Sentinel Lymph Node Biopsy for Patients with Breast Cancer: Five-Year Experience

By Richard S Godfrey, MD
Dennis R Holmes, MD
Anjali S Kumar, MD, MPH
Susan E Kutner, MD

Abstract

Background: Sentinel lymph node biopsy (SLNB) is rapidly gaining acceptance as a diagnostic tool for staging breast cancer.

Objective: Analyze trends among surgeons and facilities in Kaiser Permanente Northern California (KPNC) in adopting SLNB to stage cases of breast cancer and assess success in locating the sentinel node.

Methods: Retrospective review of data for patients whose breast cancer was staged using SLNB and axillary lymph node dissection between July 1997 through December 2002 at KPNC. Rates of false-negative results were calculated and stratified by surgeons' experience with SLNB.

Results: The number of SLNB procedures performed each month increased steadily from fewer than ten (in late 1998) to about 80 per month (in mid-2002) and were done at 17 facilities. Of the 132 surgeons who performed SLNB, most had done fewer than 15 procedures. The false-negative result rate overall was 6.53% (95% CI 4.75%, 8.73%); for surgeons who performed <30 procedures the rate was 8.58% (95% CI 5.52%, 12.60%); for surgeons who performed 20 to 30 procedures the rate was 13.08% (95% CI 7.34%, 20.98%); and for surgeons who performed more than 30 procedures the rate was 5.05% (95% CI 3.07%, 7.78%).

Conclusions: SLNB is rapidly being adopted at KPNC to stage cases of breast cancer and surgeons achieve an acceptable 6.53% false-negative result rate overall. The higher false-negative rate for surgeons who performed 20 to 30 procedures suggests that departments should expand efforts to monitor and proctor these surgeons.

Introduction

The most precise prognostic indicator for progression of primary breast cancer is lymph node involvement.[1] For this reason, as well as for local disease control, most surgeons include some form of lymph node dissection in their initial case management of breast cancer. Sentinel lymph node biopsy (SLNB) has gained acceptance as a first line diagnostic approach because it is more sensitive and causes less morbidity than traditional techniques for early staging of breast cancer.

After SLNB was found successful for staging melanoma, Giuliano et al[2] in 1994, proposed use of SLNB as an alternative to more extensive node dissection for staging breast cancer. Many papers in the surgical literature subsequently established that SLNB can provide more accurate results and cause less morbidity than standard axillary node dissection.[3-7] Working at the Kaiser Permanente (KP) Los Angeles Medical Center, Guenther et al[8,9] documented efficacy and safety of SLNB. By 1999, the National Comprehensive Cancer Network (NCCN) recognized the procedure had rapidly gained acceptance as an appropriate diagnostic tool for determining whether cancer has spread to the surrounding lymph nodes. The current NCCN Breast Cancer Practice Guidelines[10] support SLNB by experienced teams of practitioners for patients who meet selection criteria.

Beginning in 1994, the KP Oakland Medical Center (KP Oakland) used SLNB to stage cases of melanoma. On the basis of this experience, SLNB was introduced in 1996 to stage breast cancer. Early results confirmed that the method was reliable, and patients were pleased with the mild degree of post-surgical morbidity and short hospital stay.

Sentinel lymph node biopsy (SLNB) has gained acceptance as a first line diagnostic approach ...

Richard S Godfrey, MD, (top, left) Department of Surgery, Kaiser Permanente Medical Center, Oakland. E-mail: richard.s.godfrey@kp.org.
Dennis R Holmes, MD, (top, right) Department of Surgery, University of California, San Francisco. E-mail: dennis.holmes@kp.org.
Anjali S Kumar, MD, MPH, (bottom, left) Department of Surgery, University of California, San Francisco. E-mail: anjali.kumar@kp.org.
Susan E Kutner, MD, (bottom, right) Department of Surgery, Kaiser Permanente Medical Center, San Jose. E-mail: susan.e.kutner@kp.org.

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Surgeons from other facilities joined KP Oakland in a collaborative trial that enrolled patients nationally. The KP Institutional Review Board approved the study. The trial provided an organized framework for accomplishing three goals: 1) to standardize use of SLNB in breast cancer staging, 2) to facilitate training of surgery and pathology teams, and 3) to establish a comprehensive database.[11] More than 40 centers from university and community hospital settings participated in this collaborative effort (titled The Early Detection of Occult Micrometastases in Invasive Breast Cancer), a prospective, multicenter trial which originated at the University of South Florida and was funded by both the US Department of Defense and the National Cancer Institute. KP patients were recruited from November 1997 through October 1999, and data from these patients constituted part of the database content. Initial results indicated that surgeons from participating facilities learned and reliably performed SLNB. Some long-term goals of the study are still in process and include determining the prognostic significance of micrometastases and evaluating use of polymerase chain reaction (PCR) as a diagnostic tool.

At regional and statewide KP symposia conducted from 1997 through 2000, KP physicians had academic and clinical training opportunities to develop and master SLNB technique. For example, a series of presentations by Daniel Navarro, MD, of KP Oakland introduced Nuclear Medicine departments to imaging requirements; and in February 2001, TPMG sponsored its first National Surgical Symposium, to which Armando Giuliano, MD, Associate Medical Director and Chief of Surgical Oncology at the John Wayne Cancer Institute in Santa Monica, was invited to update KP surgeons from California, Colorado, and Hawaii on SLNB and its relevance for breast cancer and melanoma. TPMG data and research have been presented regionally, at national meetings, and in the surgical literature.[12,13]

The Breast Cancer Tracking System of KP Northern California (KPNC) contains data on all SLNB procedures done at KPNC since July 7, 1997 for breast cancer patients. Using these data, we studied trends among TPMG surgeons and at KPNC facilities in adopting techniques of sentinel lymph node identification, dissection, and biopsy, processes that require coordination among departments of surgery, pathology, radiology, and nuclear medicine. By mid-2003, more than 2100 cases had been recorded. Although the database does not indicate rate of successfully locating sentinel lymph nodes, the database does contain false-negative results, ie, positive results of axillary node biopsy in patients with negative results of sentinel lymph node biopsy. We used this false-negative rate for limited assessment of the success of SLNB among KP surgeons. The present study was done to assess quantitatively the rate of successful SLNB in patients with breast cancer and to identify possible ways to improve the rate.

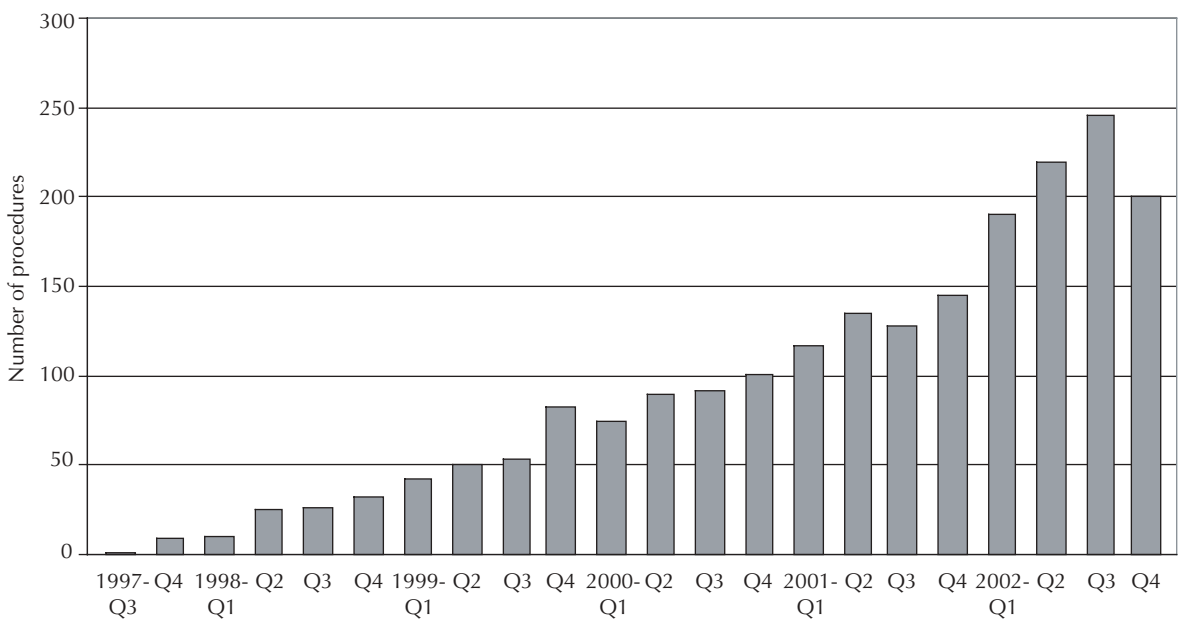

Figure 1. Trend in use of the sentinel lymph node biopsy (SLNB) procedure at Kaiser Permanente Northern California (KPNC) for patients with breast cancer and clinically negative lymph nodes.

Methods

Data in the KPNC Breast Cancer Tracking System were retrospectively reviewed to identify patients with clinically negative lymph nodes who had SLNB at KPNC facilities during the period from July 1997 through December 2002. Reviewed data included diagnosis (invasive breast cancer versus ductal carcinoma in situ), tumor size, histologic grade of tumor, nodal status of patient (test positive or negative for presence of tumor cells), and stage of primary tumor. American Joint Committee on Cancer stages T1 through T4 were used for this analysis.[14] The sentinel lymph node identification procedure combined preoperative Tc99m sulfur colloid peritumoral injection followed by lymphoscintigraphy and intraoperative isosulfan blue dye injection into the peritumoral region of the breast. Sentinel lymph nodes that were thus identified (ie, either as radioactive or blue) were removed for excisional biopsy. If no sentinel node was identified, standard level I (with or without level II) lymph node dissection and biopsy were done.

A false-negative result was defined as concurrent negative result of SLNB and positive result of axillary node biopsy. False-negative rate for the SLNB procedure (proportion of false-negative results to the sum of true positive and false-negative results) was calculated, both overall and stratified by surgeon experience with the procedure. Patients who had SLNB and biopsy without axillary node dissection were excluded from analyses of false-negative rate.

In almost all cases, serial sections of the node were permanently mounted, stained with hematoxylin-eosin, and microscopically examined to determine status of the sentinel lymph node. Initial pathologic examination was performed on-site at the surgical facility. At the KP San Francisco Medical Center, tissue was examined immunohistochemically for micrometastases, estrogen and progesterone receptors, and for over-expression of the HER-2/Neu gene.

Results

Between July 1997 and December 2002, 2098 patients with clinically negative lymph nodes had SLNB procedures. Of these 2098 patients, 437 patients did not have axillary node dissection and were excluded from the analysis of false-negative rates, and 1660 patients had standard level I or level II lymph node dissection with lumpectomy or modified radical mastectomy. The median age of patients was 59 years (range 23-95 years).

The monthly number of SLNB procedures increased steadily. Although fewer than ten per month were done in the first and second quarters of 1998, more than 30 procedures per month were done during the first quarter of 2001; by the third quarter of 2002, about 80 procedures were done per month (Figure 1).

The procedures were performed by 132 surgeons, most

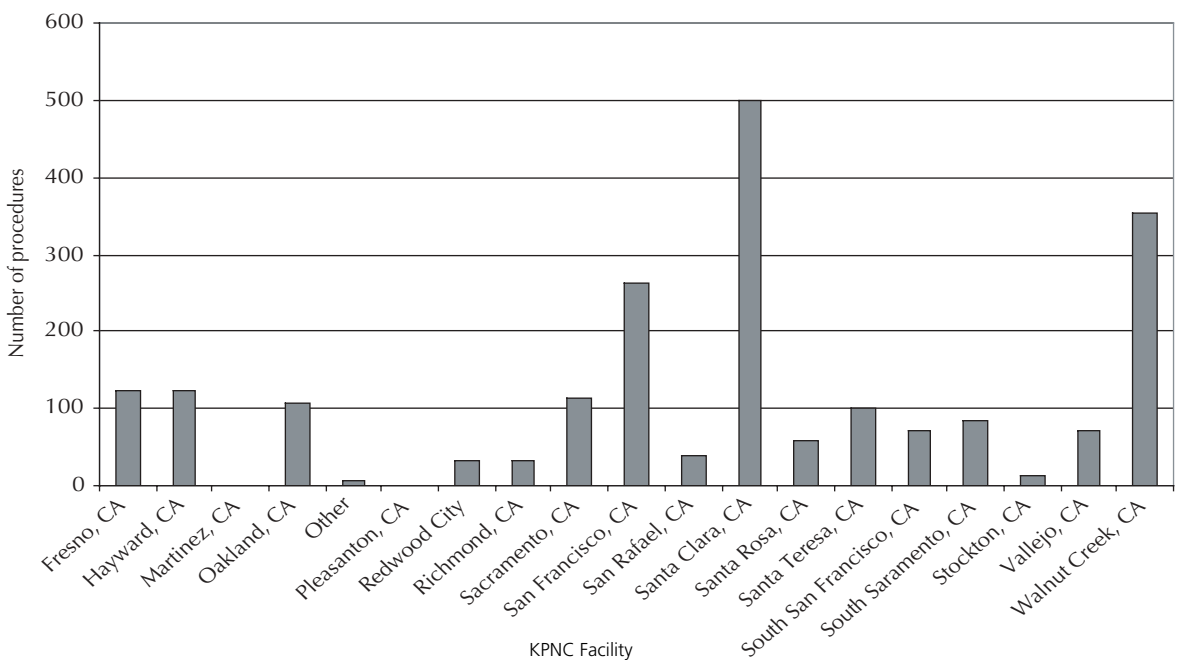

Figure 2. Graph shows number of SLNB procedures done at KPNC facilities from July 1997 through December 1997.

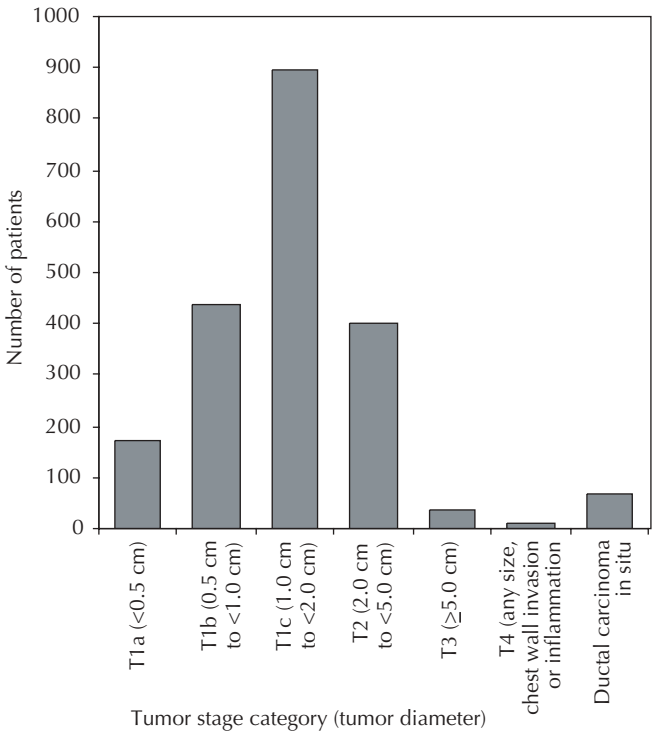

Figure 3. Graph shows tumor stage for 2097 breast cancer patients who received SLNB.

of whom were performing SLNB for the first time; 93 surgeons did fewer than 15 procedures, 17 surgeons did between 15 and 30 procedures, and 22 surgeons did 30 or more procedures. Procedures were done at 17 KP facilities; most were done at the KP medical centers in Santa Clara (n = 498), Walnut Creek (n = 352), San Francisco (n = 263), and Hayward (n = 123) (Figure 2).

Size of primary tumor varied among patients. Most patients had lesions that measured between 1.0 cm and 2.0 cm in diameter (tumor stage T1c) (Figure 3). Lesions in 69 (3.4%) of the patients were graded as ductal carcinoma in situ.

The overall false-negative rate was 6.53% (95% confidence interval [CI] 4.75%, 8.73%). The false-negative rate for surgeons who performed fewer than 30 procedures was 8.58% (95% CI 5.52%, 12.60%); the rate for surgeons who performed between 20 and 30 procedures was 13.08% (95% CI 7.34%, 20.98%); and the rate for surgeons who performed more than 30 procedures was 5.05% (95% CI 3.07%, 7.78%) (Figure 4).

Discussion

Surgical management of breast cancer has evolved in stages. Use of Halsted radical mastectomy was replaced first by modified radical mastectomy and later by conservative breast surgery. Treatment of axillary lymph nodes in patients with invasive breast cancer has always been controversial. Because as many as 70% of patients who undergo lymph node dissection have negative biopsy results[15] and because node dissection is often accompanied by postsurgical complications and morbidity, less-invasive methods were developed for staging breast cancer. This development was facilitated in particular by use of mammography and by earlier diagnosis of breast cancer (ie, when the tumor is small). Because the axillary lymph nodes of most breast cancer patients seen today are clinically and pathologically negative, the need for less invasive breast cancer staging is being met by SLNB.

The KPNC Breast Cancer Tracking System shows that SLNB is now performed regularly by Northern California TPMG surgeons. Introduction of new surgical procedures usually follows a pattern: Selected surgeons become familiar with the technique and then proctor other surgeons until the procedure becomes widely practiced. This pattern was suggested by our data. Of the 132 surgeons in the study, 58 performed SLNB fewer than five times during the period analyzed, and most (56%) of the 2098 procedures were performed by only 20 (15%) of the surgeons. This pattern also reflects a current trend in surgical practice: surgical subspecialization (ie, more breast cancer management is being done by fewer surgeons).

The ability to perform SLNB is measured primarily by the surgeon's rate of success in finding the sentinel lymph node and by the corresponding false-negative rate. Because this study was retrospective, the rate of successfully finding the sentinel lymph node could not be tracked. Combined use of blue dye and radioisotope allows surgeons to find the sentinel lymph node in 81% to 94% of patients.[16] In a prospective study conducted throughout 1998 and 1999, TPMG surgeons had a 97% rate of successfully locating the sentinel lymph node. Although no data verify similar success for the surgeons in our study, early prospective study data are reassuring. Further, surgeons who could not locate a sentinel lymph node proceeded with standard lymph node dissection.

The rate of false-negative results best defines the accuracy of sentinel lymph node biopsy. If a sentinel node which tests negative for tumor cells at histologic examination is removed while a tumor-positive lymph node remains in the axilla, the disease will be understaged, leaving the patient at risk both for local and regional recurrence of disease and for metastasis.

A false-negative rate of 5% or less is mentioned frequently in surgical literature as a goal for surgeons performing SLNB.[17,18] All TPMG surgeons combined had a 6.5% false-negative rate for the SLNB procedure. Because this rate was calculated for a large number of surgeons gaining early experience with the SLNB technique, the 6.5% rate affirms that promising introduction of a technology and technique.

How many times must surgeons perform SLNB before they achieve proficiency in this procedure? The 6.5% false-negative rate for all KP surgeons compares favorably with the goal of a 5% or less rate of false-negative results advocated in the general literature.[17,18] However, our data show some conflicting trends: Whereas surgeons who performed fewer than 30 or more than 30 SLNB procedures had low false-negative rates (8.6% and 5%, respectively), surgeons who performed an intermediate number of SLNB procedures (20 to 30 procedures) had a higher rate of false-negative results (13%). Although the rates of false-negative results in national SLNB trials range from 0% to 17%[17] and surgeons less experienced in the technique have higher false-negative rate,[18] surgeons in our series who had an intermediate level of experience (20 to 30 SLNB procedures completed) had the highest rate of false-negative results. This unexpectedly high rate may reflect inadequate proctoring, lack of surgical proficiency, or inappropriate selection of patients (ie, selecting patients who have advanced disease). The better false-negative rate among surgeons who performed fewer than 20 procedures may represent the combined experience of apprentice surgeons and their proctors; the false-negative rate may then have increased among the apprentice surgeons after they began to perform the SLNB procedure unassisted (especially after only a few proctored SLNB procedures) until more experience was gained. Data analysis (not presented here) confirmed that the entire group of KP surgeons and the group with an intermediate level of experience performed SLNB for similar percentages of patients with advanced disease. Data were not available describing surgical proficiency, selection of patients with advanced disease, or availability of a proctor during the SLNB procedure.

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The proposed number of times a surgeon must perform the SLNB procedure before achieving proficiency in it ranges from 10 to 150.[19-21] However, many authors suggest that experience with 20 to 30 SLNB procedures may be adequate,[17] if the surgeon has received good proctoring and case management is coordinated jointly by a team of surgeons, radiologists, nuclear medicine specialists, and pathologists. Our data

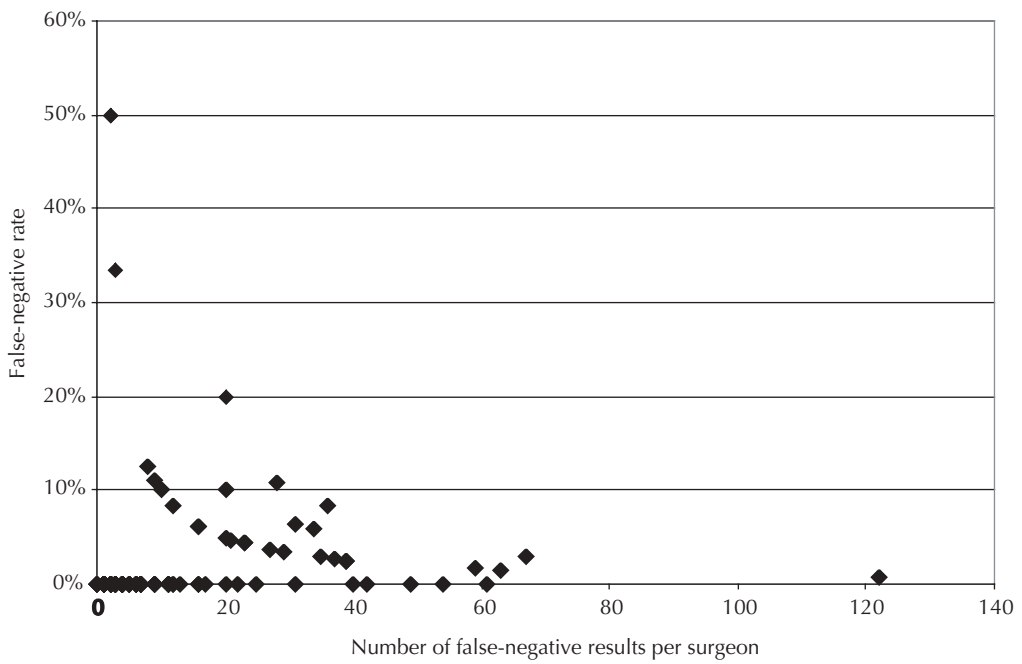

Figure 4. Graph shows SLNB experience of KP surgeons.

showed that TPMG surgeons who performed more than 30 SLNB procedures achieved an acceptable rate of false-negative results of 5% or less. However, because of the 13% rate of false-negative results achieved by TPMG surgeons who performed 20 to 30 SLNB procedures, further efforts in monitoring and proctoring should be encouraged. Until national SLNB credentialing programs are developed, we advocate use of the NCCN guidelines.[10] In addition, our data justify adopting a departmental policy which specifies the minimum surgical caseloads and monitors surgical results to verify a low rate of false-negative results (5% or less) for surgeons who have performed SLNB 20 or more times.

This focus of all our departments will help ensure that KP surgeons remain at the forefront of advances in therapy …

Continuing to Provide High-Quality Service

TPMG surgeons should be encouraged to monitor patients prospectively and to support development of a national database. To advance toward these goals, TPMG surgeons should participate in sentinel node biopsy trials such as the National Surgical Adjuvant Breast and Bowel Project study (NSABP) B32[22] or the American College of Surgeons Oncology Group trials (ACSOG) Z-10 or Z-11.[23] The NSABP B32 trial compares patients undergoing full axillary dissection and patients receiving SLNB only. However, all patients with positive sentinel lymph nodes will have complete axillary node dissection. In contrast, the ACSOG trials will include patients with positive sentinel lymph nodes who do not undergo further surgery. The Z-10 trial will further assess the benefit of bone marrow biopsy for determining presence of metastatic disease.

Dr Lou Fehrenbacher of KP Vallejo has provided infrastructure for NSABP and other trials regionally, and TPMG surgeons have already contributed to the first national prospective SLNB trial.[11] In addition, using the Breast Cancer Tracking System, we have monitored 2098 cases and have established an independent database which facilitates prospective and retrospective quality review. As these data are transferred from a local database to the Population and Condition Tracking System (PACTS)—a Web-based application designed to track multiple conditions, including many types of cancer—clinical outcome must remain the focus in all surgical cases. This focus of all our departments will help ensure that KP surgeons remain at the forefront of advances in therapy and that we offer our patients the best possible treatment for breast cancer and other conditions. ❖

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Quality of Service

For the past few years, I have had the opportunity
to observe the development of the Kaiser Foundation Hospital.
I am prepared to state that the quality of service
to the sick is of a very high order.
The members of the staff are interested
in advances in medical science and practice.
Their group contribution to our community is inspiring.

— William Kerr, MD, Professor of Medicine, University of California Medical School