

Advances in the care of head and neck cancer patients at Baylor University Medical Center

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Editor's note: The Society of Baylor Surgeons held a meeting on August 10 to 11, 2007: "Advances in Surgery and Surgical Education: The Past 20 Years," in honor of Dr. Ronald C. Jones' 20th year as chairman of the Department of Surgery at Baylor University Medical Center. This society was founded in 1981 by Dr. Robert Sparkman, past chief of the department, as a way to reunite former Baylor surgery residents and provide continuing surgical education for residents and members of the medical staff.

Under the direction of program director John Preskitt, MD, the 2007 CME-accredited meeting included presentations from four prominent guest speakers: Edward M. Copeland, MD, president of the American College of Surgeons; R. Scott Jones, MD, professor and chairman of surgery emeritus for the University of Virginia Health System; Kirby I. Bland, MD, chairman of the Department of Surgery at the University of Alabama; and Stanley Dudrick, MD, chairman of the Department of Surgery at St. Mary's Hospital, Waterbury, Connecticut. In addition, 12 physicians from Baylor made presentations at this meeting, and some provided summaries, which are reproduced in this issue of *Proceedings*.

We gather here this weekend to pay honor to our chief of surgery, Dr. Ronald C. Jones. Under his leadership, our residency program has attained national stature as the largest private hospital program and one of the best in the United States. Upon the foundation built by Drs. Robert Sparkman and Jesse Thompson, he has taken the department to new heights. We are thankful for his leadership and guidance.

The inexorable march of time through the last 20 years has brought many new and exciting changes in our diagnostic, imaging, and treatment capabilities for patients with head and neck cancer.

In pathology, the fine-needle aspiration biopsy has become routine as clinicians and pathologists have honed their skills in doing the procedure and characterizing the resulting cytology. Immunohistochemical staining has helped make and confirm diagnoses. Characterization of the human genome has allowed microarray techniques to study thousands of genes or gene products on a single slide. Sentinel node biopsy has helped to limit extensive node dissections for selected high-risk patients, sparing most patients the potential morbidity of these dissections.

Imaging techniques have improved with the advent of rapid-acquisition spiral computed tomography (CT), which uses increasing numbers of sensors and slices, allowing for three-dimensional reformatting. Entire scans can be done in the time it used to take for one slice. This technique has been most advantageous for the head and neck cancer patient, who may not be able to lie supine for a long time due to aspiration, secretions, or respiratory compromise. CT angiography and magnetic resonance imaging and angiography have made some intra-arterial studies unnecessary, while giving an excellent view of the vasculature. Positron emission tomography (PET) scanning has made it possible to canvas a patient for metastasis with a single test; when PET is combined with CT scans, localization of metastasis is improved.

Studies of demographics have elucidated some of the causal relationships of these cancers. Studies of the biology of cancers have helped researchers study novel techniques, which have had some very exciting results.

Chemotherapy is improved with new drugs and methods of administration. The introduction of three-dimensional conformal treatment and intensity-modulated radiation therapy has allowed some mucosa and salivary glands to be spared, lessening the problem of xerostomia, dysphagia, and fibrosis. These techniques target the diseased tissue and spare much of the normal structures.

Studies have proven that the modifications of the radical neck dissection are efficacious in properly selected patients. This technique saves many patients from the morbidity of the eleventh nerve palsy seen after accessory nerve resection.

SENTINEL NODE BIOPSY

Historically, the first sentinel node article in the world literature was that of Ernest Gould (1). He presented the paper at the meeting of the James Ewing Society (now the Society of Surgical Oncology) on April 3, 1959. For parotid cancer, the sentinel node is at the tail of the parotid, adjacent to the external jugular vein, and Dr. Gould felt that doing a biopsy of this node would help the surgeon decide whether radical neck dissection

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was necessary. With parotid cancer, this node was often positive, reflecting the nature of the neoplasm in the parotid.

Sentinel node biopsy was described by Cabanas in 1977 (2) for penile cancer, and the procedure was publicized and popularized subsequently by Morton (3, 4) in the early 1990s using the blue dye technique. The use of radionuclide was added by Krag (5) of Vermont. Joseph Kuhn, MD, brought this technique to Baylor University Medical Center (BUMC) in 1995. Shoaib (6) and colleagues at Canniesburn in Glasgow published much of the original work in head and neck sentinel node biopsies for mucosal lesions. They reported that sentinel nodes are found in 97% of patients; 29% are positive for occult metastasis, and 4% of nonsentinel nodes are positive. They used the hematoxylin and eosin stain plus immunohistochemistry for cytokeratins. Sentinel node biopsy in the head and neck is more technically difficult than that for cutaneous malignancies because of the proximity of the primary tumor and the propinquity of the first echelon of nodes, but it can be done well.

THE HEAD AND NECK CANCER PROBLEM

In 2007, according to the American Cancer Society, there will be 45,660 new cases of head and neck cancer and 11,210 deaths (7). These cancers primarily affect men in the sixth and seventh decades of life. Smoking and alcohol are primary risk factors. More than 50% of patients present with advanced-stage disease, and more than 90% of the cancers are squamous cell carcinoma.

But, the situation is improving: the incidence of head and neck squamous carcinoma and the use of tobacco in the population are decreasing. Coincident with this decrease is the increase of thyroid cancers and melanomas.

In 2011, the baby boomers (those born between 1946 and 1964) will begin to turn 65. In 1900, 4% of the population was aged 65 or older. In 2030, 20% will be. Those aged 85 and older are the fastest-growing segment of the population, giving rise to the term “oncogeriatric patient” (8). Over the age of 60, most patients have one chronic illness, and almost a third have three or more; however, the severity rather than the number of conditions is more relevant to medical and surgical decision making (9). Presently, patients over 65 represent 12% of the population and account for approximately 56% of cancer cases and 69% of all cancer deaths (10). These patients have increased costs of treatment and rehabilitation due to their comorbidities and potential for complications during and after treatment.

Head and neck surgeons are faced with many problems. The four leading causes of death in the population aged 60 to 79 are cancer, heart disease, chronic lung disease, and cerebral vascular disease. Taking all age groups into consideration, stroke is the third overall leading cause of death, but in the 69 to 79 age group, chronic lung disease ranks third. The head and neck treatment team will be seeing older and sicker patients due to the population’s increased life expectancy.

HISTORICAL PERSPECTIVE OF A NEW TREATMENT TECHNIQUE

In 1992, Byers reported on a series of 35 patients with neck masses >3 cm and with primary tumors thought to be curable

with radiation therapy. These patients had selective neck dissections followed by definitive radiation therapy to the primary tumor and neck. The patients were accrued over a 16-year period. The median age was 61 years. Primary tumors were treated with up to 70 Gy. The entire neck received 50 Gy plus a boost to nodal areas. Delay in starting radiation therapy after surgery caused problems. With 14 days or less, the 5-year survival was 82%. Delay >14 days resulted in a survival of 36%. If the delay was >29 days, survival was 0. Neck recurrences occurred in 4 of 35 patients, or 11%.

At M. D. Anderson Hospital in the early 1970s, most patients had been irradiated in the 1960s, and some faced recurrent disease. Few flaps were available; the forehead and deltopectoral flaps were the most common. After resection, wounds failed to heal, and postoperative rounds were dedicated to opening wounds and draining the infection away from the carotid arteries and tracheostomies. In this setting in 1972, Dr. Robert Byers decided to try something new: operate before radiation therapy in selected patients. Radiation was given mainly with cobalt 60 units with parallel opposed ports, with an anterior port for the lower neck. Eliot Strong had published a series in 1969 (11) confirming the benefit of combined preoperative radiation therapy plus surgery. The treatment group had fewer local and regional recurrences. Hence, Byers used combined surgery and radiation therapy for his series. Chemotherapy at that time consisted of methotrexate, 5-fluorouracil, and bleomycin. These agents were not very effective and weren’t used often.

For preirradiation neck dissections, the group chose patients who had advanced resectable cervical nodes and relatively early stage primary tumors that could be cured by radiation. Radiation therapy was used to treat the primary tumor for cure, as it often preserves function well, particularly in the soft palate, pharynx, and larynx. When necessary, teeth were removed at the same time as the neck dissection, allowing 2 weeks for healing of the extraction sites before beginning radiation therapy. Thus, the dissections did not cause an undue delay in getting the patient to radiation therapy. The judgments of the head and neck surgeons and the radiation oncologists were important, as they had to select appropriate patients and ensure that the procedure could be done with an acceptable morbidity. Hospitalization was usually of short duration.

Incisions and drain sites were placed where they could be covered by the primary irradiation field. This neck dissection was not a “cherry-picking” procedure; selective node groups and all gross disease were removed. Important functional structures, if not directly invaded, were preserved, including the vagus, spinal accessory, and hypoglossal nerves. Microscopic disease could be left behind (12).

For patients treated first with radiation therapy and then with neck dissection, control of the primary site was considered. If the primary site was not cured, then the neck and primary site were dissected simultaneously. Byers’ plan removed the involved structures, preserved functional structures when possible, sacrificed what was requisite for a clean dissection, and used meticulous dissection techniques.

Table 1. Patient characteristics for 29 patients treated for head and neck cancer at Baylor University Medical Center

Variable	N	%
Age		
<60	17	59
>60	12	41
Gender		
Male	23	79
Female	6	21
Race		
White	26	90
Black	2	7
Asian	1	3
Tobacco		
Never	6	21
Past	8	28
Present	15	51
Alcohol		
Never	2	7
Past	6	21
Present	21	72
Both tobacco and alcohol	22	76
Neither tobacco nor alcohol	1	3

BAYLOR UNIVERSITY MEDICAL CENTER SERIES Patient and disease characteristics

In a similar personal study of 29 selected patients treated between 1994 and 2007, the median follow-up period was 31 months, with 100% follow-up within the last 4 months. The average age of the patients was 55.5 years (range, 33–75). Performance status was 0 to 1 on the Eastern Cooperative Oncology Group scale and 80 to 100 on the Karnofsky scale. Demographic characteristics are shown in *Table 1*. Our patients were 5 years younger than those in the Byers study.

The 29 patients had 32 operations. One patient had an additional procedure for local recurrence and another patient had an additional procedure for regional recurrence. In a third patient, initially a neck dissection was done for metastatic carcinoma of unknown origin, and 15 months later the unknown primary became manifest and was resected.

Tumor and nodal characteristics (*Table 2*) show that most patients had small primary tumors in the oropharynx with advanced nodal disease. The average number of nodes retrieved was 39.7 (range, 1–90), and the average number that were positive for metastasis was 4.4 (range, 1–25). The largest positive node was an average of 3.0 cm (range, 0.2–6.2).

Four patients had nodes <3 cm. This was one of Byers' inclusion criteria. One patient had a small (0.2 cm) sentinel node. The other three had multiple nodes in their necks, resulting in an N2B classification.

Several patients had a high percentage of nodes positive for cancer: 29/44 (66%; bilateral dissection), 25/43 (58%), and 17/90 (19%; bilateral dissection). The last patient had

Table 2. Disease characteristics for 29 patients treated for head and neck cancer at Baylor University Medical Center

Variable	N	%
Primary site	29	100
Oropharynx	23	79
Base of tongue	18	62
Tonsil	5	17
Nasopharynx	1	3
Larynx	3	10
Unknown primary	3	10
T stage	32*	100
X	3	9
0	1	3
1	10	31
2	9	28
3	8	25
4	1	3
pN stage	32†	100
0	1	3
1	4	12
2	26	81
2A	4	
2B	13	
2C	9	
3	1	3

*The total is 32 rather than 29: one patient moved from TX to T1 when the unknown primary was identified; one patient moved from T2 to T4 after a primary recurrence; and one patient moved from T3 to T0 after a neck recurrence.

†One patient who was N2B with a primary recurrence was N0 after resection of the primary; one patient had metachronous neck dissections; one patient was N2B with a neck recurrence of N2B.

a cancer with neuroendocrine features. Although CT scans showed no metastasis less than a month before surgery, the patient had pulmonary metastases 6 weeks after surgery and died at 3 months.

Treatment

In these patients, we did 40 neck dissections: 20 unilateral dissections in 19 patients and 20 bilateral dissections in 10 patients (*Table 3*). In contrast to the superselective dissections preferred by Byers, we have tended to do more complete dissections, particularly after one patient experienced a neck recurrence that might have been avoided if a more complete dissection had been done. Another reason for aggressive dissection is the possibility of alteration in lymphatic flow, which can be caused by previous surgery, previous radiation therapy, and lymphatic obstruction due to enlarged nodes. In our group, 30% of patients had involvement of level IV nodes, making more aggressive dissection appropriate.

Twenty of the 29 patients received chemotherapy. Initially, cisplatin was used as a single agent in the neoadjuvant setting. Five patients received such therapy. More recently, concomitant chemotherapy and radiation therapy has been used,

Table 3. Neck dissections in 29 patients treated for head and neck cancer at Baylor University Medical Center

Neck dissection	N
Unilateral*	20
Bilateral†	20
Type‡	
Superselective	7
Selective	13
Supraomohyoid	7
Extended supraomohyoid	4
Lateral	2
Modified radical neck dissection	17
Radical neck dissection	3

*In 19 patients.

†In 10 patients. In nine patients, the bilateral dissection was synchronous, and in one it was metachronous.

‡Superselective indicates involved nodal levels; supraomohyoid, node levels IB, II, III; extended supraomohyoid, levels IB, II, III, IV; lateral, levels II, III, IV; modified radical neck dissection, levels I to V; radical neck dissection, levels I to V.

Table 4. Radiation treatment in 29 patients treated for head and neck cancer at Baylor University Medical Center

Variable	Range	Mean
Primary dose (Gy)	61.8–74.6	67.3
Neck dose (Gy)	45–63	53.7
Duration (days)	32–85	47
Initiation after surgery (days)*	8–65	26

*0–30 days, 17 patients; 0–42 days, 27 patients; >42 days, 2 patients.

with cisplatin (3 patients) or a combination of paclitaxel and carboplatin (12 patients).

Irradiation was given to all patients as part of a standard treatment plan (Table 4). After initial evaluations by the head and neck surgeon and radiation oncologist, the patient underwent radiation therapy or the combination of chemotherapy and radiation therapy as soon as wound status permitted. We made an effort to start radiation therapy within 6 weeks of surgery and met this goal in 27 of 29 patients. The two who were treated after 54 and 65 days had chemotherapy between surgery and radiation therapy. The first patient had no evidence of disease after 155 months; the other died of metastases at 20 months. We did not see the decrease in survival when radiation was started later, as was seen in Byers' series.

Treatment results

As shown in Table 5, six patients (21%) had recurrences. One patient had a local recurrence in the tonsil 5 months after radiation therapy. This tumor was resected, and the patient had no evidence of disease at 34 months. One regional recurrence occurred 15 months after a selective neck dissection for an unknown primary. The patient developed metastases on the other side of his neck from a newly identified base of tongue cancer. The neck was

Table 5. Treatment results for 29 patients treated for head and neck cancer at Baylor University Medical Center

Outcome	N	%
Recurrences	6	21
Local	1	3
Regional	1	3
Distant	4	14
Deaths	6	21
From distant metastases	4	14
From noncancer causes	2	7

dissected and the patient had radiation therapy for his carcinoma. The patient had no evidence of disease at 72 months.

Four patients (14%) had distant metastases. These four patients died of disease at 3, 10, 20, and 29 months. Two other patients died of other causes: one at 31 months of neurologic problems and one at 68 months of chronic obstructive pulmonary disease. Both had no evidence of disease at the time of death. Overall, the 2- and 4-year disease-free estimated survival rates were 89% and 84%, respectively (Figure 1).

INDUCTION CHEMOTHERAPY AND ORGAN PRESERVATION TREATMENT

The development of efficacious treatments with cisplatin and bleomycin (13) and then cisplatin and 5-fluorouracil (14) was exciting. These combinations, given before therapy with surgery or irradiation, resulted in a high response rate, with 60% to 70% partial and complete responses. Medical oncologists who previously did not care to see head and neck cancer patients were now vying with one another to see who would have the most complete responses. The scene had changed! The Veterans Affairs cooperative study, which was begun in 1985 and published in the *New England Journal of Medicine* in 1991 (15), put induction chemotherapy and organ preservation on the map. At present, some centers use induction chemotherapy plus combined chemotherapy/radiation treatment for large primary tumors and/or questionable resectability of large nodal groups.

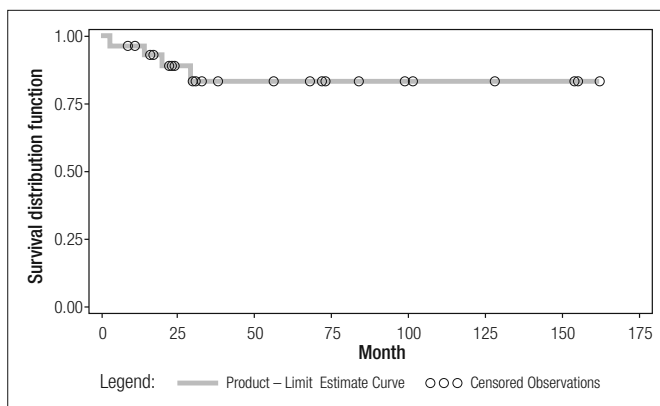


Figure 1. A Kaplan-Meier survival curve showing 89% and 84% 2- and 4-year survival estimates for patients with head and neck cancer treated at Baylor University Medical Center.



Figure 2. A pantheon of heroes. **Top row:** Drs. William S. Halsted, Ronald C. Jones, Mont R. Reid. **Bottom row:** Drs. C. Rollins Hanlon, Robert S. Sparkman, Allan Bookatz. Dr. Halsted trained Dr. Reid, who trained Drs. Hanlon and Sparkman, who trained me. Dr. Bookatz also trained me. Dr. Jones is current chief of surgery.

In a recent study from the Dana-Farber Cancer Institute (16), Haddad reported on 72 previously untreated patients, most of whom had T3 or T4 primary tumors and N2 or N3 nodal disease. They were treated with three cycles of induction chemotherapy with docetaxel, cisplatin, and 5-fluorouracil. Following treatment, all primary sites were biopsied in the operating room. Primary biopsies were negative for cancer in 64 of 72 patients, or 89%. Treatment was completed with combined chemotherapy/radiation therapy.

Neck dissections were done for all patients presenting with N3 nodal disease and for those patients with less than a complete response after induction chemotherapy treatment. Seven of 29 neck dissections were positive for cancer. All patients were without evidence of disease on follow-up—including 6 of the 12 with N3 disease. Pathologic examination showed that 22 of 29 necks had no trace of cancer, and of these 22, 21 remained without evidence of disease. The progression-free survival was 85% at both 2 and 5 years. The overall survival was 95% at 2 years and 90% at 5 years.

SURGICAL CONSIDERATIONS

Surgeons must remember several important points when operating on patients with head and neck cancers:

1. Do not get emotionally attached to structures.
2. Do not save structures that are unnecessary for function and/or life.
3. Remember why you are there: cancer ablation, preservation of function, aesthetic appearance. Take care of business in that order!

Most head and neck cancer patients smoke and hence heal more slowly than nonsmokers because of their lower serum levels of vitamin C. Nicotine induces vasoconstriction, which reduces blood flow to the skin, increases platelet adhesiveness, and reduces proliferation of red cells, fibroblasts, and macrophages. Carbon monoxide is also produced and decreases

oxygen and metabolism. Hydrogen cyanide in the smoke inhibits enzyme systems necessary for cellular metabolism and oxygen transport (17).

All of these patients should be treated preoperatively and postoperatively with vitamin C, zinc, and multiple vitamins. Attempts are made to optimize nutrition orally, enterically, or parenterally (with total parenteral nutrition). Supplements with calories and proteins are used. We make liberal use of hyperbaric oxygen therapy for wounds that have been heavily radiated or that have healing problems, dehiscences, necrosis, and infections. We often start hyperbaric oxygen in the preoperative stage or as soon as the patient is stable after the operation (18).

EPILOGUE

Many wonderful people have played significant roles in my development as a person and a surgeon. I would like to make special mention of Dr. Allan Bookatz, who was a taskmaster in the operating room but was responsible for the technical training of many surgeons of my generation. He preached, “Don’t get in the habit of doing less than perfect work just because you can get away with it. Do everything as perfectly as you can because you will have complications with your best efforts.” He felt that practice did not make perfect but that perfect practice made perfect. He also was active in teaching gross anatomy at the Baylor College of Dentistry, and twice a week I accompanied him to the anatomy lab as a teaching (learning) assistant during my first 2 years of surgery training. He felt that “a blind man works on wood the same way as a surgeon on the body, when he is ignorant of anatomy” (19).

I have included many of my heroes in a pantheon, a Greek word that means temple of all the gods. Dr. Hanlon was the chief of surgery at St. Louis University when I was a medical student. Dr. Sparkman was the chief of surgery at BUMC when I trained here. Both Dr. Hanlon and Dr. Sparkman trained under Dr. Mont Reid at the University of Cincinnati. Dr. Reid was the 16th of 17 chief residents who trained under Dr. William Stewart Halsted at Johns Hopkins University. In a presentation to the Michael E. DeBakey International Surgical Society, Dr. Hanlon stated that teachers and mentors must be able to instruct pupils and pass on information; be exemplars worthy of emulation by their students; and have personal characteristics that help form attitudes and virtues in their pupils. Many teachers are commemorated also because they developed schools or philosophies in surgery (20).

To this pantheon, I would like to add another hero (*Figure 2*), and that is Dr. Ronald Coy Jones, chief of the Department of Surgery at BUMC. He is a man of honesty and integrity. He is a teacher who is fair and even-handed. He is an operating surgeon with tremendous organizational, administrative, and leadership skills. He is politically savvy and attracts good residents. He was able to expand our residency while others couldn’t fill positions or lost positions. I believe that each day he recites this prayer: “God, grant me the serenity to accept the things I cannot change, the courage to change the things I can, and the wisdom to know the difference.” We are proud and happy to honor Dr. Ronald Coy Jones.

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