Absolute quantitation of gallium-67 citrate accumulation in the lungs and its importance for the evaluation of disease activity in pulmonary sarcoidosis

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Abstract. Our modification of a method for the absolute quantification of gallium-67 uptake in lungs with a scintillation camera and computer is described. The uptake of 67Ga in lungs, expressed in percentage of administered radioactivity, was determined by the transmission-emission method. We proved theoretically and experimentally that a 67Ga planar source could be replaced with a 57Co planar source. The performance of lung perfusion scans allows a more accurate delineation of the regions of interest on gallium scans. The method was applied to control subjects (n=27) and to patients (n = 114) suffering from biopsy-proven pulmonary sarcoidosis (28 with inactive and 86 with active disease). The obtained results were compared with chest X-ray findings, the percentage of lymphocytes in the bronchoalveolar fluid (BAF-ly%), and serum angiotensin-converting enzyme (SACE) values. The method seems suitable for the assessment of disease activity in sarcoidosis. It is more accurate in detecting parenchymal involvement in lung sarcoidosis than the commonly used X-ray criteria. No correlation was found between 67Ga uptake and the BAF-ly% and SACE values.

Key words: Gallium-67 – Quantitation – Gamma camera imaging – Lungs – Sarcoidosis


Introduction

The uptake of gallium-67 citrate in the lungs provides crucial information about the degree of activity of lung sarcoidosis (Alberts et al. 1981; Beaumont et al. 1982; Bisson et al. 1983; Hayes et al. 1990). Therefore, it is important that it be determined as precisely as possible (Bourguet et al. 1986). Most studies have evaluated this problem qualitatively (Alberts et al. 1981; Nosal et al. 1979) or semiquantitatively (Rohatgi and Baier 1983; Duffy et al. 1986; Line et al. 1978). The fact that these subjective methods of evaluation of gallium scintigrams do not have a high degree of accuracy is especially obvious when the accumulation of gallium in the lung parenchyma is low (Bourguet et al. 1985, 1986). It seems that more precise and objective evaluation is achieved using quantitative methods (Bourguet et al. 1985, 1986; Fernandez et al. 1982; Grossman et al. 1985; Alberts and Van der Schoot 1988; Mysliveček et al. 1988).

The present paper describes our modification of a method for the absolute quantification of 67Ga uptake in the lungs, used for the assessment of patients with morphologically verified sarcoidosis. The results obtained were compared with simultaneous chest X-ray findings, the percentage of lymphocytes in the bronchoalveolar fluid (BAF-ly%), and serum angiotensin-converting enzyme (SACE) values.

Patients and methods

A control group of 27 healthy persons was examined (17 men, 10 women, mean age 42 years, age range 19–75 years), of whom 12 were smokers and 15 non-smokers.

In addition, 114 patients with biopsy-proven sarcoidosis were examined (69 women, 45 men, mean age 48 years, age range 25–74 years). In 28 patients, the sarcoidosis displayed no clinical activity. These patients had not had any symptoms of the disease for at least 2 years, laboratory findings were in the normal range, and chest X-ray findings were normal or displayed no deterioration. Employing the widely accepted classification of Siltzbach et al. (1974), the X-ray findings were considered stage 0 in 20 patients, stage I in three patients, stage II in two patients, and stage III in three patients. In the group of 86 patients with clinically active disease (as evidenced by symptoms, laboratory data, and functional progress), five patients had chest X-ray findings corresponding to stage 0, 42 patients were in stage I, 29 in stage II and 10 in stage III (Table 1).

Gallium scintigraphy was performed 72 h after the i.v. administration of 110–150 MBq 67Ga citrate, using a scintillation LFOV
Table 1. Patients with active and inactive sarcoidosis

<table>
<thead>
<tr>
<th>X-ray stage</th>
<th>0</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive sarcoidosis</td>
<td>20&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>2</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Active sarcoidosis</td>
<td>5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>42</td>
<td>29</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>45</td>
<td>31</td>
<td>13</td>
<td>114</td>
</tr>
</tbody>
</table>

<sup>a</sup> Patients with stage 0 did not exhibit any X-ray symptoms of intrathoracic sarcoidosis at the time of 67Ga uptake examination
<sup>b</sup> Patients with extrapulmonary sarcoidosis

The frequently encountered problem of ambiguity of lung borders on gallium scans was avoided by delineating regions of interest (ROIs) automatically on perfusion scans [performed after the administration of 99mTc-macroaggregated albumin (Figs. 1g, h, 2g, h). The ROIs were then transferred to gallium scans, the geometry of the measurement being precisely retained. A correction of the chosen ROIs is usually required because their borders interfere with the activity in the liver and with the activity in accumulating hilar lymph nodes in the case of active sarcoidosis. With respect to the evaluation of alveolitis activity, accumulating hilar nodes should be avoided when delineating ROIs. A similar approach has been used by other authors (Hayes et al. 1990).

For the assessment of 67Ga uptake in the lungs the following relationship given by Macey and Marshall (1982) is used

\[ A_L = \frac{(I_{AP} I_{PA})^{1/2}}{E} \cdot \frac{\mu T/2}{\sinh(\mu T/2)} \]

where \( A_L \) is the activity of the emitter in the lungs, \( I_{AP} \) and \( I_{PA} \) the count rates (s\(^{-1}\)) obtained for the regions of interest delineated around the lungs on anterior and posterior views, respectively (Figs. 1e, f and 2e, f), \( E \) the sensitivity of the camera/collimator system (s\(^{-1}\)MBq\(^{-1}\)), \( \mu \) the effective linear attenuation coefficient of the tissue between the lungs and body surface (cm\(^{-1}\)) for 67Ga gamma-rays, \( T \) the thickness of the chest (cm) and \( \mu \) the linear attenuation coefficient of lung tissue (cm\(^{-1}\)) for 67Ga gamma-rays.

The factor \( \mu T/2 \) in Eq. 1 is the correction for the attenuation of gamma-rays in the tissue between the lungs and body surface. Its calculation is difficult due to the complicated nature of the determination of the effective attenuation coefficient \( \mu \), (the differing density and configurations of various body tissues have to be taken into account) and also due to the fact that the results obtained may be affected by scatter of gamma-rays in tissues. Therefore it is more suitable to determine the patient’s own transmission coefficient experimentally, employing the relationship

\[ f = \frac{I_T}{I_T} = \left( \frac{I_T}{I_T} \right)^{1/2} \]

where \( I_T \) is the count rate (s\(^{-1}\)) measured with a 67Ga planar source placed beneath the patient prior to 67Ga administration, and \( I_s \) is the count rate (s\(^{-1}\)) with the 67Ga planar source in the absence of the patient (Figs. 1a, b, 2a, b). In place of the 67Ga source, we used a 57Co planar source.

Rather than absolute 67Ga activity, it is advantageous to determine the accumulation \( U \) of this radionuclide in the lungs, i.e. the ratio of the activity in the lungs \( A_L \) and the administered activity \( A_{ad} \). Equation 1 is rewritten as

\[ U_L = \frac{A_L}{A_{ad}} \cdot 100 \left( \frac{I_{AP} I_{PA}}{I_s} \right)^{1/2} \cdot \frac{\mu T/2}{\sinh(\mu T/2)} \cdot 100\% \]

where \( I_s = E A_{ad} \) is the count rate corresponding to the 67Ga activity administered. The count rate \( I_s \) is calculated as

\[ I_s = I_{sb} - I_b \]

where \( I_{sb} \) is the count rate (s\(^{-1}\)) recorded with a syringe filled with 67Ga placed beneath a camera detector (Figs. 1c, 2c) and \( I_b \), the count rate (s\(^{-1}\)) measured with an empty syringe containing the 67Ga remnants after administration (Figs. 1d, 2d).

Fig. 1a-h. Individual steps during the examination of 67Ga uptake in the lungs.