# Sublobar Resection for Lung Adenocarcinoma Meeting Node-Negative Criteria on Preoperative Imaging

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*Background.* **This study evaluated the usefulness of sublobar resection for patients with clinical stage IA lung adenocarcinoma that met our proposed node-negative criteria: solid tumor size of less than 0.8 cm on high-resolution computed tomography or maximum standardized uptake value of less than 1.5 on [18F]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography.**

*Methods.* **A multicenter database of 618 patients with completely resected clinical stage IA lung adenocarcinoma who underwent preoperative high-resolution computed tomography and [18F]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography was used to evaluate the surgical results of sublobar resection for patients who met our node-negative criteria.**

*Results.* **No patient who met the node-negative criteria had any pathological lymph node metastasis. Recurrence-free survival (RFS) and overall survival (OS) rates at 5 years were significantly higher for patients who met the node-negative criteria (RFS: 96.6%; OS: 95.9%) than for patients who did not (RFS: 75.5%, $p < 0.0001$; OS: 83.1%, $p < 0.0001$). Among patients who met the node-negative criteria, RFS and OS rates at 5 years were not significantly different between those who underwent lobectomy (RFS: 96.0%; OS: 95.9%) and those who underwent sublobar resection (RFS: 97.2%, $p = 0.94$; OS: 95.9%, $p = 0.98$). Of 264 patients with T1b (2-cm to 3-cm) tumors, 106 (40.2%) met the node-negative criteria.**

*Conclusions.* **Sublobar resection without systematic nodal dissection is feasible for clinical stage IA lung adenocarcinoma that meets the above-mentioned node-negative criteria. Even a T1b tumor, which is generally unsuitable for intentional sublobar resection, can be a candidate for sublobar resection if it meets these node-negative criteria.**

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Early-stage lung cancer, particularly lung adenocarcinoma, is now frequently being detected because of advanced radiographic techniques, such as high-resolution computed tomography (HRCT), and the widespread use of low-dose helical CT for tumor screening [1–3]. In a prospective randomized controlled study, the Lung Cancer Study Group reported that the outcomes of limited resections, such as segmentectomy and wedge resection, were inferior to those of standard lobectomy in patients with clinical T1 node-negative (N0) M0 non-small cell lung cancer (NSCLC) [4]. However, several studies have demonstrated the usefulness of sublobar resection for peripheral small-sized NSCLC [3, 5–10].

Theoretically, true N0 lung cancer can be treated by sublobar resection without nodal dissection when surgical margins are adequate. We previously reported that preoperative HRCT and [18F]-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT) were useful for predicting N0 clinical stage IA lung adenocarcinoma [11].

The objective of this study was to evaluate the usefulness of sublobar resection for clinical stage IA lung adenocarcinoma that met our previously proposed N0 criteria: solid tumor size of less than 0.8 cm on HRCT or a maximum standardized uptake value (SUVmax) of less than 1.5 on FDG-PET/CT [11].

## Patients and Methods

### *Patients*

Between August 1, 2005, and June 30, 2010, we enrolled 618 patients with clinical T1 N0 M0 stage IA lung adenocarcinoma from 4 institutions in Japan (Hiroshima University, Kanagawa Cancer Center, Cancer Institute Hospital, and Hyogo Cancer Center). For this study, we retrospectively analyzed the data for all 618 patients in

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**Abbreviations and Acronyms**

CI = confidence interval
CT = computed tomography
F = female
FDG = [18F]-fluoro-2-deoxy-D-glucose
HR = hazard ratio
HRCT = high-resolution computed tomography
IRB = Institutional Review Board
LI = lymphatic invasion
LN = lymph node
LNM = lymph node metastasis
M = male
N0 = node-negative
NSCLC = non-small cell lung cancer
OS = overall survival
PET = positron emission tomography
PI = pleural invasion
Pt = patient
RFS = recurrence-free survival
SUVmax = maximum standardized uptake value
VI = vascular invasion

this multicenter database. The database included patients who underwent preoperative staging using HRCT and FDG-PET/CT, followed by curative resection without neoadjuvant chemotherapy or radiotherapy, with a definitive histopathologic diagnosis of lung adenocarcinoma. Excluded were those with incompletely resected tumors (R1 or R2) and those with synchronous multiple tumors or previous lung operations. This database has been prospectively collected and maintained.

HRCT and FDG-PET/CT, followed by curative R0 resection, had been performed for all patients who were staged according to the TNM Classification of Malignant Tumours, 7th Edition [12]. Mediastinoscopy and endobronchial ultrasonography were not routinely performed because all patients had undergone preoperative HRCT and FDG-PET/CT. HRCT revealed less than 1-cm enlargement of mediastinal or hilar lymph nodes and FDG-PET revealed a SUVmax of less than 1.5 in these lymph nodes.

Segmentectomy was considered for patients with clinical stage IA tumors that could be completely resected with ample surgical margins. No lymph node metastasis was intraoperatively confirmed on rapid frozen sections for enlarged lymph nodes or lymph nodes that were suspected with disease in the thoracic cavity. In cases of apparent or suspected nodal metastasis, lobectomy was chosen. Systematic lymphadenectomy, including hilar and mediastinal node dissection, was performed during segmentectomy but not during wedge resection. Therefore, wedge resection was performed for tumors, of which a ground glass opacity component accounted for great majority on HRCT. All patients who had pathologically diagnosed lymph node metastases received four cycles of platinum-based chemotherapy after the operation. None of the study patients received adjuvant radiotherapy.

Patients were divided into two groups. One group included patients who met the N0 criteria of solid tumor size of less than 0.8 cm on HRCT or a SUVmax of less than 1.5 on FDG-PET/CT [11]. The other group included patients who did not meet these N0 criteria.

This multicenter study was approved by the Institutional Review Boards (IRBs) of Hiroshima University Hospital (IRB No. EKI-644), Kanagawa Cancer Center (IRB No. KEN-31), Cancer Institute Hospital (IRB No. 2008-1018), and Hyogo Cancer Center (IRB No. H20-RK-15). All IRBs waived the requirement for informed consent from individual patients for this retrospective review of a prospective database.

### *HRCT Acquisition*

Chest images were acquired with 16-row multidetector CT independently of subsequent FDG-PET/CT examinations. For high-resolution tumor images, the following parameters were used: 120 kVp; 200 mA; 1- to 2-mm section thickness; 512- × 512-pixel resolution; 0.5- to 1.0-second scanning time; a high-spatial reconstruction algorithm with a 20-cm field of view; and mediastinal (level: 40 HU; width: 400 HU) and lung (level: −600 HU; width: 1,600 HU) window settings. Ground glass opacity was defined as a misty increase in lung attenuation that did not obscure underlying vascular markings. We defined solid tumor size as the maximum dimension of the solid component in the lung windows, excluding the ground glass opacity [13]. Radiologists from each participating institution reviewed the CT scans and determined the tumor sizes.

### *FDG-PET/CT Acquisition*

Patients were instructed to fast for more than 4 hours before intravenous injection of 74 to 370 MBq of FDG, which was followed by a relaxation period of at least 1 hour before FDG-PET/CT scanning. Blood glucose levels were determined before the tracer injection to confirm a level of less than 150 mg/dL. Patients with blood glucose levels of 150 mg/dL or more were excluded from PET/CT imaging. For imaging, we used a Discovery ST (GE Healthcare, Little Chalfont, UK), Aquiduo (Toshiba Medical Systems Corp, Tochigi, Japan), or Biograph Sensation16 (Siemens Healthcare, Erlangen, Germany) integrated 3-dimensional PET/CT scanner.

Following a standard protocol, low-dose, nonenhanced CT images (2- to 4-mm section thickness) for attenuation correction and localization of lesions identified by PET were obtained from the head to the pelvic floor of each patient. Immediately after CT, PET covered the same axial field of view for 2 to 4 minutes per table position, depending on the condition of the patient and scanner performance.

An iterative algorithm with CT-derived attenuation correction was used to reconstruct all PET images with a 50-cm field of view. An anthropomorphic body phantom (NEMA NU2-2001; Data Spectrum Corp, Hillsborough, NC) was used to minimize variations in SUVs among the institutions. A calibration factor was evaluated by dividing the actual SUV by the gauged mean SUV in the