Radionuclide Assessment of the Effects of Chest Physical Therapy on Ventilation in Cystic Fibrosis

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This study assesses the use of krypton 81m scintigraphy as a measurement tool in evaluating the effectiveness of bronchial drainage with percussion and vibration on peripheral ventilation in patients with cystic fibrosis. Ten patients with cystic fibrosis participated. Each patient underwent a krypton 81m ventilation study and traditional pulmonary function tests. Forty-five minutes later, these studies were repeated before and after a chest physical therapy treatment. Each patient acted as his own control. All krypton 81m scintiscans were recorded and analyzed visually and numerically using a digital computer to assess distribution of ventilation. Visual analysis of the scintiscans indicated individual variation in treatment response: in some patients ventilation improved with therapy; in others, no change was noted; still others had changes independent of treatment. Numerical data derived from the scintiscans and pulmonary function tests showed no important differences among the three studies of each patient. Airway abnormalities characteristic of cystic fibrosis, progression of the disease, sputum production, or a combination of these factors may account for the individual variation in response to treatment. Krypton 81m scintigraphy is a reliable measure of regional ventilation and should be useful for assessing the efficacy of chest physical therapy because of the consistent, high quality visual data retrieved.

Key Words: Cystic fibrosis, Bronchial drainage, Physical therapy.

Bronchial drainage with manual percussion and vibration is an integral part of the daily care of patients with cystic fibrosis. Studies have shown that bronchial drainage when used on patients with cystic fibrosis is effective in improving certain aspects of pulmonary function and in increasing sputum removal when compared to coughing alone. However, results of these and other studies of chest physical therapy are varied and controversial. If we accept the premise that bronchial drainage techniques are designed to remove secretions from specified areas of the lung and hence affect ventilation, but the study results do not show this occurring, then we should question the capability of the measurement tool to discern the changes. Commonly used measurements of sputum volume or viscosity do not indicate from what depth of the bronchopulmonary tree secretions have been removed. Traditional pulmonary function test results indicate overall lung function and not specific regional lung function. We were interested in finding an objective measurement tool that provides regional specificity as well as measures peripheral ventilatory changes.

Inhalation of radionuclides tagged to aerosol particles for imaging of the lung has been used recently to evaluate the effects of bronchial drainage alone and in combination with percussion and vibration on tracheal and peripheral mucus clearance. Radionuclide imaging of the lung (known as pulmonary scintigraphy) can also be used to evaluate regional ventilation when a gaseous radionuclide is...
inhaled.\textsuperscript{13-15} Krypton 81m (\textsuperscript{81m}Kr) is one such radionuclide that provides details of regional ventilation because of alveolar penetration upon inhalation. This radionuclide offers the least amount of radiation exposure of the radionuclides currently available for pulmonary studies.

The purpose of this study was to assess the use of pulmonary scintigraphy with \textsuperscript{81m}Kr as a tool for evaluating changes in peripheral ventilation after bronchial drainage with percussion and vibration in patients with cystic fibrosis.

**METHOD**

Ten patients (five men and five women) with cystic fibrosis, ages 13 to 28 years, with a mean age of 19 years, participated in the study. (Written informed consent was obtained from each patient or a parent before the study.) Two patients were studied during a routine clinic visit; eight were studied while they were in the hospital for treatment with intravenous antibiotics and chest physical therapy because of an exacerbation of their pulmonary disease. Patients were classified into three clinical categories based on their most recent chest radiographs, pulmonary function tests, and arterial blood gas findings. Mild disease was suggested by a rare or absent cough, minimal abnormalities seen on chest radiographs, nearly normal pulmonary function tests, and minimal reduction of the partial pressure of arterial oxygen (Pao\textsubscript{2}). Patients classified with moderate disease demonstrated moderate chronic changes seen in chest radiographs, moderate increases in residual volume, and reductions in Pao\textsubscript{2} of 65 to 75 mmHg. Also considered were decreases in forced expiratory flow in the middle 50 percent of forced vital capacity (FEF\textsubscript{25-75}) and modest reductions in forced expiratory volume in one second (FEV\textsubscript{1}). Patients with severe disease showed marked pulmonary obstructive and bronchiectatic changes seen in chest radiographs, marked decreases in FEF\textsubscript{25-75}, marked increases in residual volumes, and Pao\textsubscript{2} values of less than 65 mmHg.

The numbers of patients in the study classifications were four severe, three moderate, and three mild. No patient had complications such as hemoptysis. No aerosol or chest physical therapy treatments were administered for at least five hours before the study to eliminate the effects of these variables on results. Four patients were receiving their usual oral bronchodilator drugs.

**Experimental Design**

The study was designed so each patient acted as his own control. A ventilation study and the pulmonary function tests were done first. These were followed by a 45-minute control period during which the patient relaxed or returned to his room. The ventilation study and pulmonary function tests were repeated before and after a 45-minute chest physical therapy treatment. Each patient received a total of three \textsuperscript{81m}Kr ventilation studies.

**Scintigraphic Ventilation Studies**

Regional lung function was measured with a gamma camera\textsuperscript{*} linked to a computer.\textsuperscript{†} Each patient sat upright and breathed at tidal volume a mixture of oxygen and the radionuclide \textsuperscript{81m}Kr. This radionuclide has a physical half-life of 13 seconds and is produced in a rubidium 81→krypton 81m generator. The generator was eluted with humidified oxygen at 4 liters a minute, and this gas mixture was delivered to the patient by a face mask attached to a rebreathing bag. Static images in anterior, posterior, and oblique views of the lung were recorded for a total of 300,000 counts of radioactivity.

The administered dose of radiation for each study was approximately 245.25 mrads to the lungs and 5.19 × 10\textsuperscript{-3} mrads to the whole body (estimates by Radiopharmaceutical International Dosimetry Information Center, Oak Ridge, TN 37830). These scans were analyzed by computer in nine of the patients (computer data were lost on one patient with severe disease). For purposes of calculation, each lung field was divided into upper, middle, lower, central, and peripheral regions. Percentages of regional intensity of radioactivity were calculated so that any changes in percentages of radioactivity among the three scans could be evaluated. We were interested in whether an increase in percentages of radioactivity would occur following therapy. All calculations were corrected for extraneous background radioactivity, and radioactivity found in the trachea was excluded from analysis.

In six of the patients (one with severe, two with moderate, and three with mild disease), dynamic studies were recorded. A dynamic study entails continuous, sequential monitoring of radionuclide flow in an organ, in this case the lungs. Images of the lung were recorded by the computer, at a rate of five frames a second for 30 seconds, showing the lung during inspiration and expiration. Using these functional images, numerical data were obtained, representing ejection fractions and residual radioactivity remaining in the lung during washout of the radionuclide from the lung at the end of the ventilation studies. (The ratio between the amount of radioactive material ejected or exhaled during expiration and the amount in the lung at the end of inspiration is the ejection fraction. The interval from cessation of in-

\* Seimens Corp, 470 Tottan Pond Rd, Waltham, MA 02154.

\† Digital Equipment Corp, Gamma II, 129 Parker St, Maynard, MA 01754.
halation of the radionuclide until all radioactive particles have been exhaled from the lung represents washout.) The natural decaying process of the radionuclide over time was figured into calculations. Percentages of the residual isotope remaining in the lung 25 seconds after washout began were computed. We supposed that patients with chronic obstructive pulmonary disease, such as cystic fibrosis, would demonstrate air trapping resulting in decreased ejection fractions and increased percentages of residual radioactivity during washout. We were interested in any change in these variables after chest physical therapy, given the possibility that mucus plugging would be relieved by therapy.

Visual data, in the form of color photographs of the lung scintiscans, were analyzed by three physicians from our Nuclear Medicine Department at Children’s Hospital Medical Center. The anterior and posterior views of the lung from the static studies were analyzed; the oblique views were not reviewed. Each lung was divided into two regions (upper and lower) rather than five, as outlined for numerical analysis. We believed this simplified division would facilitate examining the photographs and promote more uniform evaluations by three raters. Analysis was based on a weighted rating scale grading upper and lower regions of each lung. The image with the highest overall score was chosen as the best scan. The raters were unaware of the sequence of the three scans, thus promoting objective analysis. Interrater reliability was 80 percent.

Figure. Visual scan data for examples of three types of variations in ventilation. A—improvement following chest physical therapy (CPT), B—variability independent of treatment intervention, and C—no change throughout study.

**Pulmonary Function Tests**

Baseline values of forced vital capacity (FVC), peak expiratory flow rate (PEF), FEV$_1$, and the FEF$_{25-75}$ were obtained on a Vanguard DS 500 preprogrammed pulmonary function test computer.‡ The best of three FVC maneuvers was recorded and used for analysis. Baseline pulmonary function tests were included as a measurement tool to allow for comparisons of traditional methods of measurement with those of radionuclide imaging.

**Chest Physical Therapy**

The treatment consisted of bronchial drainage to all bronchopulmonary segments (excluding apical segments of the lower lobes) in conjunction with percussion and vibration techniques. The treatment was standardized by proceeding sequentially from upper-lobe to lower-lobe drainage positions. In each position, every patient received percussion for two minutes and vibration during five expirations. Patients were encouraged to cough and expectorate sputum after treatment in each position. The amount of sputum expectorated was measured and recorded. The same physical therapist administered all treatments.

**RESULTS**

The visual analysis data of the lung scans showed that regional ventilation improved in three patients after chest physical therapy. Each of these patients had severe disease. (As was mentioned, computer data were lost on the remaining patient with severe disease.) Comparison of the scintiscans of each of the three patients with mild disease showed no obvious changes in ventilation. The scintiscans of the remaining three patients with moderate disease showed variability in distribution of ventilation independent of treatment. Examples of the three types of variations are shown (Figure).

Mean percentages of distribution of radioactivity for designated areas of interest were calculated for the three studies of each patient and displayed in graphic form. Likewise, ejection fractions and percentages of residual radioactivity during washout were presented graphically for the six patients who had undergone dynamic studies. Review of these data indicated no important differences among the three studies in patients examined. In view of this, more elaborate statistical analysis was considered unnecessary. Of note, however, were the isolated results of the dynamic study of one patient with moderate disease. An obvious decrease in the ejection fraction

‡ Life Support Equipment Corp, Woburn, MA 01801.
and increase in residual radioactivity during washout indicated compromised lung function following therapy. This patient was the only one noted to wheeze audibly after treatment.

Mean values for the pulmonary function test data showed that no major change in pulmonary function had occurred when the control study was compared with studies before and after treatment (Table).

Eight patients produced sputum during therapy (mean volume 15 ml). The mean volume of sputum for patients with severe disease was 20 ml. Patients with severe disease reported subjective improvement, while the patients with mild disease reported feeling no different and produced relatively little sputum.

**DISCUSSION**

Finding an objective tool for evaluating the effects of bronchial drainage techniques with percussion and vibration upon peripheral ventilation in patients with cystic fibrosis was the primary intent of this pilot project, because a measuring instrument that is both reliable and valid is essential.

Neither measurements of sputum volume or viscosity nor traditional pulmonary function testing can be used to evaluate function in specific regions of the lung. If we accept that bronchial drainage techniques are designed to remove secretions from specific areas of the lung and hence effect regional ventilation, then it is important to find an evaluation tool that offers sufficient specificity.

We questioned methods using inhalation of radioactive aerosols to measure mucus clearance following therapy.\(^\text{11,12}\) Particle sizes (3.2 µm-5 µm) of these radioactive aerosols are large in comparison to the gas particles of \(^{81}\text{mKr}\). Uniform penetration of these aerosols into diseased peripheral airways is likely to be impeded because of bronchial thickening and retained secretions. This probably results in more deposition of the aerosol in larger airways, making it difficult to accurately assess peripheral mucus clearance.\(^\text{17,18}\) Because of this limitation of the mucus clearance method of evaluation, we elected to assess regional ventilation following chest physical therapy through the use of a radionuclide in gaseous form, \(^{81}\text{mKr}\), to assure maximal airway penetration for definitive detailing. Krypton \(^{81}\text{m}r\) also offered a significant reduction in radiation exposure for the patient when compared to other radionuclides such as those used in the mucus clearance method. We think \(^{81}\text{mKr}\) scintigraphy is a reliable, concrete means of evaluating regional lung function after chest physical therapy because visual data are accurately and consistently retrieved and displayed.

Both numerical scan data and pulmonary function test data failed to show any important changes in lung function following bronchial drainage with percussion and vibration. Through the visual analysis of lung images, however, there was evidence of improvement in ventilation in three patients as determined by qualified raters. This points out the value of having

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**TABLE**

Pulmonary Function Test Results Data\(^a\)

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Study</th>
<th>FVC(^b) (% pred)</th>
<th>PEF(^c) (liter/sec)</th>
<th>FEV(_1)(^d) (% pred)</th>
<th>FEF(_{25-75})(^e) (% pred)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (n = 3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>77</td>
<td>9.0</td>
<td>68</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>(52–91)†</td>
<td></td>
<td>(6.8–12.9)</td>
<td>(46–81)</td>
<td>(27–96)</td>
<td></td>
</tr>
<tr>
<td>Before CPT’</td>
<td>77</td>
<td>9.4</td>
<td>69</td>
<td>60</td>
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<tr>
<td>(61–91)†</td>
<td></td>
<td>(5.4–13.1)</td>
<td>(56–77)</td>
<td>(37–81)</td>
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<tr>
<td>After CPT</td>
<td>78</td>
<td>7.0</td>
<td>70</td>
<td>63</td>
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<tr>
<td>(58–91)†</td>
<td></td>
<td>(6.1–8.3)</td>
<td>(53–83)</td>
<td>(34–98)</td>
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<tr>
<td>Moderate (n = 3)</td>
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<tr>
<td>Control</td>
<td>62</td>
<td>4.6</td>
<td>43</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>(53–83)‡</td>
<td></td>
<td>(3.2–5.9)</td>
<td>(40–48)</td>
<td>(20–24)</td>
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</tr>
<tr>
<td>Before CPT</td>
<td>65</td>
<td>4.5</td>
<td>44</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>(48–89)‡</td>
<td></td>
<td>(3.3–5.6)</td>
<td>(42–54)</td>
<td>(20–24)</td>
<td></td>
</tr>
<tr>
<td>After CPT</td>
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<td>4.2</td>
<td>43</td>
<td>21</td>
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<tr>
<td>(42–89)‡</td>
<td></td>
<td>(2.8–5.6)</td>
<td>(32–54)</td>
<td>(19–22)</td>
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<tr>
<td>Severe (n = 4)</td>
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<tr>
<td>Control</td>
<td>38</td>
<td>3.6</td>
<td>24</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>(33–43)‡</td>
<td></td>
<td>(1.5–4.8)</td>
<td>(19–26)</td>
<td>(8–15)</td>
<td></td>
</tr>
<tr>
<td>Before CPT</td>
<td>37</td>
<td>3.8</td>
<td>24</td>
<td>11</td>
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</tr>
<tr>
<td>(31–46)‡</td>
<td></td>
<td>(1.5–4.6)</td>
<td>(20–26)</td>
<td>(8–14)</td>
<td></td>
</tr>
<tr>
<td>After CPT</td>
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<td>3.9</td>
<td>24</td>
<td>11</td>
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<tr>
<td>(32–41)‡</td>
<td></td>
<td>(1.7–5.0)</td>
<td>(21–28)</td>
<td>(8–15)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Results are expressed as mean values and ranges.

\(^b\) FVC = forced vital capacity.

\(^c\) PEF = peak expiratory flow rate.

\(^d\) FEV\(_1\) = forced expiratory volume in one second.

\(^e\) FEF\(_{25-75}\) = forced expiratory flow in the mid 50% of FVC.

\(^\text{1}^{}\) CPT = chest physical therapy.
visual displays as supplementary data to further substantiate clinical findings.

Patients with cystic fibrosis were studied because of the generalized pulmonary involvement and the chronic, relatively stable characteristics of their disease. Patients with different degrees of pulmonary involvement were chosen because daily, routine bronchial drainage techniques are recommended for mildly involved and more severely involved patients. We believed that by using this chronic type of patient, we were eliminating the influence of resolving pulmonary problems, which may be seen in acutely ill medical patients with pneumonia or atelectasis, on our data. We were sure any changes in ventilation detected by $^{81m}$Kr scintigraphy would likely be the result of therapeutic intervention and not resolving disease. When using a sensitive measurement tool to evaluate chest physical therapy, however, the characteristics of the disease being studied must be considered carefully.

An example of disease characteristics influencing study results is in the study by Wood and associates. They used xenon 133 ($^{133}$Xe) perfusion/ventilation scans to study the effects of bronchial drainage with percussion and vibration in 10 patients with cystic fibrosis. They discovered varying responses to chest physical therapy: some patients improved, some did not, and some worsened. They postulated there may be a dynamic component to the lung disease in cystic fibrosis dependent on the relationship between rates of sputum production and its clearance or on the irreversible processes resulting from fibrosis or bronchiectasis. Perhaps this dynamic process associated with cystic fibrosis was detected through the impressive sensitivity of pulmonary scintigraphy and might very well be the contributing factor to the variability seen in the analysis of our data.

To further validate the use of pulmonary scintigraphy as a measurement tool, we recommend $^{81m}$Kr scintigraphy be used to evaluate the effects of chest physical therapy on other pulmonary conditions. It would be interesting to study patients with acute, reversible lung problems. It may be difficult to control for a resolving lung condition in these patients, but the complexities of an underlying disease process, as seen in cystic fibrosis, would be eliminated, and the researcher could perhaps more clearly determine if any observed changes are attributed to treatment intervention. Studies of patients with chronic lung disease other than cystic fibrosis might reveal differences in response to therapy resulting from variations in the disease process or rheological properties of the sputum.

Though the primary intent of this study was to assess the use of $^{81m}$Kr scintigraphy to evaluate the effects of chest physical therapy, some interesting observations were made with regard to sputum volume and visual changes in the lung scans. Recent literature suggests that bronchial drainage with percussion is appropriate in patients with large amounts of secretions but may be inappropriate in patients with little or no sputum. Though limited conclusions can be drawn from this recent study, one might suspect that appropriate use of bronchial drainage, percussion, and vibration is desirable in patients who expectorate large amounts of sputum, both to remove sputum and to improve regional ventilation. The mean volume of sputum from the patients we studied with severe disease was approximately 20 ml—higher than the group mean volume of approximately 15 ml. In three of these patients with severe disease, there seemed to be some correlation between large amounts of sputum produced and visible improvement seen in ventilation. Conversely, the three patients with mild disease showed no visible change in ventilation throughout the three studies. Two of these patients had nonproductive coughs, while the third raised relatively little sputum. Bronchial drainage with percussion and vibration may have little or detrimental effect on ventilation in patients who are producing little or no sputum (as was demonstrated by Connors and associates). Unfortunately, in our study numerical scan data showed no important difference between the patients producing large amounts of sputum and patients producing small amounts with regard to changes in ventilation. More studies are needed to define the processes involved in identifying those patients who best respond to our treatment technique and the techniques that best meet patient needs. Identification of such patients would be beneficial in treating diseases, such as cystic fibrosis, where daily prophylactic chest physical therapy is recommended for all patients from the time of diagnosis.

We believe $^{81m}$Kr scintigraphy is a reliable measurement tool because of its reproducible detail of peripheral ventilation and its retrievable, high quality visual representations of lung images. Its use as a measurement tool to assess ventilatory changes following bronchial drainage with percussion and vibration must be further evaluated in patients with other lung dysfunctions. The tool might be valuable in assessing the effectiveness of other chest physical therapy techniques, such as breathing exercises, or the effects of coughing alone. Careful consideration should be given to the underlying lung problems of patients being studied when interpreting test results. Pulmonary scintigraphy using radionuclides that offer little radiation exposure and definitive detailing of lung function may help to further substantiate chest physical therapy techniques currently in use. The measurement tool might also help identify what complex of treatment techniques offers the best results with the least amount of patient effort.
CONCLUSIONS

Krypton 81m scintigraphy was evaluated as a tool to measure regional ventilatory changes after bronchial drainage with percussion and vibration techniques in 10 patients with cystic fibrosis. Patients with mild, moderate, and severe disease were studied. Visual analysis of the scintiscans demonstrated improvement in ventilation in three patients with severe disease. The patients with mild disease showed no change in ventilation, while the remaining patients had ventilatory changes independent of treatment intervention. Numerical analysis of static and dynamic lung scan data showed no important differences in ventilation after therapy.

We believe 81mKr scintigraphy is a reliable measurement tool for evaluating regional ventilation and is useful in evaluating the effects of bronchial drainage with percussion and vibration because of the high quality of the visual data that are retrieved and displayed. However, careful consideration must be given to the underlying lung problem of patients studied. To further validate the use of 81mKr scintigraphy as a measurement tool for evaluating chest physical therapy techniques, patients with other lung dysfunction should be studied. We noted indications of a relationship between ventilatory changes and the amount of sputum produced. This relationship should be studied further to aid in determining which patients best respond to treatment intervention. Varied chest physical therapy procedures may be evaluated using techniques such as 81mKr scintigraphy.

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REFERENCES