INTRODUCTION

The histopathological status of tumor-draining regional lymph nodes is one of the most significant predictors of recurrence and overall survival for most clinical stage I/II solid tumors, and is often used to justify stratification of patients for adjuvant therapy.1-8

The sentinel lymph node (SLN) is defined as one or more lymph nodes that first receive lymphatic drainage from the site of a tumor.9 The SLN hypothesis was advanced to specifically address those patients at high risk of having lymph node (LN) metastasis based on the characteristics of their primary tumors, but who had no evidence of clinically detectable regional metastatic disease. SLN mapping and biopsy was first applied to melanoma, and was subsequently extended to breast cancer and, more recently, to many other solid tumors.10-28 The SLN concept for other solid tumors, including colorectal, esophageal, gastric, gynecologic, head and neck squamous cell, thyroid, urologic, and non-small-cell lung cancers, is still in the early stages of development. This concept has revolutionized the approach to the surgical staging of both melanoma and breast cancer, and has fundamentally resolved nagging questions as to the proper indications for extensive LN dissections in the former and, perhaps, in the latter disease as well.
For melanoma, breast cancer, and most other solid tumors, the morbidity of complete axillary, inguinal, and other regional LN basin dissections is significant, often disabling, and occasionally even life threatening. The mapping and selective biopsy of the SLN(s) spares the patient significant potential morbidity, while simultaneously allowing the pathologist to perform a detailed and focused evaluation of a single or a few SLNs. It has been estimated that, prior to the development of the SLN concept, as many as 80% of patients with primary melanomas < 4 mm thick who underwent elective lymph node dissection (ELND) did so without apparent benefit.

Prior to the advent of the SLN concept, standard histopathologic assessment involved the cutting of several sections from multiple paraffin-embedded archival tissue (PEAT) lymph nodes, the staining of these sections with hematoxylin and eosin (H&E), and visualization under the light microscope by the pathologist. At this level of analysis, the detection of occult or small clumps of tumor cells within a background of mononuclear lymphoid cells in multiple LNs is a very tedious process and has been shown to have limitations in terms of sensitivity particularly for various carcinomas. Before the advent of SLN mapping, the necessity of sampling multiple regional LNs for evidence of micrometastases was a labor-intensive and inefficient process, frequently resulting in "understaging" of the patient. The detailed analysis of multiple LNs, including serial sectioning, immunostaining, and assessing numerous serial LN sections, is costly, time-consuming, and also impractical for most community hospitals. In terms of today's health care logistics and costs, this is of major concern.

**HISTOPATHOLOGICAL EVALUATION**

Both H&E and IHC staining have been extensively used, in combination with thin serial sectioning of frozen and paraffin-embedded specimens, in the detection of micrometastatic disease in the SLN/LN. The application of IHC has markedly improved the sensitivity of micrometastatic disease detection in the SLN/LN beyond the capability of routine H&E staining alone.

The antibodies against tumor markers of interest must reproducibly be highly specific and sensitive for detection of tumor cells and virtually non-reactive to the adjacent nontumor cells in the SLN/LN. When searching for occult metastasis, the sensitivity of the antibody must be high. The most commonly used IHC target for epithelial carcinomas are the cytokeratins (CK), which are ubiquitously expressed as intermediate filaments in normal eukaryotic epithelial cells. The risk of false-positive results with the use of individual anticytokeratin antibodies