local-regional recurrence in the adequately treated neck.
• Local-regional treatment failure more commonly presents as a recurrence in the neck rather than the primary site.
• The most common site of distant metastasis is the lungs.

The senior author and the physicians at the University of Pittsburgh in the early 1980s performed surgery followed by radiation therapy in all patients with ECS. However, they found that their patients with ECS treated with combined surgery and radiation therapy, as a group, still had a poor outcome. As a result of these observations, a program of adjuvant chemotherapy was instituted. As part of a prospective, nonrandomized study, patients with ECS who had been treated with surgery and radiation were offered outpatient chemotherapy consisting of 18 courses of methotrexate and 5-fluorouracil. The findings were encouraging in that the determinate 5-year, disease-free survival was 54% compared with 17% for those who did not have chemotherapy. Further results on the use of chemotherapy and radiation treatment in a larger but similar cohort of patients was recently reported in Cancer. At the University of Pittsburgh, we have continued the application of chemotherapy to this high-risk group of patients but with a change in the protocol to include concomitant postoperative chemoradiation using carboplatin.

While we recognized at that time the morbidity of a classic RND, we were willing to accept the deformities and decreased functionality associated with it because it was the gold standard for patients with identifiable cervical lymph node metastasis. We also continued to use it because of our preoccupation with the “new” information about the poor prognosis associated with ECS. The RND did not seem acceptable, however, for patients with an N0 neck, and most particularly for those who had a lesion in the midline and faced the possibility of a bilateral RND.

It is unfortunate that the work of Cachin and Bocca and Pignataro, who were doing ENDS, was not recognized or accepted in the United States in the 1970s. Dr Yves Cachin and his surgical group from the Institut Gustave-Roussy addressed the issue of whether the early removal of the nodes confers a survival benefit on the patient, and they established general principles in the treatment of cervical lymph node metastasis:
• The treatment of the cervical lymph nodes is inseparable from that of the primary tumor.
• The treatment of cervical lymph nodes depends on the volume and character of the adenopathy.
• The choice of surgical technique must be made in accordance with precise rules.
• The choice of radiotherapy techniques must also obey stringent rules; in this regard, a distinction must be made between cases with and without palpable adenopathy.

Pallpable Adenopathy Present

If the primary tumor is treated surgically, the lymph nodes are treated by neck dissection, possibly followed by postoperative radiotherapy, depending on the results of the histologic examination of the operative specimen. If the primary tumor is treated by radium implants, the lymph nodes are handled in the same manner. If the primary tumor is treated by external radiation, the lymph nodes are likewise treated by radiotherapy, with surgery reserved for those cases with residual palpable disease present after primary therapy.

No Palpable Adenopathy

One must first determine whether it is necessary to treat the cervical lymph nodes systematically or if it is possible to await the appearance of palpable adenopathy. The results of a therapeutic trial carried out at the Institut Gustave-Roussy from 1967 to 1973 in a group of patients with cancer of the oral cavity compared systematic performance of neck dissection with therapeutic abstention (with later dissection performed in the cases of eventual appearance of palpable lymph adenopathy). A study of these results demonstrates the effectiveness of systematically performed neck dissection, although the difference in the 5-year survival of the 2 groups (about 10% higher in the treated group) is not quite statistically significant. The difference is probably the result of the more frequent evolution of the lymph node invasion to ECS allowed by the delay engendered by waiting for palpable nodes to develop.

Cachin went on to say that the classic (total) RND should be used for N3 nodes or N2 and N1 nodes larger than 2 cm in diameter, whereas functional neck dissection is reserved for N0, N1, and N2 nodes smaller than 2 cm in diameter. The functional neck dissection does according to these indications offers the same degree of anatomic excision as the classic dissection in that it removes all the lymphatic and adipose tissue of the neck within the aponeurosis. He made 2 points:
• Functional neck dissection should be performed only by a skilled head and neck surgeon.
• It should be followed, as is the classic dissection, by postoperative radiotherapy as indicated by the histologic aspect of the operative specimen.

Vandenbrouck et al conducted a randomized clinical trial to look at elective vs therapeutic RND in epidermoid carcinoma of the oral cavity. This study was carried out in patients with squamous cell carcinoma of the oral cavity who were treated with brachytherapy. Two options were proposed by the authors: (1) perform END, and (2) wait until there is evidence of disease and then carry out a delayed therapeutic dissection. The authors note that proponents of the first method cited the high rate of histologically positive nodes (36%-49%) in clinically disease-free necks found at elective surgery and the often rapid growth of the nodes when they ultimately appear. Opponents believed that RND was useless or even harmful when histologic involvement was not evident, causing pain, shoulder disability, and long-term adverse cosmetic effects. Furthermore, acute nodal growth was not often observed, and the value of an elective operative procedure designed to increase the survival rate was never proven.
Another interesting observation of Vandenbroucke et al.\textsuperscript{23} was that when they looked at the level of histologic involvement, it was impossible to predict the absence of growth in nodes in the inferior aspect of the neck by sampling only the jugulodigastric area. This important observation indicated that the histologic involvement rate was the same for patients with and without END, but that the incidence of ECS was quite different, occurring more frequently in the group without END. The difference in ECS incidence was nearly statistically significant, considering the number of involved cases. Extracapsular spread had been demonstrated to be an ominous prognostic sign; therefore, means to a better prognosis should be sought for patients undergoing END.

However, even though the 2 main prognostic factors, nodal involvement and ECS, were taken into account, the authors\textsuperscript{23} were unable to detect a difference between the survival curves in the 2 groups of patients. Over the years, certain doubts have been raised about this study, such as sample size or failure to control for certain factors such as positive margins in the primary site. Unfortunately, this flawed study is still often cited by those opposed to the concept of systematic use of elective END.

**THE ERA OF THE MODIFIED RND**

The transition into the era of the modified RND (MRND) was driven by the growing understanding from many of the studies already cited that the N0 neck was often pN positive. When the spinal accessory nerve was spared, the patients had fewer problems with pain and decreased functionality, while the oncologic outcome was not changed.\textsuperscript{20} Lingeman et al.\textsuperscript{27} reported that of 98 patients with a clinically negative neck who underwent MRND, none had a regional recurrence. In 1980, Molinari et al.\textsuperscript{28} also indicated a low regional recurrence rate in patients with cancer of the larynx who underwent MRND.

In 1985, Byers\textsuperscript{29} reported that during the 1960s, Ballantyne and others at The University of Texas M. D. Anderson Cancer Center and Tumor Institute at Houston had begun to explore the possibilities of a tailored (less than radical) resection in which the groups of nodes at highest risk for metastatic involvement were removed, and nerves, vessels, and muscles not grossly invaded with tumor were preserved. Dr Byers\textsuperscript{30} suggested that if multiple unilateral or bilateral positive nodes were discovered on pathologic examination, or extracapsular nodal spread identified, postoperative radiation therapy should be added to the treatment of the neck. The improvement in regional control set the stage for a conceptual revolution in the surgical treatment of cervical metastases from SCCHN.

Subsequent studies confirmed these good control rates and improved functional outcomes.\textsuperscript{30,32} In the 1980s, the senior author and his colleagues began to use MRND type 1 electively, preserving only the spinal accessory nerve for any primary SCCHN thought to have a significant metastatic rate. Excellent results were achieved with primary control (eg, in the oral cavity), which was attributed to the systematic use of frozen sections during the surgical procedure.\textsuperscript{33} McGuirt et al.\textsuperscript{34} did a retrospective analysis of 129 patients with squamous cell carcinoma of the floor of the mouth with an N0 neck treated between 1973 and 1992 with a mean follow-up of 6 years. Occult disease was detected in 23\% of the patients who underwent END (MRND). High metastatic rates of early oral cavity cancer had also been published in multiple studies.\textsuperscript{35-37} Recurrence in the neck occurred in 36\% of 103 patients who did not undergo END, whereas the determinate survival at 3 years was 100\% for patients with occult disease who underwent END. Eighty-five percent of the patients who received no initial treatment of the neck were cured.

Before the senior author’s surgical team began to perform ENDS, some of their patients under the watchful waiting scheme returned with an inoperable cancer in the neck. Disappointing 3-year survival results also occurred in those patients in the watchful waiting group who underwent surgical salvage for recurrence in the neck. Although the first report from this group of researchers\textsuperscript{39} showed a very small number of electively treated necks, several teams had already reported improved survival with END.\textsuperscript{38-40} Knowing that the occult rate was even worse in higher stages and that stage alone was not the only predictor of metastasis, the senior author and his colleagues at the University of Pittsburgh included elective MRND in their treatment regimen for the N0 neck. Moreover, with decreased morbidity they were able to improve results with contralateral metastases, such as in supraglottic cancer, by performing elective bilateral neck dissections.\textsuperscript{41} Ultimately, improved survival in these patients increased confidence levels in this treatment strategy.\textsuperscript{41-44} Based on numerous studies, head and neck surgeons began performing elective MRND for patients with an occult metastasis rate of 20\% or higher for any SCCHN.\textsuperscript{34,45,46}

Spiro and Strong\textsuperscript{46} reported a series of 563 patients who were treated for invasive epidermoid carcinoma of the tongue between 1957 and 1963. Of this group, 185 patients had partial glossectomy alone as the initial definitive treatment. Seventy-one (38.4\%) of these 185 patients who developed cervical metastasis also had recurrence in the primary site in the tongue. An RND was subsequently performed in most of the individuals in whom metastasis developed. Two of the patients had unresectable disease in the neck. The authors concluded that cervical metastasis was successfully treated in only 35\% of the patients. More than 60\% of the patients who developed metastasis died of uncontrolled neck disease.

In the 1980s, the use of computed tomography (CT) and later magnetic resonance imaging (MRI) improved the accuracy of preoperative assessment of patients with SCCHN. These technologies further validated the initial use of END because now more patients were being diagnosed with N-positive disease than had been the case with physical examination alone.\textsuperscript{47-49} However, while studies have shown that CT scans can help determine more accurately when a tumor is is N positive, truly pN0 necks cannot be accurately identified.\textsuperscript{50} For instance, one report showed that 50\% of metastatic lymph nodes are smaller than 5 mm, well under the size criteria for radiographic identification.\textsuperscript{51}

The initial driving force for adopting MRND and END was to reduce or eliminate the morbidity associ-
ated with RND and to decrease the rate of recurrence in the neck, and we have witnessed improved functional outcome with these procedures, particularly a decrease in sensory deficits and shoulder dysfunction. However, during the 1980s, the utility of END for staging began to be recognized. Pathologic examination of lymph nodes might yield an untapped resource for prognostic and potentially therapeutic information. It was already reputed in 1959 that when more than 1 lymph node harbored metastatic disease, the survival rate was dramatically reduced. Johnson and others, including the senior author, had demonstrated that ECS was also known to have significant prognostic ramifications. It was frequently found in lymph nodes smaller than 1 cm, thereby being undetectable by imaging. It was later determined that the disease-free period between treatment and the development of recurrent disease was also markedly decreased in patients with ECS. Based on these studies, the utility of adjuvant therapies like radiation and chemotherapy came to be better understood. Other groups confirmed the use of adjuvant therapy and demonstrated that in necks found to harbor advanced occult disease, postoperative radiation therapy decreased recurrence rates after END.

THE ERA OF THE SND

Lest we think that the issue of comprehensive vs partial neck dissection is a new one, Dr George Crile, who is considered to be the first to describe RND, also described in 1906 the value of partial neck dissections. Dr Crile categorized his group of cases into those that involved enlarged lymph nodes and those that did not:

The enlarged lymph nodes often proved to be metastatic cancer, although this was not always correct. In this group, the lymphatic-bearing tissue was widely excised (the entire lymphatic-bearing tissue of that side) because once the lymph stream is choked by metastasis, further dissemination may travel in any direction. When there were no palpable glands only the lymphatic drainage area was excised. . . . We have seen most encouraging results not only in the immediate recovery rate but in permanent cure.

Bocca and Pignataro in 1967 and Bocca again in 1975 described the use of conservation neck dissection. This procedure involved dissection of the fascial space in the neck, where the lymphatic system was contained, without removal of other anatomic structures that bear no direct relationship to the lymph nodes, although they are closely adjacent to them. This work was based on the surgical anatomic description of the fascial compartments in the neck by Dr Oswaldo Suarez of Spain as quoted by Bocca and Pignataro. They noted that a conservation neck dissection may also be performed in the neck dissection should be added to the surgical treatment of supraglottic carcinoma for the control of regional disease.

Around 1990 (the time of the study by Lutz et al), relying on the evolving literature in the field, we had begun to use the SND in certain cases at the University of Pittsburgh. Patients with supraglottic cancer were good candidates because they have a high incidence of bilateral lymph node metastasis. Subsequently, Weber et al studied the impact of bilateral SND, either alone or in combination with a therapeutic neck dissection in the case of an N-positive neck. We determined that there was a substantial decrease in the rate of recurrence using bilateral neck dissection. In a subsequent study, these same researchers indicated that bilateral neck dissection did not result in more complications for the patient or greater use of resources.

One of the landmark articles in the area of SND is the work of Spiro and his colleagues from the Memorial Sloan-Kettering Cancer Center, New York, NY. They found that supraomohyoid neck dissection, which had been used with increasing frequency in their hospital since 1980 for patients with cancer of the oral cavity, currently accounted for about 25% of the neck dissections carried out at the time of their research. They performed a neck dissection on 115 patients that included the submental, submandibular, and upper and middle lymphatic drainage of various sites in the head and neck. These studies have since been confirmed clinically by the analysis of cervical lymph nodes at risk in patients with SCCHN. The type of SND is based on the observations of Shah, who studied 1119 RNDs and analyzed the lymph node levels at highest risk for metastasis from a variety of anatomic sites. This information has been invaluable in helping surgeons to determine exactly which lymph node groups needed to be removed based on the site of the primary cancer.
deep jugular nodes (levels I, II, and III, respectively). The sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve were spared. Most, but not all, of the patients operated on had squamous cell carcinoma. The authors found that occult nodal metastases were present in 31% of the necks that underwent an elective supraomohyoid neck dissection for squamous cell carcinoma of the oral cavity. This is comparable to the incidence of occult nodal disease that has been reported in patients with oral cavity cancer.29 Of the total of 64 pN0 necks dissected, 3 patients (5%) experienced recurrence in the ipsilateral neck. One of these was in the area of the prior neck dissection, and 2 were outside the operative field. Microscopic nodal disease was found in 26 of 83 supraomohyoid neck dissections performed electively, including 3 specimens that demonstrated ECS. Twenty of these patients were treated with postoperative radiation therapy.

When microscopic or occult nodal disease is discovered after supraomohyoid neck dissection, treatment options include completion neck dissection, postoperative radiation therapy, or observation. Spiro et al61 were reluctant to perform a completion RND as a second procedure when microscopic nodal involvement was reported in permanent sections. They achieved an 86% control rate of neck disease through postoperative radiation therapy, and they quote Byers,28 who reported 100% control of neck metastasis in patients with pathologically confirmed N1 disease who had undergone supraomohyoid neck dissection and postoperative radiotherapy. Byers’ conclusions were somewhat different in that he advocated supraomohyoid neck dissection alone as adequate treatment for pathologic N1 disease that did not show any evidence of ECS.

Those who argue against SND note the lack of boundaries between anatomic sites and point out that surgeons routinely convert to an MRND when they encounter positive lymph nodes. Using various studies Leemans and Snow62 have calculated a statistically improved control rate for MRNDs compared with SNDs. In addition, skip lesions may occur during lymphatic spread of SCCHN.63 The concern is that because studies advocating SNDs are nonrandomized and retrospective, they might not demonstrate the true metastatic potential of SCCHN. If this is the case, SND might be a less than adequate prognostic and therapeutic tool.

The reality of treatment of patients who have squamous cell carcinoma with an N0 neck is that there are 2 options: perform END or wait until there is evidence of disease and then carry out a therapeutic neck dissection. The proponents of the SND have agreed that ultimately only a properly designed multi-institutional study would answer these important criticisms. So far these types of studies confirm the efficacy of SND, at least in laryngeal and hypopharyngeal cancers.64,65 A prospective trial65 compared the results of END vs type 3 MRND in 132 patients with cancer of the larynx. The researchers concluded that the rate of recurrence in the neck and 5-year overall survival were similar in both groups, confirming the efficacy of SND in elective treatment of the N0 neck not only oncologically but also with preservation of form and function.

In terms of converting to a more extensive type of neck dissection intraoperatively, Rassekh et al66 have shown that surgeons are poor predictors of nodal positivity, even intraoperatively, unless they can rely on the results of frozen sections. Furthermore, SND proponents point out that the therapeutic role of the MRND is limited in that patients still require postoperative irradiation if extensive occult positive findings or ECS is encountered.20 In the case of SND, if the most at-risk nodes demonstrate adverse histologic findings such as multiple metastatic nodes or ECS, these same patients ultimately will receive postoperative radiation therapy.67

Despite the absence of a multi-institutional, prospective, well-controlled clinical trial, information has been accumulated that verifies the effectiveness of END in the treatment of SCCHN. Yuen et al,68 at the University of Hong Kong, studied a group of 63 patients with cancer of the tongue. Their department policy had been surgical resection of the cancer of the tongue together with watchful waiting in the management of patients with an N0 neck, with surgical salvage used for recurrence in the neck. In the 30 patients with an N0 neck who had no END, the regional recurrence rate was 47%, and eventually 23% died of cancer-related regional recurrence. Later, the systematic use of END reduced the regional recurrence rate to 9% and also significantly reduced the mortality related to regional recurrence to 3%. Elective neck dissection also increased the 5-year disease-free survival rate to 86% compared with 55% under watchful waiting. No significant difference in outcome was noted between the elective RND, which was used early in the study, and SND, including levels I, II, and III, which has been performed since May 1990. The 5-year disease-free survival rate was 55% for the watchful waiting group and 86% for the END group. Another very important outcome of this study was that only 50% of the cases in the watchful waiting group who had recurrence in the neck were successfully salvaged.

Our department began to use SND for the N0 neck in the 1990s. Our researchers assessed the utility of this procedure by retrospectively analyzing SND data and comparing the results with the department’s experiences in the 1970s and 1980s with RND and MRND. Through the use of SND, surgeons were able to detect occult metastases in approximately 90% of patients, which correlated well with the results from other groups.69 Our researchers further investigated the effectiveness of SND and found, as others have reported, that when properly used, it is as effective as the MRND.69,70-73

In 1997, Pitman et al69 compared SND with RND for effective management of the clinically negative neck in SCCHN. This study included 280 patients treated with 322 RNDs between 1974 and 1989, and 114 patients treated with 168 SNDs between January 1990 and March 1994. The overall regional recurrence rate for RND was 5.8%, which was not statistically different from the regional recurrence rate of 3.5% in the SND population. These results indicate that SND is as effective as RND for treating the N0 neck.

In a study done in our department,74 none of the patients with occult-positive, ECS-negative nodes treated with SND had regional recurrence. We showed that ECS in
occult metastasis influences the rate of distant metastasis as the sole site of recurrence, and a trend exists toward decreased survival compared with pathologically positive lymph nodes without ECS. Additionally, ECS was present in at least 33% of patients with occult metastases.\textsuperscript{74}

Medina and Byers\textsuperscript{75} recommended the use of postoperative radiation therapy for patients with 3 or more positive nodes without ECS. Ambrosch et al\textsuperscript{76} strongly recommended postoperative radiation therapy in patients with at least 2 positive lymph nodes. They stated, however, that survival rates were similar with or without postoperative radiotherapy in the patients with pN-positive necks. They further stated that this result needs to be interpreted with caution in view of an inherent selection bias.

Hosal et al\textsuperscript{77} studied the efficacy of SND in the management of the clinically N0 neck. The results of 300 neck dissections performed on 210 patients with an N0 neck between January 1, 1990, and June 30, 1996, were studied retrospectively. Thirty-three percent of the patients were node positive on pathologic examination. In those necks with positive nodes, 24% had ECS. The median follow-up time was 41 months. Recurrent disease developed in the dissected neck of 11 patients (4%), twice outside the dissected field. Regional recurrence developed in 3% of patients without ECS and 18% of patients with ECS. Of importance was that patients having more than 2 metastatic lymph nodes had a higher incidence of recurrent disease than patients with carcinoma limited to 1 or 2 lymph nodes. We now systematically include radiation therapy as part of our program in patients who have more than 2 positive lymph nodes without ECS, and all patients with ECS are treated with chemoradiation. Hosal et al\textsuperscript{77} concluded that SND is effective for controlling neck disease and serves to detect patients who require adjuvant therapy.

Alvi and Johnson\textsuperscript{78} demonstrated that of 103 patients with an N0 neck who had an END, occult metastasis was observed in 34% of the patients, and ECS was present in 49% of patients in this group who were pN positive. Of this group, 68 patients had histologically negative nodes, of whom 56 (82%) were free of disease. Of the patients with ECS, only 5 (31%) of 16 were free of disease. This is in contrast to patients with metastasis confined to the lymph nodes, of whom 9 (47%) of 19 were free of disease. Statistical analysis of these data shows that for this sample size, this difference is significant. The presence of ECS appears to predict a worse outcome in patients with occult cervical metastasis.

Myers et al\textsuperscript{79} at the M. D. Anderson Cancer Center analyzed a group of 64 cases of squamous cell carcinoma of the tongue in an age group younger than 39 years. Whether the patients were initially treated elsewhere or at the M. D. Anderson Cancer Center, those who had a neck dissection as part of the initial treatment had a better outcome. Three- and 5-year survival rates were 81% and 72%, respectively, in patients who had a neck dissection and 44% and 22%, respectively in patients whose necks were not dissected. The other important factor affecting survival was adequate resection of the primary cancer.

Kowalski et al\textsuperscript{80} studied a series of 513 consecutive cases of squamous cell carcinoma of the oral cavity. There was a poorer prognosis associated with patients who did not have END and were managed instead with watchful waiting. Importantly, among the cases that had metastases at follow-up, 50% were not candidates for salvage treatment.

Kligerman et al\textsuperscript{81} examined a cohort of 67 patients with T1/T2 squamous cell carcinoma of the tongue and floor of the mouth. They focused on the importance of determining the thickness of the tumor and the presence or absence of END in these cases. Patients treated by supramohyoid END at the time of their surgery had fewer recurrences in the neck and a better survival rate than those who had undergone resection of the primary tumor alone. These authors used radiation in a small number of patients in this group. Most importantly, the authors found a poor salvage rate among patients who have not undergone END and who develop cervical metastasis after resection of the primary tumor. The salvage rates after neck recurrence in these patients were low, and the authors suggested that this might be owing to the large number of patients from lower socioeconomic levels who had returned to follow-up with already advanced recurrence in the neck.

Fritz et al\textsuperscript{82} looked at the recurrence rate after selective neck dissection in the N0 neck treated with radiation and concluded that SND in previously irradiated patients with recurrent primary disease but clinically negative necks resulted in excellent tumor control in the neck. The usual patterns of nodal spread did not appear to be significantly altered with primary site recurrence after radiation therapy. The presence of more than 2 positive nodes in the neck specimen correlated with poor prognosis.

More recently, the senior author has begun to use the SND to treat the N-positive neck without fixed lymphadenopathy. In selected cases, in association with radiation therapy, we have found it to be an effective way of managing patients with pN-positive disease. Our rationale is that the management of occult N-positive necks and that of necks found on physical examination or CT to be N positive should only differ in the sensitivity of the preoperative devices used for assessment. Also our department has demonstrated that the SND alone is adequate treatment of the neck for patients with 2 or fewer positive occult lymph nodes.\textsuperscript{83} Other studies evaluating the SND in a field that has been prophylactically treated with radiation after recurrence of the primary tumor or even for salvage therapy also show promise.\textsuperscript{84,85} The recurrences in what were reported as N0 necks may be related to micrometastasis that cannot be detected on routine pathologic evaluation.

While studies investigating the use of SND in clinically N-positive necks are currently limited, several recent articles report excellent results.\textsuperscript{86,87} Additionally, Chepeha et al\textsuperscript{88} recently reported the use of the SND for the treatment of clinically detectable metastasis (N positive) in patients with SCCHN. Their objectives were to determine the outcome in a cohort of patients whose primary site was controlled, who had clinically detectable cervical metastasis smaller than 3 cm (N1), and who were...
treated with SND for squamous cell carcinoma. Of the 52 patients who had 58 SNDs for cervical metastasis, 26 had a clinically negative neck (pN0) and 26 patients had a clinically positive neck (pN1). Indications for postoperative radiation therapy were ECS, more than 2 positive lymph nodes, and T3 or T4 primary tumors. The regional control rate with SND was comparable to control rates obtained with MRND. In this cohort, 94% of the patients who had been treated with SND for squamous cell carcinoma of the upper aerodigestive tract and cervical metastasis smaller than 3 cm remained disease free in the neck with the primary site controlled.

Kolli et al\textsuperscript{41} studied the role of supraomohyoid neck dissection in patients with clinically positive nodes (pN+). The group was composed of 69 patients: 30 with clinically negative nodes and 39 with clinically positive nodes in the neck. Locoregional control rates were 88% for pN0 compared with 71% for pN positive. Adjuvant radiation therapy significantly improved regional control in patients with pathologically positive nodes but not in those with N0 disease. The supraomohyoid neck dissection alone in patients with pathologically positive nodes in the neck proved inadequate therapy for regional control without postoperative radiation therapy. With radiation therapy, this procedure can achieve regional control comparable to that of comprehensive neck dissection and postoperative radiation therapy.

Pellitteri et al\textsuperscript{82} looked at the expanded application of neck dissection with regard to nodal status. The authors questioned whether SND is oncologically safe for patients in whom clinical assessment of nodal disease is not more extensive than N1. They studied a cohort of 92 patients who had received SND as part of their initial therapy for cancer of the head and neck. The primary site was controlled following initial therapy in each case. Supraomohyoid and lateral neck dissections were used, depending on the primary site. All patients with histopathologically proven positive nodes at multiple levels or ECS received postoperative radiation therapy. The recurrence rate for necks staged pN0 was 1 of 26. In the necks staged N1, 1 of 10 experienced recurrence. The authors concluded that SND represents an acceptable modality for management of the N0 and selected N1 necks in the treatment of squamous cell carcinoma. The application of SND in the management of more advanced nodal disease, N2a, N2b, and N3, has not been studied.

We believe that SND in the N0 neck with SCCHN from most anatomic sites in the head and neck is an indispensable technique for diagnosis and treatment. A critical mass of information verifies the efficacy of this procedure. We also believe that enough evidence has been developed to demonstrate the efficacy of SND in selected patients with an N-positive node.

THE NEXT ERA: THE “SUPERSELECTIVE” NECK DISSECTION AND BEYOND SURGERY

In the course of trying to be oncologically safe and to decrease the morbidity of surgery, researchers have devised a number of novel procedures. For instance, Dulguerov et al\textsuperscript{84} in Geneva, Switzerland, have been investigating the use of endoscopic neck dissections. Although this technique is challenging, once mastered it gives excellent visualization of the surgical field and should decrease the morbidity of surgery.

A number of groups have been looking at ways to perform a type of "superselective" neck dissection.\textsuperscript{85-87} One novel method is sentinel lymph node mapping. In this approach, analysis of a biopsy specimen of the sentinel or first-echelon lymph nodes may help the surgeon decide whether a neck dissection should be performed. Some groups using a radiolabeling technique have found that they can adequately predict the presence of occult metastases on the basis of a sentinel lymph node.\textsuperscript{88,89} In one study, the authors accurately defined the sentinel lymph node by a radiolabeling technique and effectively performed a biopsy on this node using ultrasound-guided fine-needle aspiration.\textsuperscript{90} Other studies demonstrate that the sentinel lymph node may be multiple and in unexpected locations, which might change the type of neck dissection.\textsuperscript{91,92} Using other techniques, members of our group have demonstrated that sentinel lymph node mapping may not yet be accurate enough for use in determining whether to perform a neck dissection, and currently this procedure remains controversial.\textsuperscript{93}

Careful examination of a particular lymph node may increase the utility of sentinel node mapping.\textsuperscript{93-95} Ambrosch et al\textsuperscript{79} analyzed a series of 76 neck dissection specimens from patients originally staged as pN0. The authors used serial sectioning in 10-µm intervals, hematoxylin-eosin staining, and immunostaining with an antibody against cytokeratin and revealed 8 micrometastases in 6 specimens from 6 patients resulting in upstaging. Although common use of serial sectioning is impractical except under specific situations, the END might be therapeutic in more necks than previously shown. Certainly in the case of examination of a sentinel lymph node, serial examination would be paramount.

Although the light microscope continues to be the "gold standard" by which tumors are diagnosed, we are at the dawn of a new era in which molecular-genetic studies may become the new standard of care for patients with cancer of the head and neck. Newer cellular and molecular biology techniques will also increase the utility of lymph node analysis.\textsuperscript{96,97} With these new technologies, we may learn that the true micrometastatic rate is even higher than previously thought. At the University of Pittsburgh, reverse transcriptase–polymerase chain reaction (RT-PCR) and Taqman quantitative RT-PCR have been shown to improve our ability to detect micrometastatic disease.\textsuperscript{88,98} With newly defined overexpressed molecules in SCCHN being discovered rapidly, these techniques have been used to identify micrometastatic cancer in patients with SCCHN, and these techniques may help physicians decide which patients are at risk for local or even distant metastases.\textsuperscript{101-103}

Russolo et al\textsuperscript{104} studied the importance of several tumor factors related to predicting the presence of occult metastases in patients with squamous cell carcinoma of
the oral cavity. They conclude that there is a significant correlation between invasive-cell grading equal to or greater than 13 (range, 5-20) and the presence of occult metastases \((P = .002)\). The authors state that the invasive-cell grading parameter correctly identified 9 of 10 patients with N-positive disease and could have reduced overtreatment from 65.5\% to 17.2\% in histopathologically positive necks. The authors also studied the relevance of tumor thickness as a means of identification for local-regional occult metastases. They note that 10 of the patients with T1/T2 cancers of the oral cavity (34.4\%) had occult metastases, and 6 of these patients had ECS. They also indicate that patients with a clinically N0 neck who do not undergo neck dissection but who later develop metastases of the neck, albeit cured for tumor and followed up correctly, have, on average, a greatly reduced chance of survival compared with patients classified as N positive who undergo END. The authors conclude that the invasive-cell grading parameter enables correct identification of 90\% of patients with occult metastases and T1/T2 oral cancer. The use of it could greatly reduce overtreatment from 65.5\% to 17.2\% in patients classified as N0.

Other modalities for lymph node analysis being tested include combining biological assays and imaging. For instance, combining positron emission tomography and CT scanning may increase the specificity of lymph node assessment (Figure 4).105,106 In addition, it has been shown that central necrosis even in very small cervical lymph nodes may be a sign of metastasis.48 New techniques to define cell death now exist for a variety of imaging techniques and may have potential in evaluating metastatic SCCHN.107,108

There is considerable attention being paid to the advancement of neoadjuvant therapies for the treatment of SCCHN, particularly for the prevention of regional or distant recurrence. Trials using various gene therapies are already being conducted.109,110 One approach is the development of vaccines through the manipulation of cytoxic T cells.111 Some of these adoptive cell therapies rely on the acquisition of tumor cells. Through experience in our department, we have found that the best sterile supply of tumor specimens is from the neck. With an adequate quantity of cancer cells we are able to grow these tumors in culture. These cultured tumor cells can then be used to (1) generate various neoadjuvant therapies, (2) test for expression of various genes and proteins, and (3) give prognostic information. They may also be used in the further study of SCCHN.112,113

In conclusion, our standard practice at the University of Pittsburgh of performing elective SNDs for pa-

![Figure 4. Positron emission/computed tomographic images of a previously unknown primary tumor with metastasis to the neck in a 70-year-old man. The images were taken after a biopsy of the right neck mass proved positive for poorly differentiated squamous cell carcinoma. A, Anteroposterior view demonstrating the primary cancer in the base of the tongue with metastasis to the neck. B, Cancer in the base of the tongue (arrow) with metastasis to the neck (brightest area).](https://www.archoto.com)
Patient with SCCN and an N0 neck evolved over years of trial and error as well as many clinical investigations to prove the efficacy of this plan of management. In recent years, others have also documented very positive experiences with this approach. We now believe that not doing an SND in patients with squamous cell carcinoma of most sites in the upper aerodigestive tract may deprive the patient of an opportunity to be cured. We and others have also demonstrated the efficacy of SND in selected patients with an N-positive neck.

Our hope is that one day clinicians and scientists will obviate the need for surgery with newer molecular diagnostic and therapeutic approaches. Until that time, we encourage surgeons to adopt the systematic use of SND in most anatomic sites in the head and neck for the treatment of selected patients with SCCN.

Accepted for publication August 9, 2002.

This article was presented as the Hayes Martin Lecture at the annual meeting of the American Head and Neck Society, Boca Raton, Fla, May 12, 2002.

Reprints not available from the authors.

REFERENCES


