

# Innovations in surgical oncology at Baylor University Medical Center

Joseph A. Kuhn, MD, Tammy Fisher, RN, and Sheryl Livingston, RN

It is a great pleasure to review clinical and research contributions in the field of surgical oncology under the leadership and guidance of Dr. Ronald C. Jones. He arrived at Baylor University Medical Center (BUMC) in 1987 with a national reputation as a leader in organized surgical oncology based on his role as a leader in the American College of Surgeons Commission on Cancer. He served as state chairman prior to becoming national chairman of the Cancer Liaison Program and vice chairman of the Commission on Cancer (*Figure*). This commission has created national guidelines that have led to standardized requirements for hospitals across the country as they seek certification as a Commission on Cancer–approved cancer center (1).

Upon his arrival at Baylor, Dr. Jones encouraged resident research, allowed for recruitment of dedicated research nurses, and encouraged participation in cooperative group trials. He served as a mentor and leader for the surgical staff, who became active in research trials involving breast cancer, melanoma, esophageal cancer, colon cancer, liver cancer, pancreas cancer, and head and neck and endocrine cancer.

The improvements in each disease state can best be seen by considering the changes in modern management brought about in part through the clinical and research efforts of the staff and residents in the Department of Surgery.

## BREAST CANCER

In 1987, a 39-year-old patient presenting with a 2-cm breast mass would likely have undergone an open biopsy in the operating room, followed by a thoughtful discussion of lumpectomy plus complete axillary node dissection versus a modified radical mastectomy.

The innovations developed at BUMC during the late 1980s included standardized screening, awareness of the hormone status of tumors, and participation in national trials comparing



**Figure.** Dr. Richard Wilson giving a plaque to Dr. Ronald C. Jones in recognition of his tenure as vice chairman of the Commission on Cancer, 1982–1983.

lumpectomy and mastectomy through the efforts of Dr. Jones, Dr. Harold Cheek, and Dr. George Peters (2, 3). Cooperative clinical trials with sentinel node biopsy were introduced by Dr. Kuhn. This work led to national presentations by Dr. Kathleen Crews showing that the sentinel node is the predictive node for breast cancer patients; when these nodes are negative for cancer, patients can be spared complete node dissection (4). Several other residents presented research on the impact of micrometastases, the impact of patient weight, injection techniques around the nipple, appropriate timing for breast reconstruction, and ultimately the long-term results of sentinel node biopsy (4–13).

Magnetic resonance imaging (MRI) in patients with breast cancer was introduced at BUMC by Dr. Steve Harms (14). Continued experience led to a recent report by Drs. Tuoc Dao and Sally Knox suggesting the role of MRI as a potential screening tool for patients with early stage breast cancer (15). Other residents have emphasized the role of office-based breast ultrasound for the staging and optimal biopsy for breast cancer patients (16). Dr. Michael Grant has been a consistent leader with clinical trials of the National Surgical Adjuvant Breast and Bowel Project (NSABP) that involve breast cancer prevention and hormonal therapy of breast cancer. Strategies for periareolar fine-needle biopsy and nipple duct wash techniques to identify patients for prevention trials have also been presented by BUMC residents (8).

Recent research involving circulating tumor cells to stage systemic disease for early stage breast cancer patients has been presented by Dr. Jeffrey Lamont and others (17). Finally, the Department of Surgery is actively involved in a collaborative effort to obtain molecular profiling of breast cancer patients as a means to identify the genomic and proteomic differences between the malignancy and the normal tissue.

As a result of the above contributions and improvements, the modern treatment for the 39-year-old breast cancer patient with a 2-cm tumor would be considerably different in 2007. The surgeon would likely assess the patient with ultrasound-guided core biopsy and ultrasound evaluation of the axillary

From the Department of Surgery, Baylor University Medical Center, Dallas, Texas.

**Corresponding author:** Joseph A. Kuhn, MD, 3409 Worth Street, Suite 420, Dallas, Texas 75246 (e-mail: JosephKu@BaylorHealth.edu).

nodes. The patient would be informed of the protocols involving circulating tumor cells, genomic profiling with a portion of the tumor, or possible neoadjuvant hormonal or molecular therapy. The patient would undergo MRI prior to discussion of possible skin-sparing mastectomy versus lumpectomy plus sentinel node biopsy. If the patient chose lumpectomy, she would be offered the opportunity to participate in a clinical trial with intracavitary radiation dose instead of external beam radiation. Genetic testing might also be considered in this young patient before discussing the possible option of bilateral mastectomy with reconstruction. The complexity of the modern management of breast cancer is a testament to the contributions of many BUMC surgeons and residents.

## MELANOMA

In 1987, the typical patient with a 2.5-mm Clark's level III malignant melanoma on the foot might be managed with a 5-cm-wide excision along with a possible complete axillary node dissection. A positive node might be managed with simple observation.

Surgeons and residents at BUMC have contributed to the management of melanoma through participation in cooperative group trials involving sentinel node biopsy techniques. Presentations have included discussion on the early and late results of sentinel node biopsy from a technical standpoint (18–22). Later reports identified the patterns of recurrence following this technique when applied to extremity and head and neck melanoma (23, 24).

Other technical advancements were introduced by Dr. Alexandra Dresel with use of the node biopsy skin as the graft source with extremity melanoma (25). Nodal and local failure was shown to be similar for shave versus excisional biopsy of the primary melanoma (26). In addition, active involvement in the Sunbelt Melanoma Trial led to greater understanding of the role of polymerase chain reaction for detection of minute amounts of melanoma DNA in the sentinel node and circulating plasma of melanoma patients. Recent work with circulating tumor cells has revealed detection of occasional positive cells in patients with metastatic melanoma. Surgeons at BUMC have collaborated on innovative dendritic cell research for metastatic melanoma as well as various gene therapy trials (27).

Modern management of the above example would entail wide excision with a 2-cm margin and a simultaneous sentinel node biopsy. With a positive sentinel node, the patient would be invited to participate in a clinical trial with circulating tumor cell measurement and would be offered interferon in addition to genomic and proteomic assessment.

## ESOPHAGEAL CANCER

Surgeons at BUMC have been active participants in the development of transhiatal esophagectomy and endoscopic ultrasound for optimal staging of esophageal cancer (28). The department also participated in the American College of Surgeons Oncology Group clinical trial investigating the role of position emission tomography (PET) scans for preoperative staging of esophageal cancer. Surgeons have been involved in

experimental research involving gene therapy for esophageal cancer with injection of a gene construct allowing for intratumoral release of tumor necrosis factor (29). Recent work with laparoscopic esophagectomy was presented by Drs. Shawn Steen and Kuhn (30).

Improvements in management of esophageal cancer have led to better staging, less invasive surgical options, and unique adjuvant therapy options that didn't exist 20 years ago.

## COLON CANCER

Drs. Warren Lichliter, Robert Jacobson, and R. D. Dignan have been key contributors to colorectal surgical innovations through participation in NSABP protocols and improvements in technique (31). Presentations by residents and fellows have included innovative strategies for the role of PET scans, a PET probe, and the gamma detection probe with monoclonal antibodies (32–34). Dr. James McLoughlin presented the early work of Drs. Kuhn and Lamont related to the role of intraperitoneal hyperthermic chemotherapy for colon carcinoma with peritoneal metastases (35–37). Other residents have presented research work involving laser ablation or stenting of obstructive rectal cancer. Dr. Lichliter and colleagues participated in institutional studies and a national protocol investigating molecular biomarkers in young patients with colorectal carcinoma (38). The institution continues to participate in studies of genetic testing in high-risk patients.

## LIVER MALIGNANCY

The changes in clinical management of liver tumors continue to evolve through the efforts of surgeons in the BUMC Department of Surgery and the Baylor Regional Transplant Institute. Technical aspects of caudate lobe resection, cryosurgical ablation, hepatic artery pumps, and radiofrequency ablation have been presented by surgical staff and residents (39–43). Improved imaging strategies with MRI, intraoperative ultrasound, and PET scans have contributed to optimal staging and optimal surgical approaches (44, 45). Recent work with stapled liver resections and laparoscopic resections has characterized the types of innovations through the department (56). Surgeons have taken an active role in the introduction of focused radiation with the CyberKnife system (47) and SIR-Spheres via the hepatic artery. Collaboration with the Mary Crowley Medical Research Center has led to participation in several clinical trials involving gene therapy products designed to work preferentially with liver tumors (48).

## PANCREAS CANCER

Technical proficiency in the surgical management of pancreas malignancies has always been a strong component of the surgery department, with an early presentation by Dr. Jeff Stephens regarding the role of portal vein resection (49). Improved imaging with endoscopic ultrasound or intraoperative ultrasound offers better staging and diagnosis (50). Surgeon-directed focused radiation therapy (CyberKnife) and gene therapy with tumor necrosis factor release and radiation therapy have been areas of unique strength at BUMC.

## HEAD/NECK/ENDOCRINE CANCER

The surgeons and residents at BUMC have helped to modify and improve the surgical management of head and neck cancer through the aggressive acceptance of the multidisciplinary organ-preserving efforts of Dr. John O'Brien and others. Participation in novel gene therapy protocols has been possible through collaboration with the Mary Crowley Medical Research Center (51, 52).

The surgeon's role in the optimal staging of parotid and thyroid lesions based on office ultrasound has been presented at regional meetings (16, 53). The department was an early adopter of the parathyroid hormone assay as a means of less-invasive parathyroidectomy (54). Recent work with the technique of thyroid biopsy has been presented by Drs. Ernesto Garza and Kuhn, showing the preferential value of a 25-gauge needle (55).

## SUMMARY

The pathway to innovation and clinical changes in the management of the cancer patient has been directly related to the leadership, vision, and support of the chairman of surgery, Dr. Ronald C. Jones. He has encouraged the surgical staff to become involved with the residents and resident research. He has recruited and funded the research nurse position at BUMC, leading to a greatly more efficient process. He has encouraged residents to be involved with research and has supported travel to appropriate meetings. He has actively reviewed virtually every abstract that has left the department, leading to an improved research product in the Department of Surgery.

The formula for continued innovation in the Department of Surgery can be tied to the enormous strides made over the past 20 years. Stay current. Go to meetings. Read journals. Assume that there is always a better way. Participate in national trials. Work under a great chairman, like Dr. Jones.

1. Jones RC. Challenge of the field liaison program. *The Bulletin [published by the American College of Surgeons]* 1979;649:20–21.
2. Moot SK, Peters GN, Cheek JH. Tumor hormone receptor status and recurrences in premenopausal node negative breast carcinoma. *Cancer* 1987;60(3):382–385.
3. Hobar PC, Jones RC, Schouten J, Leitch AM, Hendler F. Multimodality treatment of locally advanced breast carcinoma. *Arch Surg* 1988;123(8):951–955.
4. Crews KA, Kuhn JA, Fisher TL, Grant MD, Peters GN, Knox SM, Krag DN. Sentinel node biopsy for breast cancer: preliminary results. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 1997, and the Southeastern Surgical Congress, January 1998.
5. Stratmann SL, McCarty TM, Kuhn JA. Radiation safety with breast sentinel node biopsy. *Am J Surg* 1999;178(6):454–457.
6. Ganaraj A, Kuhn JA, Jones RC, Grant MD, Andrews VR, Knox SM, Livingston SA, McCarty TM. The significance of micrometastasis in the sentinel lymph node for breast cancer. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2000, and the Southwestern Surgical Congress, April 2000 (best poster award).
7. Styperek KE, Kuhn JA, Grant MD, Andrews VR, McCarty TM, Knox SM, Newsome TW, Griffith LK, Livingston SA, Stratmann SL, Jones RC. Phase II results with sentinel lymphadenectomy for breast cancer staging. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2000.
8. Harrison JM, Kuhn JA, O'Shaughnessy J, Andrews VR, Knox SM, Grant MD, Pippin J, Blum J, Jones SE, Fisher TL, Pratt K, Fabian C. Periareolar fine needle aspiration cytology for breast cancer prediction: technical results. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2001, and the Southwestern Surgical Congress, April 2001.
9. Brady B, Fant J, Jones R, Grant M, Andrews V, Livingston S, Kuhn J. Sentinel lymph node biopsy followed by delayed mastectomy and reconstruction. *Am J Surg* 2003;185(2):114–117.
10. Krag D, Weaver D, Ashikaga T, Moffat F, Klimberg VS, Shriver C, Feldman S, Kusminsky R, Gadd M, Kuhn J, Harlow S, Beitsch P. The sentinel node in breast cancer—a multicenter validation study. *N Engl J Med* 1998;339(14):941–946.
11. Ganaraj A, Kuhn JA, Jones RC, Grant MD, Andrews VR, Knox SM, Netto GJ, Altrabulsi B, Livingston SA, McCarty TM. Predictors for nonsentinel node involvement in breast cancer patients with micrometastases in the sentinel lymph node. *Proc (Bayl Univ Med Cent)* 2003;16(1):3–6.
12. Carlo JT, Grant MD, Knox SM, Jones RC, Hamilton CS, Livingston SA, Kuhn JA. Survival analysis following sentinel lymph node biopsy: a validation trial demonstrating its accuracy in staging early breast cancer. *Proc (Bayl Univ Med Cent)* 2005;18(2):103–107.
13. Fant JS, Grant MD, Knox SM, Livingston SA, Ridl K, Jones RC, Kuhn JA. Preliminary outcome analysis in patients with breast cancer and a positive sentinel lymph node who declined axillary dissection. *Ann Surg Oncol* 2003;10(2):126–130.
14. Cross MJ, Harms SE, Cheek JH, Peters GN, Jones RC. New horizons in the diagnosis and treatment of breast cancer using magnetic resonance imaging. *Am J Surg* 1993;166(6):749–753.
15. Dao TN, Lamont JP, Knox SM. Clinical utility of breast magnetic resonance imaging in patients presenting with primary breast cancer. *Proc (Bayl Univ Med Cent)* 2007;20(3):227–230.
16. Gogel BM, Ferry KM, Livingston SA, McCarty TM, Kuhn JA. The effect of surgical office-based thyroid ultrasound on clinical decision making. *Proc (Bayl Univ Med Cent)* 2000;13(3):207–209.
17. Dao T, Thepajatri N, Kuhn JA, Knox SM, Grant MD, Nemunaitis JJ, Livingston SA, Lamont JP. Preliminary results of a pilot study of circulating tumor cells in patients undergoing surgery for primary breast cancer. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2007.
18. Kuhn JA, McCarty TM. Malignant melanoma and the sentinel lymph node biopsy. *Cancer Invest* 1999;17(1):39–46.
19. Gogel BM, Kuhn JA, Ferry KM, Fisher TL, Preskitt JT, O'Brien JC, Lieberman ZH, Stephens JS, Krag DN. Sentinel lymph node biopsy for melanoma. *Am J Surg* 1998;176(6):544–547.
20. Harlow SP, Krag DN, Ashikaga T, Weaver DL, Meijer SJ, Loggie BW, Tanabe KK, Whitworth P Jr, Kuhn J, Kusminsky R, Carp NZ, Gadd M, Rawlings M Jr, Slingluff CL Jr. Gamma probe guided biopsy of the sentinel node in malignant melanoma: a multicentre study. *Melanoma Res* 2001;11(1):45–55.
21. Moore TO, Kuhn JA, Hoover TC, Stroman DL, Fisher TL, Netto GJ, McCarty TM. The need for completion lymph node dissection following positive sentinel lymph node biopsy for cutaneous melanoma. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 19, 1999.
22. Moore TO, Kuhn JA, Hoover TC, Stroman DL, Fisher TL, Netto GJ, McCarty TM. Completion lymph node dissection following positive sentinel lymph node biopsy for cutaneous melanoma. Presented at the Southwestern Surgical Congress, April 2000.
23. Fincher TR, McCarty TM, Fisher TL, Preskitt JT, Lieberman ZH, Stephens JF, O'Brien JC, Kuhn JA. Patterns of recurrence after sentinel lymph node biopsy for cutaneous melanoma. *Am J Surg* 2003;186(6):675–681.
24. Fincher TR, O'Brien JC, McCarty TM, Fisher TL, Preskitt JT, Lieberman ZH, Stephens JF, Kuhn JA. Patterns of drainage and recurrence following sentinel lymph node biopsy for cutaneous melanoma of the head and neck. *Arch Otolaryngol Head Neck Surg* 2004;130(7):844–848.
25. Dresel A, Kuhn JA, McCarty TM. Sentinel node biopsy site used as full thickness skin graft donor for cutaneous melanoma. *Am J Surg* 2002;184(2):176–178.

26. Carlo J, Nelson B, Kuhn JA, Fincher T, Fisher TL, McCarty TM. Does a shave biopsy of cutaneous melanoma increase the risk of nodal or local recurrence? Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2004.
27. Nemunaitis J, Bohart C, Fong T, Meyer W, Edelman G, Paulson RS, Orr D, Jain V, O'Brien J, Kuhn J, Kowal KJ, Burkeholder S, Bruce J, Ognoskie N, Wynne D, Martineau D, Ando D. Phase I trial of retroviral vector-mediated interferon (IFN)-gamma gene transfer into autologous tumor cells in patients with metastatic melanoma. *Cancer Gene Ther* 1998;5(5):292-300.
28. Patel AN, Preskitt JT, Kuhn JA, Hebel RF, Wood RE, Urschel HC Jr. Surgical management of esophageal carcinoma. *Proc (Bayl Univ Med Cent)* 2003;16(3):280-284.
29. McLoughlin JM, McCarty TM, Cunningham C, Clark V, Senzer N, Nemunaitis J, Kuhn JA. TNFerade, an adenovector carrying the transgene for human tumor necrosis factor alpha, for patients with advanced solid tumors: surgical experience and long-term follow-up. *Ann Surg Oncol* 2005;12(10):825-830.
30. Steen S, Lamont J, Westmoreland M, Fisher T, Kuhn JA. Laparoscopic esophagectomy. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2007.
31. Goss MG, Kuhn JA, Lichliter WE. Anal canal squamous cell cancer: results of combined modality treatment. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 1995.
32. Goss MG, Kuhn JA, Lichliter WE, Franko ER, Dignan RD. Laser ablation of rectal tumors. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 1997.
33. Conrad J, Kuhn JA, Grossman S, Griffith L, McCarty TM. Identification of metastatic cancer with handheld PET probe. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2000.
34. Kuhn JA, Nochumson J. Operative probe scintimetry with indium and technetium for colorectal cancer. *J Surg Onc* 2007;96(4):290-296.
35. McLoughlin JM, Talaasen LJ, McCarty TM, Kuhn JA. Intraperitoneal hyperthermic chemotherapy for peritoneal carcinomatosis: analysis and outcomes. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2003 and February 2004.
36. McLoughlin J, Kuhn JA, Lamont JP, McCarty TM, Livingston S. Pseudomyxoma peritonei and intraperitoneal hyperthermic chemotherapy. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 25, 2005, and at the Southwestern Surgical Congress.
37. Kuhn JA, McLoughlin JM, Harris DC, Talaasen LJ, Sutton SW, McCarty TM. Intraperitoneal hyperthermic chemotherapy: experience at Baylor University Medical Center. *Proc (Bayl Univ Med Cent)* 2002;15(4):359-362.
38. Farner RE, Fisher TL, Jacobson RM, Tulanon P, Franco ER, Dignan RD, Kuhn JA, Lichliter WE. Colon cancer in patients 40 years old or younger. *Proc (Bayl Univ Med Cent)* 1998;11(4):175-178.
39. Burton L, Kuhn JA, Preskitt JT, Klintmalm G. Caudate lobe resection for metastatic colon carcinoma. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 1993.
40. Crews KA, Kuhn JA, Fisher TM, McCarty TM, Goldstein RM, Preskitt JT, Derrick HC. Hepatic cryosurgical ablation. Presented at the Southwestern Surgical Congress, April 1997, Rancho Mirage, CA.
41. Warner MT, Goldstein RM, Kuhn JA, Derrick HC, McCarty TM. Radiofrequency interstitial thermal ablation of hepatic tumors. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 19, 1999.
42. Kuhn JA, McCarty TM, Hurst DC. Cryosurgical ablation of colorectal metastasis to the liver. *Proc (Bayl Univ Med Cent)* 1994;7(3):3-7.
43. Ditrack G, Lamont JP, Livingston S, Kuhn JA. The role of hepatic artery infusion chemotherapy in metastatic colorectal cancer. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2006.
44. Schultz JF, Bell JD, Goldstein RM, Kuhn JA, McCarty TM. Hepatic tumor imaging using iron oxide MRI: comparison with computed tomography, clinical impact, and cost analysis. *Ann Surg Oncol* 1999;6(7):691-698.
45. Gogel BM, Goldstein RM, Kuhn JA, McCarty TM. Screening for hepatocellular carcinoma in the multinodular, cirrhotic liver. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2000, and the meeting of the Society of Surgical Oncology, March 2000.
46. Emerson N, Kuhn JA, Lamont JP, McCarty TM, Livingston S, Goldstein R. Comparison of stapled vs nonstapled hepatic transection during lobectomy. Poster presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2006.
47. Pool M, Wood R, Berger B. Frameless stereotactic radiosurgery (Cyber-Knife) therapy for lung tumors: an early clinical experience. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2007.
48. Kuhn JA, Steen S, Senzer N, Maples P, Nemunaitis J. Genomic and proteomic analysis of high-risk cancer patients. Abstract submitted to the 2008 meeting, Society of Surgical Oncology.
49. Stephens J, Kuhn J, O'Brien J, Preskitt J, Derrick H, Fisher T, Fuller R, Lieberman Z. Surgical morbidity, mortality, and long-term survival in patients with peripancreatic cancer following pancreaticoduodenectomy. *Am J Surg* 1997;174(6):600-603.
50. Carlo GT, DeMarco DC, Polter DE, Smith BA, Livingston SA, Wisner PK, Kuhn JA, Lamont JP. The utility of capsule endoscopy and its role for diagnosing pathology in the GI tract. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 25, 2005, and at the Southwestern Surgical Congress, April 2005.
51. Nemunaitis J, Ganly I, Khuri F, Arseneau J, Kuhn J, McCarty T, Landers S, Maples P, Romel L, Randlev B, Reid T, Kaye S, Kirn D. Selective replication and oncolysis in p53 mutant tumors with ONYX-015, an E1B-55kD gene-deleted adenovirus, in patients with advanced head and neck cancer: a phase II trial. *Cancer Res* 2000;60(22):6359-6366.
52. Lamont JP, Kuhn JA, Nemunaitis JJ, McCarty TM. Gene therapy for head and neck cancers. *Oncology* 2001;15(3):303-308.
53. Lamont JP, Kuhn JA, Fisher TL, McCarty TM. Prospective evaluation of office-based parotid ultrasound. Poster presented at the meeting of the Society of Surgical Oncology, March 2001, and the Southwestern Surgical Congress, April 2001.
54. Stratmann SL, Kuhn JA, Bell MS, Preskitt JT, O'Brien JC, Gable DR, Stephens JS, McCarty TM. Comparison of quick parathyroid assay for uniglandular and multiglandular parathyroid disease. *Am J Surg* 2002;184(6):578-581.
55. Garza E, Fisher T, Adair C, Lamont J, Kuhn JA. Thyroid nodule sampling: comparison of 22-gauge versus 25-gauge needles. Presented at the meeting of the North Texas Chapter, American College of Surgeons, February 2007.