Application of Electrical Impedance Analysis for Diagnosis of a Pulmonary Mass*


The electrical impedance of a pulmonary mass was measured in 53 patients of whom 44 had primary lung cancer, 5 had metastatic lung tumor, and 4 had organizing pneumonia. Because biologic tissue can be regarded, electrically, to consist of extracellular resistance (Re), intracellular resistance (Ri), and the electrical capacitance of the cell membrane (Cm), these three parameters were calculated from the measured electrical impedance of tissue by a curve-fitting technique using a computer program. The Re of lung tissue was significantly greater (p<0.01) and the Cm of lung tissue was significantly less (p<0.01) than that of a pulmonary mass. The Re of malignant tumors (both lung cancer and metastatic tumors) was significantly greater (p<0.01) and the Cm of malignant tumors was significantly less (p<0.01) than that of organizing pneumonia. With this information, we used a biopsy needle to diagnose nine intrathoracic lesions. This technique additionally allowed us to confirm the proximity of the needle tip of the mass. The electrical impedance of the lung mass was measured through the biopsy needle using a modified impedence analysis system before the biopsy was performed. There were no false-negative results, and one false-positive result. The rapid measurement of the electrical impedance of a pulmonary mass, preoperatively, may be of value in the clinical evaluation of a pulmonary mass both by facilitating needle guidance and by permitting diagnosis based on electrical impedance.

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Cm=cell membrane; CT=computed tomography; Re=extracellular resistance; Ri=intracellular resistance

T he electrical properties of biologic tissues differ depending on their structural characteristics and differences in the electrical properties of various neoplasms that have been reported previously.1 Because impedance is one of the most important electrical properties, we performed intraoperative impedance analysis to measure the impedance of pulmonary masses, pulmonary tissue, and skeletal muscle. On the basis of our data, we developed hardware and software programs to measure real-time impedance and assessed whether the in vivo measurement of electrical impedance was applicable to needle biopsy of the lung.

MATERIALS AND METHODS

We conducted intraoperative measurements in 53 patients ranging in age from 43 to 77 years (mean, 64 years); radiography showed mass sizes varying in size from 10 to 100 mm (mean, 42 mm). The electrical impedance of 53 pulmonary masses, including 44 lung cancers, 5 metastatic lung tumors, and 4 organizing pnomias, was determined. In computed tomographic (CT) examinations of these lesions, no differences were seen between them in density; and therefore, CT findings were not of any help in making differentia diagnosis. In nine cases in which a preoperative needle biopsy was performed, the size of the masses by radiography varied from 15 to 65 mm (mean, 32.4 mm) and the patients’ ages ranged from 41 to 71 years (mean, 67.4 years). All patients signed informed consent.

Measurements were also determined at the time of thoracotomy by inserting a coaxial bipolar needle electrode into the skeletal muscle, pulmonary tissue, and pulmonary mass under direct observation. In each patient, the measurements were determined once for skeletal muscle, once for pulmonary tissue, and twice for the pulmonary mass. A plate electrode consisting of a counter electrode plate (80x160 mm2) from an electrosurgical knife was placed on the lower leg. The time required for the measurements was 1 min. We subsequently modified the conventional analytical system to create a real-time analytical system equipped with a monitor mode that could measure values in real-time. Subsequently, the electrical impedance of a pulmonary mass in nine patients was performed during needle biopsy using the modified impedance analytical system.

A pulse response method was used to measure impedance. The pulse response to a pulsed current containing multiple frequency components was determined. Impedance could be measured up to approximately 200 kHz. In these measurements, a host computer (PC9801E, NEC; Tokyo, Japan) and a slave computer (Microprocessor 8086, Intel; United States) were used. The host computer was used to generate pulse current waves, calculate impedance, display the vector trajectory, and process other data. The slave computer was used to control measurement circuits and eliminate noise from the measured data by synchronous addition (256-fold addition). Pulse currents were applied through measurement circuits and the data were sampled at high speed (0.2

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Tip of needle

0.5 mm

Inner electrode

Outer electrode

\[ i(t) \]

\[ v(t) \]

\[ \text{measurement system} \]

\[ \text{needle} \]

\[ \text{lung} \]

\[ \text{Electrical Circuit} \]

\[ \text{Circuit elements} \]

A pulse current, 5-μA peak, was applied between the outside conductor of the needle electrode and the plate electrode, and a response voltage, between the inside conductor and the plate electrode, was measured. The impedance was calculated by the host computer. The coaxial needle electrode was created by inserting a silver wire (0.2 mm in diameter) into a stainless-steel tube (0.5 mm in diameter and 40 mm in length). The lumen and surface were insulated with teflon and only the tip was exposed as an electrode. The 90 percent and 100 percent measurement ranges were about 2 mm and 7 mm from the center of the electrode, respectively (Fig 1).

In the modified impedance analysis system, a sinusoidal current of two different phases was applied to the body; the pulse current and the extracellular resistance (Re), intracellular resistance (Ri), and cell membrane (Cm) were calculated. The speed was displayed three times per second and the hardware and software were modified to permit entry into the measurement mode when necessary.

Biologic tissue and cells can be modeled as an equivalent circuit, in which the Re, Ri, and Cm represent extracellular resistance, intracellular resistance, and cell membrane capacitance, respectively. Cells are composed of intracellular fluid, extracellular fluid, and the cell membrane. As the intracellular and extracellular fluids are electrolytes, they can be considered as resistances. Assigning these as Ri and Re, respectively, and the cell membrane capacity as Cm, the most simple equivalent electric circuit connects Ri and Cm in series and Re in parallel to it (Fig 2); Re, Ri, and Cm were calculated on the basis of this equivalent circuit from the measured impedance value by means of a curve-fitting technique using a computer program.

Differences between mean values were assessed by one-way analysis of variance and an unpaired Student's t test.

RESULTS

Table 1 shows intraoperative impedance values (mean ± SD) of the lung tissue, muscle, and pulmonary mass measured at the time of thoracotomy. The Re and Ri were significantly greater in malignant tumors than in organizing pneumonias (p<0.01) and the Cm was significantly less in malignant tumors than in organizing pneumonias (p<0.01). The Re and Ri were also significantly greater in normal lung tissue than in pulmonary masses or muscle tissue (p<0.01). From these data we derived a discrimination function:

\[ F = 5.3041 - 0.0004(Re) - 0.0008(Ri) \]

Simple equivalent circuit

\[ \text{Re = extracellular resistance} \]

\[ \text{Ri = intracellular resistance} \]

\[ \text{Cm = cell membrane capacitance} \]

Figure 2. Individual cells and biologic tissue can be ideally modeled with a simple equivalent circuit in which extracellular resistance (Re), intracellular fluid resistance (Ri), and cell membrane capacitance (Cm) are represented. In this study, from the measured impedance value, Re, Ri, and Cm are calculated on the basis of a bioequivalent circuit by means of the curve-fitting technique and computer program.
Table 1—Intraoperative Impedance Values*

<table>
<thead>
<tr>
<th>Measurement Items</th>
<th>10 kHz, Ω</th>
<th>Re, Ω</th>
<th>Ri, Ω</th>
<th>Cm, pF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>1,459 ± 577</td>
<td>1,663 ± 633</td>
<td>1,807 ± 718</td>
<td>3,546 ± 1,931</td>
</tr>
<tr>
<td>Metastatic lung tumor</td>
<td>1,794 ± 370</td>
<td>2,009 ± 421</td>
<td>2,623 ± 698</td>
<td>2,486 ± 696</td>
</tr>
<tr>
<td>Malignant tumor</td>
<td>1,493 ± 569</td>
<td>1,698 ± 624</td>
<td>1,890 ± 757</td>
<td>3,438 ± 1,871</td>
</tr>
<tr>
<td>Organizing pneumonia</td>
<td>586 ± 69†</td>
<td>728 ± 147†</td>
<td>604 ± 91†</td>
<td>10,042 ± 414†</td>
</tr>
<tr>
<td>Pulmonary mass</td>
<td>1,450 ± 609</td>
<td>1,650 ± 663</td>
<td>1,830 ± 834</td>
<td>3,880 ± 2,470</td>
</tr>
<tr>
<td>Muscles</td>
<td>2,257 ± 1,050</td>
<td>2,558 ± 1,326</td>
<td>1,617 ± 957</td>
<td>2,366 ± 766</td>
</tr>
<tr>
<td>Normal lung tissue</td>
<td>6,581 ± 4,177†</td>
<td>7,234 ± 4,606†</td>
<td>5,029 ± 2,546†</td>
<td>893 ± 575†</td>
</tr>
</tbody>
</table>

*Values are means ± SDs. The table shows the three computer-calculated parameters of the pulmonary mass, pulmonary tissue, and skeletal muscle. This shows 10-kHz impedance, and Re, Ri, and Cm of the lung tissue, muscle, and pulmonary mass measured at the time of thoractomy. Lung cancer and metastatic lung tumors are put together under malignant tumors. Pulmonary masses cover malignant tumors and organizing pneumonia.

†p<0.01.

-0.0008(Cm). The weight ascribed to a malignant tumor was 0.3198 and the weight ascribed to an organizing tumor was −3.4575. The frequency at which the tumors may be distinguished from organizing tumor was 95.74 percent. An F value greater than −1.5589 was diagnostic for malignant tumors and less than −1.5589 was diagnostic for an organizing tumor. The electrical impedance of lung masses was measured preoperatively using the modified impedance analytical system. There were no false-negatives and only one false-positive result. The sensitivity of impedance diagnosis was 100 percent (Table 2). Figure 3 shows values of 10 kHz, Re, Ri, Cm in lung cancer, organizing pneumonia, and metastatic lung tumor under needle biopsy. Impedance at 10 kHz was 736 ± 341Ω in organizing pneumonias, 1,879 ± 822Ω in metastatic lung tumors, and 2,115 ± 509Ω in primary lung cancers. The Ri was 1,070 ± 512Ω in organizing pneumonias, 1,830 ± 97Ω in metastatic lung tumors, and 2,115 ± 509Ω in primary lung cancers. The Cm was 7,379 ± 5023 pF.

Table 2—Comparison Between Impedance Diagnosis and Histologic Diagnosis in Nine Patients*

<table>
<thead>
<tr>
<th>Case No./Age, Yr/Sex</th>
<th>F Value</th>
<th>Impedance Diagnosis</th>
<th>Histologic Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/55/M</td>
<td>0.2846</td>
<td>Malignant tumor</td>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>2/68/M</td>
<td>0.1654</td>
<td>Malignant tumor</td>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>3/54/M</td>
<td>1.0187</td>
<td>Malignant tumor</td>
<td>Metastatic tumor</td>
</tr>
<tr>
<td>4/41/M</td>
<td>−4.838</td>
<td>Organizing pneumonia</td>
<td>Organizing pneumonia</td>
</tr>
<tr>
<td>5/61/M</td>
<td>−5.2857</td>
<td>Organizing pneumonia</td>
<td>Organizing pneumonia</td>
</tr>
<tr>
<td>6/63/M</td>
<td>0.1813</td>
<td>Malignant tumor</td>
<td>Organizing pneumonia</td>
</tr>
<tr>
<td>7/58/F</td>
<td>0.8859</td>
<td>Malignant tumor</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>8/55/M</td>
<td>0.3546</td>
<td>Malignant tumor</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>9/64/F</td>
<td>1.0837</td>
<td>Malignant tumor</td>
<td>Lung cancer</td>
</tr>
</tbody>
</table>

*Preoperative impedance values at 10 kHz and the value of Re, Ri, and Cm of the pulmonary mass and lung tissue were measured percutaneously in nine patients under local anesthesia. F value was calculated by feeding obtained data into the discriminant analysis formula prepared with intraoperative data; and based on the impedance, determination was made before the operation as to whether the lesion is malignant tumor or organizing pneumonia. Then the determination thus made from the data was compared with postoperative pathologic diagnosis. Differences were found between the two findings in eight of the nine patients.

Figure 3. Values of 10 kHz, Re, Ri, Cm in lung cancer, organizing pneumonia, and metastatic lung tumor under needle biopsy. The ordinate shows the values of 10 kHz, Re, Ri, and Cm. The abscissa shows four parameters, namely, 10 kHz, Re, Ri, and Cm. Open circle shows normal lung tissue, and solid circle shows lung cancer and organizing pneumonia. By making an improvement over the conventional system, we developed a new real-time analytical system equipped with a monitor mode that made it possible to display measured value in real time. When the new system is used, the moment the needle is inserted into the mass through the lung tissue, the type of the lesion can be determined by the differences in Re, Ri and Cm. Figure 3 clearly shows the differences between the lung tissue and pulmonary mass.
in organizing pneumonias, 3.060 ± 718 pF in metastatic lung tumors, and 2.664 ± 668 pF in primary lung cancers. In normal lung tissue, the impedance at 10 kHz was 3.857 ± 1136Ω, the Re was 4.217 ± 1.314Ω, the Ri was 1.960 ± 678Ω, and the Cm was 1.304 ± 469 pF.

**Discussion**

In general, electrical impedance of tissue depends on cell type and density. The purpose of our study was to measure tumor impedance in vivo and to determine its applicability in the diagnosis of pulmonary masses. The impedance for current in the range of 0 to 200 kHz was measured and an equivalent circuit representing the electrical characteristics of tumor tissue was calculated.1

Frike and Morse2 and Surowie et al3 measured the relative electrical permittivity of infiltrating breast carcinoma and surrounding breast tissue; and they reported that the capacitance of malignant breast tumor tissue was significantly greater than that of normal tissue or benign tumors to be of diagnostic value.

We designed an impedance analysis system for the purpose of measuring electrical impedance in organs. We detected differences in impedance between breast masses and fibroadenomas. A comparison between the mammary masses and fibroadenomas revealed that the Re and Ri were greater in the masses while Cm was greater in the fibroadenomas.4 In the present study, we applied this same analysis intraoperatively to normal pulmonary tissues and pulmonary masses and again found differences between them as well as between organizing pneumonias and pulmonary cancer.

At present, pulmonary needle biopsy may be performed under (1) radiography, (2) CT, or (3) ultrasoundography. Conventional radiography has the advantage of universal availability; however, in the case of a faint mass, precise location and needle insertion are difficult. Computed tomography required the institution to be equipped with CT and is more time-consuming as approximately 30 min is required for a single-needle insertion.5 Ultrasonography is effective in the biopsy of masses attached to the chest wall or pleural effusions but is not applicable to intrapulmonary masses due to scattering of sonic waves by air inside the lung.6 Thus, we have assessed whether the location of a biopsy needle could be easily determined by impedance measurement using conventional radiography. In this manner, an immediate diagnosis for malignant tumor vs organizing pneumonia could be obtained by the comparison of the Ri, Re, and Cm values.

We conducted impedance diagnosis at the time of lung needle biopsy by applying a discrimination function to the intraoperative data. At the same time, we determined whether the location of the biopsy needle could easily be confirmed within the pulmonary mass.

In nine cases, one case of organizing pneumonia was found among those assessed as pulmonary cancer and, thus, the sensitivity was 100 percent while the specificity was 66 percent. With real-time analysis, location of the needle tip was readily confirmed as the Ri, Re, and Cm values changed suddenly when the biopsy needle electrode moved from the pulmonary tissue into the mass.

From our data, we believe that a determination of electrical impedance permits the localization of the biopsy needle tip within the lung and can additionally provide information allowing diagnosis of the pulmonary mass. When this technique was applied to a pulmonary needle biopsy, however, it was necessary to use a coaxial bipolar needle electrode instead of the inner biopsy tube so as to perform impedance determination and tissue sampling simultaneously. We, therefore, are presently attempting to determine whether a bipolar needle electrode, produced with modification from the external and internal tubes of a pulmonary biopsy needle, is applicable to clinical use.

**References**

2 Frike H, Morse S. The electric capacity of tumors of the breast. J Cancer Res 1926; 16:310-76
5 Haaga JR, Allady BJ. Precise biopsy localization by computed tomography. Radiology 1976; 118:603-07