



Milton Rochman. *Essence of Blue*. Acrylic on canvas, 36" × 36".  
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*The staging of patients with NSCLC has improved. Anatomic surgical resection is the standard of care for treatment of stage I and II NSCLC.*

# Treatment of Stage I and II Non-Small-Cell Lung Cancer

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**Background:** *The appropriate staging and treatment of patients with stage I and II non-small-cell lung cancer (NSCLC) are important in that the potential for a lost curative opportunity in this population is greater than for those presenting with advanced NSCLC.*

**Methods:** *Treatment options — surgery, radiation therapy, and chemotherapy — for stage I and II NSCLC are reviewed, and the impact of newer staging modalities on patient survival is discussed, including altering both the lead-time and clinicopathologic stage biases that exist in the diagnosis and treatment of NSCLC. Some predictions are also made regarding how that standard may change for clinicians in the near future, and methods for further improvements in posttreatment survival in this group are discussed.*

**Results:** *Whenever possible, patients with early-stage NSCLC should be treated with surgical resection. Patients for whom resection is not an option may benefit from radiation as definitive therapy. Positive results with neoadjuvant chemotherapy have led to an ongoing randomized trial (Intergroup S9900) to compare surgery alone to neoadjuvant chemotherapy plus surgery.*

**Conclusions:** *Staging bias may affect the overall low survival of early-stage NSCLC. However, true stage-specific survival may improve with newer imaging modalities. Future advances, including closed transthoracic radiation, thermal ablative therapy techniques, and gene therapy, may supplant the need to surgically resect these tumors to achieve local control.*

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## Introduction

Of the more than 150,000 patients diagnosed with non-small-cell lung cancer (NSCLC) in the United States each year, a woeful minority will present with stage I or II disease as defined by the TNM staging system of the American Joint Commission on Cancer (AJCC). While we may appreciate a patient who presents with a 1-cm peripheral lung cancer nodule with-

out evidence of mediastinal or distant metastases rather than disseminated disease, cure of such a patient is not certain. A substantial number of patients who are treated for early-stage NSCLC will eventually die of this neoplasm. The latest Surveillance, Epidemiology and End Results (SEER) Program data analysis indicates that 15% of patients diagnosed from 1989 to 1996 with NSCLC in the United States were reported to have "localized" disease compared with 23% with "regional" disease, 48% with "distant" disease, and 14% with "unstaged" disease.<sup>1</sup> According to SEER data, NSCLC survival improved from 12.4% during the 1974-1979 reporting period to only 14.1% in the last period analyzed (1989-1996).

In a review evaluating recent published data for outcomes in patients with stage I or II NSCLC, Nesbitt and colleagues<sup>2</sup> estimated overall cumulative reported survival rates to be 64.6% for stage I and 41.2% for stage II. Naruke et al<sup>3</sup> and Mountain<sup>4</sup> published two of the largest series evaluating postsurgical survival in NSCLC. In these studies, 2,322 patients with stage I or II (1997 AJCC system designation) NSCLC were treated surgically, and survival was retrospectively assessed. The 5-year survival rate for patients with T3 N0 M0 IIB disease was no greater than 38%, and when patients in the most favorable subgroup (T1 N0 M0 stage I disease) were analyzed, the survival rates ranged from 67% to 75% (Table).

Clearly, a cure to patients with a diagnosis of NSCLC cannot be promised at any stage. However, survival following treatment of this disease is stage related, and patients with lower-stage disease have the best chance for curative treatment. With this in mind, the appropriate treatment of patients with early-stage disease assumes perhaps even greater importance than for those who present with advanced NSCLC, as the potential for a lost curative opportunity is greatest. The survival rate increase from 12.4% to 14.1% previously mentioned may seem trivial, but a 2% increase in a group of 150,000 patients/year means an additional 21,000 lives were saved during this time period compared with 20 years earlier.

This review addresses the "standard of care" for treatment of stage I and II NSCLC, as supported by past experience. Some predictions are also made regarding how that standard may change for clinicians in the near future, and methods for further improvements in post-treatment survival in this group are discussed. In addition, the impact of newer screening modalities on patient survival is discussed. by altering both the lead-time and clinicopathologic stage biases that exist in the diagnosis and treatment of NSCLC.

## Conventional Pretreatment Physiologic Evaluation and Staging of Patients With Clinical Stage I and II NSCLC

Patients being considered for treatment of NSCLC should undergo a careful history and examination. Although a general evaluation is required in all cases, one should direct the evaluation to identify problems that may lead to either a greater risk of postoperative complications or a need to more carefully evaluate for advanced or metastatic tumor. Particular attention is paid to the neurologic history, including the presence or absence of vertigo and headache, and to questions regarding new bone and/or joint pain as positive responses may lead to the discovery of metastases. A careful cardiac and respiratory history is also garnered as these organ systems are most frequently involved in postoperative complications following surgical resection for NSCLC. Patients are asked about head and neck symptoms (dysphagia, odynophagia, oropharyngeal pain or bleeding) as this may lead to the discovery of either a second primary cancer or true primary aerodigestive malignancy that first manifested by pulmonary metastasis. Symptoms of any sort related to the primary malignancy can portend a poor prognosis in stage I and II NSCLC patients. In a 10-year review of patients who recurred less than 9 months following curative-intent anatomic resection with negative operative margins, 33 stage I and II NSCLC patients were identified at The University of Texas M. D. Anderson Cancer Center within a 10-year period. The only clinical variables that correlated with this early recurrence when compared to a control group were symptoms such as weight loss ( $P=.029$ ) and unusual histologic variants such as adenosquamous carcinoma (unpublished data, 2000).

The physical examination can demonstrate sources of concern that require more involved evaluation. These include cardiac murmurs, carotid bruits, and respiratory findings out of proportion to the patient's complaints such as chronic obstructive pulmonary

Postsurgical Survival in NSCLC

	TNM Subset	Mountain (1997) <sup>4</sup>		Naruke et al (1988) <sup>3</sup>	
		Number of Patients	% 5-Yr Survival	Number of Patients	% 5-Yr Survival
Stage I-II	T1 N0 M0	511	67.0	245	75.5
	T2 N0 M0	549	57.0	241	57.0
	T1 N1 M0	76	55.0	66	52.5
	T2 N1 M0	288	39.0	153	40.0
	T3 N0 M0	87	38.0	106	33.3
	T3 N1 M0	55	25.0	85	39.0
	Any T N2 M0	344	23.0	368	15.1

disease (COPD) stigmata and wheezing. In addition, the physical examination allows recognition of unusual but well-known findings in NSCLC such as supraclavicular nodal spread in apparently early disease or undiscovered skin malignancies that represent primary tumors with metastatic spread to the lung.

## Imaging

Routine imaging prior to staging should include posterior-anterior and lateral chest films as well as a contrast-enhanced computed tomography (CT) scan of the chest with both parenchymal and mediastinal windows and upper abdomen to evaluate for occult liver and adrenal metastasis. Preoperative disease staging in patients with stage I and II disease is controversial and is rapidly evolving with the advent of positron emission tomography (PET) and other new techniques. PET is clearly more specific and sensitive than CT,<sup>5</sup> and in centers that use this modality, it is considered the key to preoperative staging for NSCLC.

Between 3%-15% of neurologically asymptomatic patients with NSCLC may harbor brain metastases when assessed by CT, although some authors have demonstrated that the reported incidence is less in earlier-stage disease.<sup>6-8</sup> Magnetic resonance imaging (MRI) may be more sensitive than CT and, in most centers, is the test of choice for this evaluation.<sup>9</sup> The bone is another favored metastatic site for NSCLC. A screening bone scan may detect abnormalities in asymptomatic patients that on follow-up plain film or MRI will be determined to be metastatic disease in approximately 9% of patients.<sup>6</sup> Although a careful study evaluating screening for occult metastatic disease in asymptomatic patients at all stages is lacking, and some have argued that such screening is not cost effective, a reasonable approach might be to screen all patients with a diagnosis of NSCLC above clinical stage IA with a head CT or MRI (especially if there are new neurologic symptoms) and a whole-body bone scan. Asymptomatic patients with stage IA disease are at low risk for metastasis, but the possibility of occult metastatic disease needs to be related in the pretreatment counseling session if screening imaging is not performed.

## Pulmonary Function

Pulmonary function testing, including spirometry and DLCO (diffusing capacity of the lung for carbon monoxide), is a routine part of the evaluation, even for early-stage disease. It should be remembered that a lobectomy carries the same potential for functional compromise in a patient with an 8-mm NSCLC tumor as in one with a tumor that measures 8 cm, and perhaps even more so as a greater number of functioning alve-

oli will be removed. Quantitative lung perfusion studies and exercise testing are performed for cases where the foregoing is inconclusive regarding the ability of a patient to tolerate an anatomic resection. Effective pulmonary toilet and presurgical treatment of patients with aggressive inhaled therapy or formal pulmonary rehabilitation may enhance the likelihood that patients with comorbidities such as COPD can tolerate indicated tumor resection procedures.

## Surgery for Stage I and II NSCLC as “Standard of Care”

Defining a standard of care for a given illness can be a daunting task. London<sup>10</sup> has argued that even the Helsinki Accords, the document to which most around the world refer to for guidance in matters of human rights, is unclear in its description of “best proven therapeutic method” in discussions of research ethics with human subjects. The “standard of care” for one community may vary from that in another, and the term “best proven method” should probably replace the former nomenclature. In the absence of known metastatic disease or a reliable marker, such as mediastinal nodal metastasis as a marker for stage IIIA disease, local tumor control has been the mainstay of treatment for stage I and II NSCLC. To date, no adjuvant or neoadjuvant treatment of any type, including radiation therapy and chemotherapy, has affected the survival of stage I and II patients. Therefore, at this time, the “best proven method” for treatment of patients with stage I and II NSCLC is aggressive local control, either by surgical resection and/or radiation therapy ablation of NSCLC primary carcinomas.

Due to the relatively discrete nature of many of the primary lesions in these stage categories, especially patients with T1 tumors, there has been a temptation in the past to perform sublobar or limited lung resection for definitive local control therapy (“wedge resection” or “segmentectomy”). However, this approach has been discredited in patients who could tolerate lobectomy, as the more limited procedures engender higher rates of local recurrence and even possibly poorer survival. Multiple retrospective studies between 1979-1990 addressed this question, although results were not conclusive. In a comparison of these two groups, Hoffmann et al<sup>11</sup> found no difference in survival at 1, 2, and 5 years, although a 5-year survival rate of 25% in the lobectomy group for early-stage NSCLC reported in this study is low. Errett et al<sup>12</sup> also reported a similar 5-year survival rate in stage I patients treated with lobectomy (n=97, 75%) and wedge resection (n=100, 69%) at 6 years. In an early report in 1979, investigators at Memorial Sloan-Kettering Cancer Center examined the results

of limited resection for stage I NSCLC.<sup>13</sup> They noted a local recurrence rate of 19% and a 5-year survival rate of only 33% in these patients. Earlier published reports from the same institution indicated no local recurrence and 5-year survival rate of more than 50% in stage I patients who were treated with lobectomy. In 1995, this same group published a more convincing 12-year retrospective controlled study evaluating limited resection vs. anatomic lobectomy or pneumonectomy in more than 500 patients.<sup>14</sup> The 5- and 10-year survival rates in those undergoing limited resection (n=61) were 59% and 35%, respectively, compared with 77% and 70% in those undergoing lobectomy (n=511). Finally, in 1995, a prospective, randomized trial was reported by the Lung Cancer Study Group in which lobectomy and limited resection were compared in patients with peripheral T1 N0 NSCLC.<sup>15</sup> In this study, more than 250 patients were randomly allocated to either approach. The authors determined that the lung cancer recurrence rate was 75% greater in the limited resection group because of a tripling of local tumor recurrences, and there was a 50% increase in death with cancer.

Thoracoscopic NSCLC resection has gained some acceptance, and modest improvement of postoperative pain control and earlier return to work have been reported.<sup>16,17</sup> Of course, thoracoscopic wedge resection suffers the same potential oncologic problems as open limited resection via thoracotomy reviewed above. Enthusiasm for this approach for lobectomy in patients with NSCLC should also be tempered because (1) the procedure can be technically difficult, (2) a full mediastinal lymph node dissection is not reliably possible, (3) careful palpation of the lung for occult extralobar metastatic disease is not always possible, and (4) thoracoscopic lobectomy with an intercostal delivery incision may offer little postoperative pain advantage over a small muscle-sparing thoracotomy in this era of routine use of epidural and intravenous narcotic analgesia.

The higher rate of local recurrence with more limited resections seems somewhat intuitive when one considers the lobar anatomy of the lung and the prevailing lymphatic drainage patterns. Ishida et al<sup>18</sup> demonstrated that 5% of patients with tumors between 1 and 2 cm and 12% of patients with tumors greater than 2 cm will have N1 (hilar) nodal disease proximal to the primary lesion. Although it may be possible to remove most N2 (mediastinal) nodes at the time of a wedge resection, removal of N1 nodal tissue, which is often intraparenchymal at the hilum, requires a lobectomy. Sublobar resections would, by definition, leave behind pathologically detectable tumor in 5% to 12% of cases since intraparenchymal lymphatics proximal to N1 nodes cannot be evaluated.

The question of whether a complete lymph node dissection or lymph node sampling is required at the time of resection in patients with early stage is also contentious. Some authors have suggested that, for small peripheral NSCLC tumors, there is neither a staging nor survival benefit achieved by a complete mediastinal lymph node dissection rather than sampling, or by a limited biopsy of hilar and mediastinal nodal stations at the time of tumor removal.<sup>19</sup> Other authors disagree with the ability of surgeons to discriminate, even in the operating room, between involved and uninvolved nodal regions. Takizawa et al<sup>20</sup> demonstrated that in 157 patients undergoing surgical resection for 1.1-2.0 cm-diameter peripheral NSCLC, 27 (17%) were found to have nodal disease, and in 19 of these 27 cases, there was no intraoperative finding that predicted this. As expected, survival directly correlated to the nodal stage, with 5-year survival rates of 91% in those truly N0 and 30% for the 27 patients with N1 or N2 disease. Graham et al<sup>21</sup> noted similar findings in 240 patients thought to be N0 or N1. N2 disease was noted in 46 patients (20%), and no clinical stage subgroup was without this upstaging. Finally, in a report evaluating staging and survival in 337 patients with stage II or III NSCLC undergoing either mediastinal nodal sampling or complete nodal dissection, although staging accuracy was equivalent, more levels of N2 disease were noted in the node-dissection group, as well as longer survival.<sup>22</sup> A large randomized study sponsored by the American College of Surgeons is currently evaluating this question in a more rigorous fashion. In addition to conventional nodal removal, many centers are currently working on a method to identify "sentinel" mediastinal lymph nodes in NSCLC at the time of resection, making sampling more reliable,<sup>23,24</sup> although cytokeratin analysis of sentinel nodes will add many questions concerning upstaging and prognosis.

## Radiation Therapy vs Surgery for Stage I and II NSCLC

Although anatomic resection is the preferred local control modality for treatment of stage I and II NSCLC, a subset of patients either refuse or are medically unfit for surgical treatment. These patients can also benefit from some form of local control modality (eg, radiation therapy) or possibly from limited resection as discussed in the previous section.

A number of published reports have recently appeared in the literature describing radiation as definitive therapy for patients with early-stage NSCLC. Morita et al<sup>25</sup> compiled results from 10 Japanese hospitals involving 149 patients with stage I NSCLC who were considered to be medically inoperable. The mean dose

administered to patients was 64.7 Gy. The actuarial 3- and 5-year survival rates were 34.2% and 22.2%, respectively, and the 5-year survival rate was 31% when concomitant mediastinal nodal irradiation was given. In another retrospective study of patients treated in the 1980s,<sup>21</sup> 103 patients with stage I and II NSCLC were treated with “radical” radiation therapy (~60 Gy, with curative intent). Overall survival rates at 3 and 5 years were only 35% and 14%, respectively, but a small subgroup of patients with T1 tumors and no history of antecedent weight loss had a survival rate of 50% at 5 years. Also, the radiation therapy group at M.D. Anderson reported on 71 patients who received definitive radiation therapy for NSCLC instead of surgery due to medical contraindications for surgical resection.<sup>26</sup> Disease-specific 3-year survival rates for T1 and T2 lesions following ~62 Gy were 49% and 47% and the local control rates were 89% and 61%, respectively.

As a possible harbinger of things to come in the field, a more contemporary group of patients treated with proton-beam radiation therapy between the years 1994 and 1998 was recently reported by Bush and colleagues.<sup>27</sup> In this study, the disease-free survival rate in patients with stage I disease at 2 years of follow-up was 86%. These studies and others suggest that a 5-year survival rate of approximately 30% should be expected in stage I patients treated with definitive radiation therapy. Wedge resection, when tolerated via a minimal incision, can lead to a 5-year survival rate of up to 50% in this same group. Although these data argue for limited surgical resection when possible, one must recognize that medically inoperable patients reported in earlier definitive radiation treatment papers often die of non-oncologic reasons, that disease-specific survival data from radiation may approach that of wedge resection, and that the newer modalities of radiation therapy (eg, proton-beam therapy, motion-gated approaches, transthoracic intratumoral treatment, continuous hyperfractionated accelerated radiotherapy, and intensity modulated radiation therapy) may prove to be superior to conventional external-beam radiation techniques.

## Chemotherapy for Stage I and II NSCLC

The two approaches studied for chemotherapy in patients with clinically resectable NSCLC have been preoperative (neoadjuvant) therapy and postoperative (adjuvant) therapy. Thus far, the adjuvant chemotherapy approach has been shown to provide no significant benefit in NSCLC, regardless of stage. A meta-analysis performed by the NSCLC Collaborative Group of England in 1995 examined the pooled results of 52 randomized trials in which adjuvant chemotherapy

was utilized in patients with NSCLC.<sup>28</sup> Chemotherapy engendered at best a 5% positive treatment effect on survival using platinum-based chemotherapy. In some cases, chemotherapy with alkylating agents appeared detrimental. Although past studies have been negative, these findings have yet to be retested with more active chemotherapy combinations. The alternative approach, neoadjuvant or preoperative chemotherapy, has been shown in at least two small randomized trials (both of which were stopped early by review committees due to a large positive effect in chemotherapy groups) to be active in later-stage (IIIA) resectable NSCLC. These studies demonstrated survival benefit for stage IIIA patients undergoing surgical resection following “induction” platinum-based chemotherapy.<sup>29-32</sup> Other similar studies, however, have had less favorable outcomes.<sup>33-35</sup> This neoadjuvant chemotherapy approach in patients with potentially resectable stage IIIA NSCLC is currently being evaluated in a cooperative group national randomized trial.

These preliminary results, along with the fact that patients with good performance status respond better to chemotherapy and that a significant proportion of patients with stage I and II NSCLC eventually succumb to the disease, have led to evaluation of neoadjuvant chemotherapy for these earlier-stage patients. A past criticism of chemotherapy in these patients is that drug toxicity might well outweigh any beneficial effect in this early-stage group that can often be cured with surgery alone. To evaluate this question objectively, investigators at M.D. Anderson Cancer Center compared the toxicity profile of neoadjuvant chemotherapy in 76 consecutive NSCLC patients to 259 control patients.<sup>36</sup> No significant differences in mortality, pulmonary morbidity, complications related to healing, length of stay, or readmission rates were noted (Fig 1).

In a phase II study, Pisters et al<sup>37</sup> have assessed the feasibility of administration of neoadjuvant chemother-

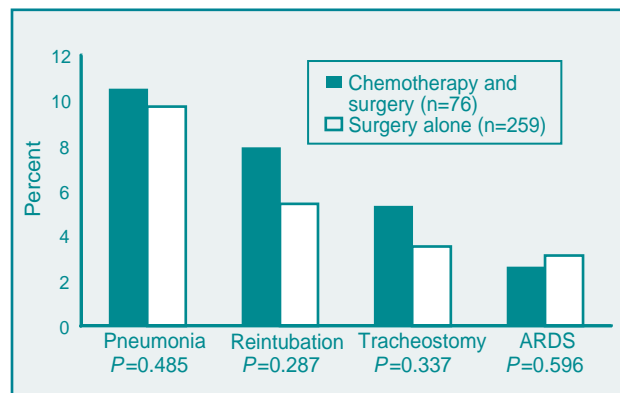


Fig 1. — Pulmonary morbidity related to the use of neoadjuvant chemotherapy in patients with NSCLC at the University of Texas M.D. Anderson Cancer Center.

apy for patients with early-stage NSCLC (IB through selected IIIA). This study, conducted by the Bimodality Lung Oncology Team (BLOT), included 94 patients treated with preoperative carboplatin at a dose based on the area under the concentration-time curve (AUC) of 6 mg/mL × min and paclitaxel at 225 mg/kg<sup>2</sup> over 3 hours every 21 days. Two cycles were administered prior to surgical resection. A major response was seen in 56% of the treated patients, 96% completed the planned preoperative chemotherapy, and 94% underwent a surgical procedure. No unexpected surgical or medical morbidity occurred. As a result of these findings, a randomized trial comparing three courses of carboplatin plus paclitaxel followed by surgery vs surgery alone — the BLOT or KNOT trial (Intergroup S9900) — is now in progress.

## Measurement Bias in Staging of Early-Stage NSCLC

Data from multiple sources, including autopsy studies, PET evaluation of patients, and nonconventional measures of micrometastasis, suggest that a form of measurement bias is one explanation that a proportion of stage I and II patients disease will succumb to recurrent disease. Simply stated, the conventional measures of metastatic disease — CT, MRI, and bone scan — are insufficiently sensitive to detect all disseminated disease, and some patients thought to be early stage by clinical and pathologic evaluation actually harbor metastases and are thus understaged. In a 10-year retrospective study of all autopsies (n=1,625) performed at the Medical Center of Louisiana, the discordance between clinical and autopsy diagnosis for malignant neoplasms was 44%.<sup>38</sup> In addition, the most common site for a misdiagnosed or undiagnosed malignancy was the respiratory tract.

The more frequent use of PET scanning as a pre-treatment screening modality for NSCLC is informative. In a recently published study evaluating PET as a screening method for patients deemed operable by clinical criteria, 11 of 102 patients were found to have metastatic disease undetected by conventional methods.<sup>5</sup> Similar results have been reported by others, with a relatively consistent finding of metastatic disease in patients cleared for resection (stage IIIA or less) by conventional screening methods in 11% to 14% of cases.<sup>39-41</sup> In addition to distant metastases, virtually all of these studies have demonstrated an increase in the rate of detection of unsuspected mediastinal and hilar nodal disease.

Finally, a number of studies demonstrate that dissemination of cancer cells at levels much below those

detected by PET scanning affect the prognosis of patients with clinical early-stage NSCLC. Examination of bone marrow using epithelial cytokeratin antigens for occult micrometastases in “operable” patients with stage I-III disease have demonstrated that 18% to 59% of patients with clinically operable stage I-III NSCLC harbor occult micrometastatic disease in the bone marrow. This finding is directly correlated with survival, exclusive of stage.<sup>42-45</sup> Passlick et al<sup>45</sup> evaluated 139 NSCLC patients with bone marrow biopsy and cytokeratin immunohistochemistry analysis at the time of thoracic surgical procedure, with a median postsurgical follow-up of 66 months. Patients with stage I and II disease had micrometastases detected in more than 48% of cases, and overall survival in node-negative patients was dramatically poorer in those with a positive bone marrow. In addition to bone marrow evaluation, similar findings have been noted with immunohistochemical and polymerase chain reaction evaluation of lymph nodes previously deemed negative in surgically treated NSCLC patients by conventional hematoxylin and eosin histopathologic examination. In a recent illustrative study, Maruyama et al<sup>46</sup> evaluated 973 regional lymph nodes from 44 patients with stage I NSCLC who were pathologically staged. Utilizing a cytokeratin antibody, 70.5% of patients were found to have positive lymph nodes, and 19 and 12 patients were restaged as having N1 and N2 disease, respectively. The median survival in these patients was shorter (*P*=.004) and more in keeping with the corrected stage category.

What about more sensitive measures of true early disease, such as extremely sensitive screening methods that will be more likely to ensure that patients are truly stage I? The Early Lung Cancer Action Project (ELCAP), an effort to screen individuals at high risk for NSCLC on the basis of smoking history, was recently published.<sup>47</sup> In this report, noncalcified nodules were noted in 233 of 1,000 patients, and 27 NSCLC tumors not discernible on conventional radiographs were found. Of these 27 lesions, 15 (56%) were 10 mm or less in size, and 26 were resectable. While such studies offer hope that lesions detected earlier may improve survival on the basis of “true” early-stage disease, the jury is still out regarding both the clinical and cost effectiveness of large screening programs for NSCLC, even using the newer technologies at our disposal. Patz et al<sup>48</sup> reported that when a large number of patients treated surgically with stage IA disease (n=510) were analyzed, no significant differences in survival were noted between stage IA patients with lesions of any size from 0.27 to 3.0 cm. The explanation for this may be that even when less than 1 cm in diameter, NSCLC lesions may exhibit vascular or lymphatic invasion in up to one third of cases.<sup>49</sup>

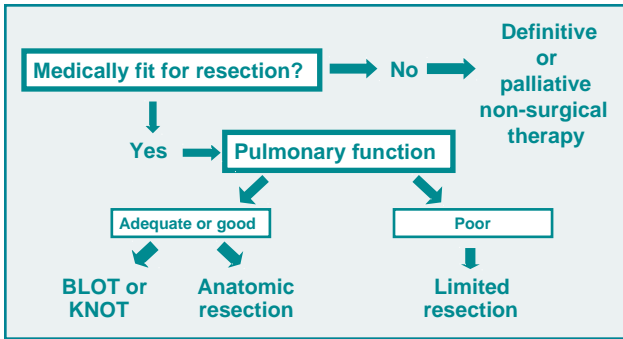


Fig 2. — A proposed algorithm of clinically determined stage I or II NSCLC based on current (non-PET) staging techniques.

## Conclusions

Marcus Aurelius (121-180 AD) stated that an individual should “look beneath the surface; let not the several quality of a thing nor its worth escape thee.” As in many areas of medicine, the issues regarding treatment of early-stage NSCLC patients, which may appear simple compared with those surrounding the treatment of patients at other stages — stage IIIA NSCLC, for example — are indeed complex. A reasonable algorithm for the current treatment of stage I and II NSCLC is presented in Fig 2.

Future advances, including closed transthoracic radiation, thermal ablative therapy techniques, and gene therapy, may well supplant the need to surgically resect these tumors to achieve local control, and PET scan is already changing the way these patients are staged.<sup>50-52</sup> The results from ongoing neoadjuvant and planned adjuvant trials utilizing newer, more active chemotherapeutic approaches for NSCLC are anticipated. One could easily envision a future treatment algo-

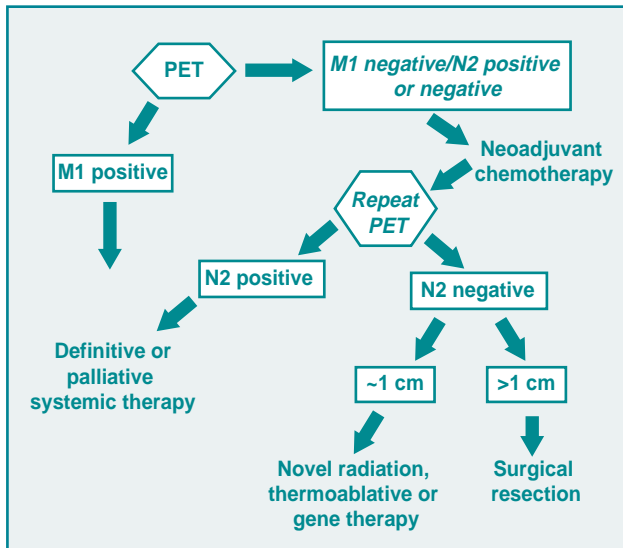


Fig 3. — A potential future algorithm for management of stage I or II NSCLC using PET staging.

rithm based on these new technologies and findings as noted in Fig 3, and we should be optimistic that the prognosis of patients I and II NSCLC can soon be further improved.

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